Research and Development

Use of Volunteers as Subjects of Research

Headquarters
Department of the Army
Washington, DC

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SUMMARY of CHANGE

AR 70-25
Use of Volunteers as Subjects of Research

This change is published to correct a serious error that occurred during the final editing of the current revision. In attempting to respond to guidance from the Office of The Judge Advocate General that a subparagraph be moved from the text of the regulation to appendix F, the wrong subparagraph was moved.

Headquarters
Department of the Army
Washington, DC
25 January 1990

*Army Regulation 70–25

Effective 24 February 1990

Research and Development

Use of Volunteers as Subjects of Research

This publication was last revised on 8 August 1988. Since that time, permanent Change 1 has been issued. As of 25 January 1990, that change remains in effect. This UPDATE printing incorporates that change into the text.

This UPDATE printing publishes a Change 2. The portions being revised by this change are highlighted.

By Order of the Secretary of the Army:

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General, United States Army
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Official:

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Summary. This revision implements Department of Defense (DOD) Directive (DODD) 3216.2. It reflects the present legal requirements pertaining to the use of humans as research subjects funded by research, development, test, and evaluation appropriations. This revision provides guidance for establishing human use committees (HUCs). Excluding limited situations, authority to approve research using human subjects can be delegated within the military chain of command.

Applicability. This regulation applies to research, development, test, and evaluation (RDTE) programs conducted by the Active Army. It does not apply to the Army National Guard (ARNG) or the U.S. Army Reserve (USAR) unless there is involvement of Active Army personnel.

Internal control systems. This regulation is subject to the requirements of AR 11–2. It contains internal control provisions but does not contain checklists for conducting internal control reviews. A checklist will be published at a later date.

Supplementation. Supplementation of this regulation is prohibited unless prior approval is obtained from HQDA (DASG–RDZ), 5109 Leesburg Pike, Falls Church, VA 22041–3258.

Interim changes. Interim changes to this regulation are not official unless they are authenticated by the Administrative Assistant to the Secretary of the Army. Users will destroy interim changes on their expiration dates unless sooner superseded or rescinded.

Suggested improvements. The proponent of this regulation is the Office of The Surgeon General. Users are invited to send comments and suggested improvements on DA Form 2028 (Recommended Changes to Publications and Blank Forms) directly to Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

Distribution. Distribution of this publication is made in accordance with the requirements on DA Form 12–09–E, block number 3724, intended for command level D for Active Army and None for the ARNG and USAR.

Contents (Listed by paragraph number)

*This regulation supersedes AR 70–25, 25 September 1989.

RESERVED

Chapter 1
Introduction

1–1. Purpose
This regulation—

a. Prescribes Army policy on the conduct and management of human subjects in testing, including—

(1) Command responsibilities.

(2) Review process requirements.

(3) Approval authorities.

(4) Reporting requirements.

b. Allows a decentralized approval option for those elements that have established review committees and an internal review process.

1–2. References
Required and related publications and prescribed and referenced forms are listed in appendix A.

1–3. Explanation of abbreviations and terms
Abbreviations and special terms used in this regulation are explained in the glossary.

1–4. Limitations
a. Nothing in this regulation is intended to supersede requirements for health hazard or other safety review required by Department of the Army (DA) regulations.

b. Nothing in this regulation limits the authority of a health care practitioner to provide emergency care under laws that apply in the jurisdiction in which care is provided.

c. Protocols for the use of drugs or Schedule I controlled substances for investigational purposes will be approved as per AR 40–7.

d. The guidance in this regulation pertains to the following, regardless of whether conducted by DA, a contractor, grantee, or other agency utilizing Army funds:

(1) Biomedical research and behavioral studies involving human subjects.

(2) RDTE 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 will be made by review committees established in accordance with paragraph 3–2*b* of this regulation.

(4) ~~Inclusion of human subjects as the indirect object of research involving minimal risk or less in the development and testing of military weapon systems, vehicles, aircraft, and other material are exempt from the requirement for obtaining informed consent from the participants. The determination of whether a proposal is minimal risk or less is made by a HUC established in accordance with paragraph 3–2*b* of this regulation.~~Research involving deliberate exposure of human subjects to nuclear weapons effect, to chemical warfare agents, or to biological warfare agents.

(5) Activities funded by non-Army resources in which the human subjects are DA military or civilian personnel.

e. See appendix F for a listing of research exempt from the requirements of this regulation.

Chapter 2
Responsibilities

2–1. The Under Secretary of Defense for Aquisition (USD (A))
In accordance with DOD Directive 3216.2, the USD (A) or designee will be the approval authority for studies involving the actual exposure of human subjects to nuclear weapons effect, chemical warfare agents, or biological warfare agents.

2–2. Assistant Secretary of Defense (Health Affairs) (ASD (HA))
In accordance with DOD Directive 3216.2, the ASD (HA) serves as the DOD representative on matters relating to implementation of Food and Drug Administration (FDA) regulatory requirements.

2–3. Assistant Secretary of the Army (Research, Development, and Aquisition) (ASA (RDA))
The ASA (RDA) will manage all DA RDTE activities, including those in which human use is planned.

2–4. The Deputy Chief of Staff for Personnel (DCSPER)
The DCSPER will—

a. Supervise and review RDTE activities under the Army Personnel Performance and Training Program.

b. Within established areas of responsibility, monitor RDTE involving human subjects to ensure implementation of policies contained in this regulation.

c. Approve or disapprove those studies involving alcohol and drug abuse programs.

2–5. The Surgeon General
The Surgeon General (TSG) will—

a. Prepare policies and regulations on research using human subjects.

b. Establish and maintain the Human Subjects Research Review Board (HSRRB), chaired by the Assistant Surgeon General for Research and Development.

c. Establish and maintain the Human Use Review and Regulatory Affairs Office (HURRAO) attached to the U.S. Army Medical Research and Development Command (USAMRDC) and reporting to the Assistant Surgeon General for Research and Development.

d. Approve or disapprove research proposals from major Army Commands (MACOMs) that do not have a HUC or an internal review process.

e. Provide an evaluation of protocols as described in paragraphs 2–1 and 2–4, above, and 2–6, below, to the following heads of offices or command:

(1) The USD (A).

(2) The DCSPER.

(3) Upon request, the Commander, SSC–NCR.

f. Be the approval authority for studies and research protocols involving human subjects using Schedule I controlled drug substances.

g. Be the approval authority for research involving minors, or other vulnerable categories of human subjects, when subjects are wards of a State or other agency, institution, or entity.

h. Be the approval authority for MACOM or agency requests to establish a HUC and a human use review process.

i. Manage the Army's Health Hazard Assessment Program and assess health hazards of medical and nonmedical materiel.

j. Direct medical followup, when appropriate, on research subjects to ensure that any long-range problems are detected and treated.

k. Report on a frequent basis, findings associated with classified investigational drug and device studies to the USD (A), the ASD (HA), and the FDA.

l. Be the approval authority for all in-house and contract research (other than that noted in paras 2–1, 2–2, 2–4, and 2–6) involving human subjects for which the Army has been designated the executive agent. Except for those categories of research noted above for which TSG is specifically designated as the approval authority, the authority to approve such research may be delegated by TSG within the military chain of command to the lowest level operating a human-subjects review process approved pursuant to paragraph 3–2*b*.

2–6. Commander, Soldier Support Center—National Capital Region (SSC–NCR)

The Commander, SSC–NCR, will be the approval authority in accordance with AR 600–46 for attitude and opinion surveys or Army occupational surveys.

2–7. Major Army commanders

These commanders will—

a. Monitor RDTE involving personnel within their command to ensure effective implementation of the policies and procedures contained in this regulation.

b. Provide assistance to volunteer recruiting teams.

c. Ensure that only individuals who freely volunteer to participate are enrolled in research protocols or studies.

2–8. Commanders of RDTE organizations

These commanders will—

a. Ensure the effective implementation of the policies and procedures contained in this regulation.

b. Use the established review process through TSG's HSRRB for all protocols and test plans or establish a HUC and implement review process consistent with the policies and procedures contained in this regulation.

c. Ensure that research volunteers are adequately informed concerning the risks associated with their participation, and provide them with any newly acquired information that may affect their well-being when that information becomes available.

d. Comply with AR 40–10, AR 70–10, AR 385–16, AR 602–1, and AR 602–2 in planning and conducting development and/or operational testing.

2–9. Other responsibilities

a. Members of the HSRRB will—

(1) Evaluate methods by which DA involves human subjects in research.

(2) Recommend policy to TSG on the treatment of volunteers consistent with current moral, ethical, and legal standards. (See app G for legal implications.)

(3) Evaluate research protocols and test plans submitted to TSG for approval.

b. The Chief of the HURRAO will—

(1) Provide, for TSG, administrative support for the HSRRB.

(2) Conduct a compliance review of all protocols submitted to TSG for approval.

(3) Submit DA-sponsored Notices of Claimed Investigational Exemption for a New Drug (INDs) and Investigational Device Exemptions (IDEs) directly to the FDA.

(4) Submit DA-sponsored New Drug Applications (NDAs) directly to the FDA.

(5) Maintain DA record files for IND and NDA submissions to the FDA.

(6) Conduct post-marketing surveillance for NDAs sponsored by DA.

(7) Serve as the DA point of contact for policies and regulations on human use in RDTE programs.

(8) Advise and assist MACOMs and DA staff agencies that conduct research or sponsor research by contracts and grants that involve the use of human volunteers.

c. Investigators will—

(1) Prepare a protocol following the policies and procedures in this regulation.

(2) Prepare adequate records on—

(a) Receipt, storage, use, and disposition of all investigational drugs, devices, controlled drug substances, and ethyl alcohol.

(b) Case histories that record all observations and other data important to the study.

(c) Volunteer informed consent documents (see app E). The principal investigator will fill in the information in parts A and B of DA Form 5303–R and inform the subject of each entry on the form.

(3) Prepare progress reports, including annual reports, as determined by the approving authority and regulatory agencies.

(4) Promptly notify the approving authority, through the medical monitor, of any changes in the research used by the research.

(5) Report serious and/or unexpected adverse experiences involving the use of an investigational device or drug to the sponsor and the FDA in accordance with AR 40–7.

(6) Ensure that the research has been approved by the proper review committee(s) before starting, changing, or extending the study.

(7) Ensure that all subjects, including those used as controls, or their representatives are fully informed of the nature of the research to include potential risks to the subject.

(8) Ensure that investigational drugs or devices are administered only to subjects under their personal supervision, or that of a previously approved associate investigator.

(9) Ensure that a new principal investigator (PI) is appointed if the previously appointed PI cannot complete the research (for example, permanent change of station (PCS), retirement, etc.).

(10) Apprise the HUC of any investigator's noncompliance with the research protocol.

(11) Seek HUC approval for other investigators to participate in the research.

(12) Ensure that research involving attitude or opinion surveys are approved in accordance with AR 600–46 (3–2*c*(5) below).

d. Volunteer recruiting teams. Members will—

(1) Establish volunteer requirements prior to recruitment.

(2) Coordinate recruiting activities with unit commanders.

(3) Undertake recruiting in a moral, ethical, and legal manner.

e. Medical monitor. The medical monitor is responsible for serving as advocate for the medical safety of volunteers. The monitor will have responsibilities as determined by the approving official and the authority to suspend or terminate the effort consistent with the policies and procedures contained in this regulation.

Chapter 3
Research

3–1. General guidance

a. Only persons who are fully informed and volunteer in advance to take part may be used as subjects in research; except, when the measures used are intended to be beneficial to the subject, and informed consent is obtained in advance from a legal representative on the subject's behalf.

b. Nothing in this regulation is intended to limit the authority of a health care practitioner to provide emergency medical care under applicable law of the jurisdiction in which care is provided.

c. Any human tissue or body fluid, obtained by autopsy, and used in research will be donated for such purpose. The donor will be the next of kin or legal representative of such person. Donation is made by written consent and relinquishes ownership and/or rights to the tissue or fluid. Consent to donate will not preclude payment for such donation. Organ donation intended for transplant will be accomplished in accordance with AR 40–3, chapter 18.

d. Any tissue or body fluid linked by identifiers to a particular person, obtained by surgical or diagnostic procedure and intended for use in research will be donated for such purpose. The donor will be the person from whom the tissue or fluid is removed or, in the event of death or legal disability of that person, the next of kin or legal representative of such person. Donation is made by written consent and relinquishes ownership and/or rights to the tissue or fluid. Consent to donate does not preclude payment for such donation.

e. The determination of level of risk in a research protocol will be made by a HUC established in accordance with this regulation. (See app G for a complete listing of legal implications.)

f. Moral, ethical, and legal concepts on the use of human subjects will be followed as outlined in this regulation. Voluntary consent of the human subject is essential. Military personnel are not subject to punishment under the Uniform Code of Military Justice

for choosing not to take part as human subjects. Further, no administrative sanctions will be taken against military or civilian personnel for choosing not to participate as human subjects.

g. RDTE using human subjects is conducted in such a manner that risks to the subjects are minimized and reasonable in relation to anticipated benefits.

h. The proposed number of subjects is the minimum needed to ensure a statistically valid conclusion.

i. The research is conducted in such a manner as to avoid unnecessary physical and mental suffering. Preparations are made and adequate facilities provided to protect the subject and investigators against all foreseeable injuries, disabilities or death. Such research is not to be conducted if any reason exists to believe that death or injury will result.

j. Volunteers are given adequate time to review and understand all information before agreeing to take part in a study.

k. Volunteers are authorized all necessary medical care for injury or disease that is a proximate result of their participation in research.

(1) Medical care for civilian employees who volunteer and who perform duty as a volunteer during their regularly scheduled tour of duty will be provided in accordance with AR 40–3.

(2) Medical care costs for all other categories of personnel, who under the provisions of AR 40–3 are routinely authorized care in a military MTF will be waived for the volunteer while in the hospital, if the volunteer would not normally enter the hospital for treatment but is requested to do so to facilitate the research. This also applies to a volunteer's extension of time in a hospital for research when the volunteer is already in the hospital.

(3) Subsistence charges for all other categories of personnel, except for active duty and retired commissioned officers, may be waived in the circumstances noted in (2) above. The costs for subsistence charges for commissioned officers may be reimbursed to the officer by the research organization.

(4) Costs of medical insurance coverage or direct charges for medical care for volunteers participating in research performed by a contract or grant may be negotiated between the DA contracting officer and the contractor or grantee. (See app G.)

l. Information obtained during, or as a result of, an epidemiologic-assessment interview with a human immunodeficiency virus (HIV) serum positive member of the Armed Forces may not be used to support any adverse personnel action against the member. (See glossary for definition of the terms "epidemiologic-assessment interview," "serum positive member of the Armed Forces," and "adverse personnel action.")

m. Research may be conducted outside the United States that involves non-U.S. citizens (for example, research on diseases of military interest, such as malaria, that are not endemic to the United States). However, in the conduct of such research, the laws, customs and practices of the country in which the research is conducted or those required by this regulation, whichever are more stringent, will take precedence. The research must meet the same standards of ethics and safety that apply to research conducted within the United States involving U.S. citizens, and will be conducted in accordance with applicable international agreements.

n. The use of prisoners of war and detainees as human research subjects is prohibited.

o. Minors may be enrolled as human research subjects when the following conditions are met:

(1) The research is intended to benefit the subject, and any risk involved is justified by the expected benefit to the minor.

(2) The expected benefits are at least as favorable to the minor as those presented by available alternatives.

(3) A legally authorized representative has been fully informed and voluntarily consents, in advance, for the minor to participate in the research.

(4) The minor, if capable, has assented in writing. In determining whether the minor is capable of assenting, the HUC will consider the minor's age, maturity, and psychological state. The HUC may waive assent for some or all minors involved in the study if it determines that the—

(a) Capability of some or all of the minors is so limited that they cannot be reasonably consulted, or

(b) Procedure involved in the research holds out a prospect for direct benefit that is important to the health or well-being of the minor, and is available only in the context of research.

p. The personnel responsible for the conduct of the research are the best qualified to recruit volunteers for a study and should be the primary recruiters whenever possible.

q. Only persons judged qualified by the appropriate approving official will conduct research involving human subjects.

r. A medical monitor is appointed by name if the HUC or approving official determines that the risk is more than minimal. A medical monitor may be appointed to minimal risk or less than minimal risk studies if so determined by the HUC or approving authority. The principal investigator may function as medical monitor only in situations where no other physician is reasonably available and approval for the principal investigator to function as medical monitor is granted by TSG. Requests for the principal investigator to function as the medical monitor will be sent to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

s. Safeguards or special conditions imposed on a protocol by a HUC may not be reduced or waived by the approving official upon approval of the protocol. The approving official may require additional safeguards, may disapprove the protocol, or may refer it to a higher review and approving authority.

t. User testing, as defined in AR 71–3, which involves the use of volunteers, is reviewed and approved by a HUC established in accordance with this regulation.

u. Research on medical devices is conducted in accordance with Part 812, Title 21, Code of Federal Regulations (21 CFR 812)

v. Emergency one-time use of an investigational drug or medical device is accomplished to the extent permitted under applicable law and in accordance with AR 40–7.

w. Public Affairs guidelines on the release of information are in AR 360–5.

3–2. Procedural guidance

a. Duties. MACOM commanders and organization heads conducting RDTE research involving human subjects will—

(1) Publish directives and regulations for—

(a) Protocol and/or test plan preparation (see app B).

(b) The use of volunteers as subjects of research conducted or sponsored by the organization.

(c) The procedures for reporting and responding to reports of improper use of volunteers as subjects of research conducted or sponsored by the organization.

(d) The procedures to assure that the organization can accomplish its "duty to warn" (see para 3–2*h* for a discussion of "duty to warn").

(2) Forward one copy of published regulations and directives (see (1) above) to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012, within 60 days of publication.

(3) Establish a HUC, if appropriate (see *b* below).

(4) Establish a system that permits the identification of volunteers who have participated in research conducted or sponsored by that command or organization. Such a system will be established in accordance with AR 340–21. (App H describes data elements which could comprise such a system.)

b. Establishing a HUC. As noted in paragraph 2–8*b*, commanders or heads of RDTE organizations will either use TSG's HSRRB or implement their own HUC.

(1) HUCs will be established for research conducted by DA in accordance with appendix C.

(2) Institutional review boards will be established by contractors or grantees in accordance with 45 CFR 46.

(3) RDTE organizations which establish an internal review process will forward the items listed below to the Assistant Surgeon General for Research and Development, c / o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

(a) See *a*(2) above.

(b) A listing of the membership of the HUC and the curriculum vitae for each member.

(4) Newly established HUCs may not review research protocols until the items in *(a)* and *(b)* above are reviewed and approved by TSG.

c. Protocol and/or test plan review before submission to a HUC.

(1) A protocol or test plan will be prepared for all research requiring approval pursuant to this regulation. Certain studies may be exempt (see app F). The format in appendix B should be followed, but may be modified to meet local requirements. DA Pam 70–21 and DA Pam 71–3 provide guidance for preparation of test plans and equivalent documents. Protocols and test plans are exempt from management information requirements per AR 335–15, para 5–2*b*. An informed consent document will be prepared using DA Form 5303–R (Volunteer Agreement Affidavit), or functional equivalent, in accordance with appendix E (see *d* below). DA Form 5303–R will be reproduced locally on 8½- by 11-inch paper. A copy for reproduction is located at the back of this regulation.

(2) If a study calls for the use of tissue or fluids obtained from a human, and is not an exempt study as defined by appendix F, paragraph *e*, then a protocol is prepared. The following must be considered in determining whether informed consent is required.

(a) Fluid or tissue obtained at autopsy: informed consent is required.

(b) Fluid or tissue obtained at surgery or as the result of a diagnostic procedure and linked by identifiers directly or indirectly to a particular person intended for research: informed consent is required.

(c) Fluid or tissue obtained at surgery or as the result of a diagnostic procedure not intended for research and not linked by identifiers: no informed consent is required.

(d) Fluid or tissue obtained from a tissue or blood bank which is linked to a personal identifier and the research data is recorded in such a manner as to identify the donor: informed consent is required.

(e) Fluid or tissue obtained from a tissue or blood bank, which is linked to a personal identifier, but the research data is recorded in such a manner that the donor's identity is unknown: no informed consent is required.

(f) Fluid or tissue obtained from a tissue or blood bank which is not linked to a personal identifier: no informed consent is required.

(The informed consent document used in these cases may be the DA Form 5303–R, an overprinted consent for surgery or autopsy, or other form approved by the HUC and the forms management office at the organization.)

(3) The protocol or test plan is submitted to a scientific review committee composed of individuals qualified by training and experience, and appointed by the commander of the unit to evaluate the validity of the protocol. The purpose of this peer review is to assure that the protocol design will yield scientifically useful data which meets the objective(s) of the study. The committee recommendations and actions taken by the investigator in response to the recommendations are submitted with the protocol to the HUC.

(4) When applicable, the protocol or test plan will be submitted to the radioisotope/radiation control committee, or equivalent, established in accordance with TB MED 525. The committee recommendations and actions taken by the investigator in response to those recommendations are submitted with the protocol to the HUC.

(5) When applicable, the protocol will be submitted to the SSC–NCR for research which calls for the use of an attitude or opinion survey, as defined by AR 600–46. If such studies are planned, the SSC–NCR will be contacted to determine whether the survey requires approval of that Center. This information should accompany the proposal when it is submitted for review. Surveys that cross command lines or are sent to other Services require approval. Inquiries should be directed to Commander, SSC–NCR, Attitude and Opinion Survey Division, ATTN: ATNC–MOA, 200 Stovall Street, Alexandria, VA 22332–0400 (AUTOVON 221–9680).

d. Informed consent documentation. The subject's agreement to participate in the study will be documented using DA Form 5303–R, or functional equivalent, in accordance with appendix E. If additional pages are required, plain bond paper will be used and each page will be initialed by the volunteer and the witness. This form is not appropriate for research performed by contract. The volunteer agreement will be written in language that is easily understood by the subject. In research conducted outside the United States involving non-U.S. citizens, a locally produced form in the subject's native language may be used. An English translation of the form will be provided to the HUC.

e. Protocol and/or test plan review after submission to the local HUC.

(1) *HUC actions.*

(a) The HUC determines the level of risk associated with the protocol or test plan.

(b) The HUC may make the following recommendations to the approving authority: Approved, approved with modification, defer review to higher authority, disapproved, or exempt from further human use review.

(c) The HUC requires that the information given to subjects as a part of the informed consent is in accordance with the applicable portions of appendix E. The committee may require that information, in addition to that specifically mentioned in appendix E, be given to the subject when, in the HUC's judgement, the information would meaningfully add to the protection of the rights and welfare of the subject.

(d) The HUC reviews research involving minors. The committee will determine if assent is required and establish the method documenting such assent. The committee may waive the requirement for assent provided the HUC finds and documents that the research could not practicably be carried out without the waiver (see para 3–1*o*(4)).

(e) The HUC reviews research involving wards of a State agency, and other vulnerable categories of human subjects. The HUC determines if the use of such a category of subjects is warranted. If, in the opinion of the committee, the use of this category of subjects is appropriate, then the protocol is forwarded through command channels to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012, for approval.

(f) The HUC conducts a continuing review of the research approved by the HUC at intervals appropriate to the level of risk, but at least annually. The format for the review (for example, progress report from the investigator) will be determined by the HUC.

(g) A HUC reviews research involving medical devices. If, in the opinion of the HUC, the device does not pose a significant risk to the research subject, the organization will not be required to submit an IDE to the FDA.

(h) Certain categories of research may be reviewed by the HUC using the expedited review procedures in g below.

(i) Exempt categories of research are discussed in appendix F.

(2) *Approving official actions.* Approving officials—

(a) Will accept or reject the recommendations of the HUC. Safeguards or special restrictions imposed on a protocol by a HUC may not be reduced or waived by approving officials upon approval of the protocol or test plan.

(b) May require additional safeguards, may disapprove the protocol or test plan, or may refer it to a higher review committee and approving authority.

(c) Appoint a medical monitor (see glossary) for all studies that are greater than minimal risk.

(d) Obtain a health hazard assessment prior to approving a research proposal involving the use of chemical agents or operation of military materiel.

(e) Notify the investigator of their decision to approve or disapprove the research proposal, or of modifications required to secure approval.

(f) Ensure the continued evaluation of research programs by the program or project manager or equivalent official to assure that the policies and procedures established by this regulation are being followed.

(g) Will, when higher approval authority is required, forward two copies of the research protocol or test plan, informed consent documentation (DA Form 5303–R, or functional equivalent if applicable), all minutes of committees reviewing the protocol, and the commander's recommendations through command channels to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.

f. Actions taken by an organization without a local HUC.

(1) The investigator accomplishes the actions noted in *c* above.

(2) The commander or organizational head accomplishes the actions noted in *e*(2)*(d)* above, and forwards the protocol with his or her recommendations, through the military chain of command, to the next level of command having an approved HUC.

g. Expedited review procedures. These procedures are as follows:

(1) Research activities involving no more than minimal risk and in which the only involvement of human subjects will be in one or more of the categories listed at appendix D may be reviewed by the HUC through the expedited review procedure.

(2) The HUC may also use the expedited review procedure to review minor changes in previously approved research during the period for which approval is authorized. Under an expedited review procedure, the HUC chairman or one or more HUC reviewers designated by the chairman may carry out the review. The reviewers may exercise all of the authorities of the HUC except that of disapproval. Research may be disapproved only after review according to the nonexpedited procedure in *e* above.

(3) Each HUC using an expedited review procedure adopts a method for keeping all members and the commander advised of approved proposals.

(4) The approving official may restrict, suspend, or end a HUC's use of the expedited review procedure when necessary to protect the rights or welfare of subjects.

h. Duty to warn. Commanders have an obligation to ensure that research volunteers are adequately informed concerning the risks involved with their participation in research, and to provide them with any newly acquired information that may affect their well-being when that information becomes available. The duty to warn exists even after the individual volunteer has completed his or her participation in research. To accomplish this, the MACOM or agency conducting or sponsoring research must establish a system which will permit the identification of volunteers who have participated in research conducted or sponsored by that command or agency, and take actions to notify volunteers of newly acquired information. (See *a* above.)

i. Determining responsibility for review of protocols when more than one DOD or DA component is involved. The commander will determine primary responsibility based upon consideration of whether the subjects are inpatients or outpatients of a DOD medical treatment facility (MTF); whether the study is conducted in-house or by contract; or whether the prospective subjects are members of a DOD component.

(1) When the research, regardless of in-house or contract status, involves use of patients in a DOD MTF, the component to which the MTF belongs organizationally will have primary responsibility; except as provided in (3) below.

(2) For research not involving the use of inpatients at a DOD MTF, primary responsibility rests as follows:

(a) If the research is done on grant or contract, primary responsibility rests with the component providing funds.

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

(c) If research is not funded by a DOD or DA component and there is no DOD or DA principal investigator, primary responsibility rests with the component to which the prospective human subject is assigned.

(3) Studies funded by the Uniformed Services University of the Health Sciences (USUHS) or the Defense Nuclear Agency are reviewed and approved in accordance with policies established by the funding activity, and DODD 3216.2.

j. Records. Organizations or agencies conducting research involving volunteers will maintain records in accordance with AR 25–400–2, which are pertinent to the research conducted. These records will include, at a minimum—

(1) Documentation of approval to conduct the study.

(2) A copy of the approved protocol or test plan.

(3) The volunteer's signed informed consent (for example, DA Form 5303–R).

(4) A summary of the results of the research, to include any untoward reactions or occurrences. (See app H for a discussion of the composition of the Volunteer Data Base.)

k. Contractors or grantees. Contractors or grantees holding an approved Department of Health and Human Services (DHHS) Form HHS 596 (Protection of Human Subjects Assurance/Certification/Declaration) are considered in compliance with this regulation. (See fig 3–1 for sample DHHS Form HHS 596.) In the absence of such an assurance, a special assurance will be negotiated by the contracting officer with the contractor or grantee. Organizations can verify that a contractor has a valid DHHS Form HHS 596 by contacting the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012. Even though a contractor has a review process which is consistent with Federal law (that is, 45 CFR 46), it is incumbent upon the approving official to administratively review the protocol to assure that it complies with the policies established in this regulation.

l. Technical reports and publications.

(1) Technical reports will be prepared in accordance with AR 70–31 and follow the format established in MIL–STD 847B or its revisions.

(2) Publications regarding the results of DA conducted research will be released by the approving official in accordance with the provisions of AR 360–5 and will contain the following statement: "The investigators have adhered to the policies for protection of human subjects as prescribed in AR 70–25."

(3) Publications regarding the results of DA sponsored research conducted by contract or grant will note adherence with 45 CFR 46, as amended.

m. Requests for exceptions to policy. Requests for exceptions to policy are submitted to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012. Requests will then be submitted to TSG's HSRRB for evaluation and recommendation to TSG; and TSG's recommendation to the ASD (HA) or USD (A), as appropriate.

SAMPLE

OMB No. 0925-0037

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PROTECTION OF HUMAN SUBJECTS ASSURANCE/CERTIFICATION/DECLARATION

☒ ORIGINAL ☐ FOLLOWUP ☐ EXEMPTION (previously undesignated)

☐ GRANT ☒ CONTRACT ☐ FELLOW ☐ OTHER

☐ New ☐ Competing continuation ☐ Noncompeting continuation ☐ Supplemental

APPLICATION IDENTIFICATION NO. *(if known)*

POLICY: A research activity involving human subjects that is not exempt from HHS regulations may not be funded unless an Institutional Review Board (IRB) has reviewed and approved the activity in accordance with Section 474 of the Public Health Service Act as implemented by Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46—as revised). The applicant institution must submit certification of IRB approval to HHS unless the applicant institution has designated a specific exemption under Section 46.101(b) which applies to the proposed research activity. Institutions with an assurance of compliance on file with HHS which covers the proposed activity should submit certification of IRB review and approval with each application. (In exceptional cases, certification may be accepted up to 60 days after the receipt date for which the application is submitted.) In the case of institutions which do not have an assurance of compliance on file with HHS covering the proposed activity, certification of IRB review and approval must be submitted within 30 days of the receipt of a written request from HHS for certification.

1. TITLE OF APPLICATION OR ACTIVITY

Evaluation of Mefloquine in the Treatment of P.falciparum malaria

2. PRINCIPAL INVESTIGATOR, PROGRAM DIRECTOR, OR FELLOW

John Boslego, MD

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION *(see reverse side)*

4. HHS ASSURANCE STATUS

☒ This institution has an approved assurance of compliance on file with HHS which covers this activity.

M1369 Assurance identification number _____ IRB identification number

☐ No assurance of compliance which applies to this activity has been established with HHS but the applicant institution will provide written assurance of compliance and certification of IRB review and approval in accordance with 45 CFR 46 upon request.

5. CERTIFICATION OF IRB REVIEW OR DECLARATION OF EXEMPTION

☒ This activity has been reviewed and approved by an IRB in accordance with the requirements of 45 CFR 46, including its relevant Subparts. This certification fulfills, when applicable, requirements for certifying FDA status for each investigational new drug or device *(see reverse side of this form)*.

Jul 31,1987 Date of IRB review and approval. *(If approval is pending, write "pending". Followup certification is required.)*
(month/day/year)

☒ Full Board Review ☐ 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 45 CFR 46 will be reviewed and approved before they are initiated and that appropriate further certification *(form HHS 596)* will be submitted.

☐ Human subjects are involved but this activity qualifies for exemption under 46.101(b) in accordance with paragraph _____ *(insert paragraph number of exemption in 46.101(b), 1 through 5)*, but the institution did not designate that exemption on the application.

6. Each official signing below certifies that the information provided on this form is correct and that each institution assumes responsibility for assuring required future reviews, approvals, and submissions of certification.

APPLICANT INSTITUTION	COOPERATING INSTITUTION
NAME, ADDRESS, AND TELEPHONE NO. Wonderful University PO Box 7 Anywhere, State 65473	NAME, ADDRESS, AND TELEPHONE NO.
NAME AND TITLE OF OFFICIAL *(print or type)* William D. Clyde, Jr Chancellor for Health Affairs	NAME AND TITLE OF OFFICIAL *(print or type)*
SIGNATURE OF OFFICIAL LISTED ABOVE *(and date)* William D. Clyde Jr 7Aug87	SIGNATURE OF OFFICIAL LISTED ABOVE *(and date)*

HHS 596 (Rev. 1/82) *(If additional space is needed, please use reverse side under "Notes.")*

Figure 3–1. Sample DHHS Form HHS 596

SAMPLE

3. FOOD AND DRUG ADMINISTRATION REQUIRED INFORMATION *(from front side)*

According to 45 CFR 46.121, if an application is made to HHS requiring certification and involving use of an investigational new drug or device, additional information is required. In addition, according to 21 CFR 312.1(a)(2), 30 days must elapse between date of receipt by FDA of Form FD-1571 and use of the drug, unless the 30 day delay period is waived by FDA.

3a. INVESTIGATIONAL NEW DRUG EXEMPTION *(if more than one is involved, list others below under NOTES):*

SPONSOR NAME

Hoffman LaRoche, Inc

DRUG NAME

Mefloquine, 250 mg tablet

DATE OF END OF 30-DAY EXPIRATION OR WAIVER	NUMBER ISSUED
1 Apr 85	IND 1423

3b. INVESTIGATIONAL DEVICE EXEMPTION:

SPONSOR NAME

DEVICE NAME

Unless notified otherwise by FDA, under 21 CFR 812.2(b) (ii) a sponsor is deemed to have an approved IDE if: (1) the IRB has agreed with the sponsor that the device is a nonsignificant risk device; and (2) the IRB has approved the study. *(Check applicable box.)*

☐ The IRB agrees with the sponsor that this device is a nonsignificant risk device.

OR

☐ The IDE application was submitted to FDA on *(date)* _____ . Number issued _____ .

NOTES:

HHS 596 (Rev. 1/82) BACK

GPO 865-826

Figure 3–1. Sample DHHS Form HHS 596—Continued

Appendix A References

Section I
Required Publications

AR 25–400–2
The Modern Army Recordkeeping System (MARKS). (Cited in paras 3–2*j* and C–6*b*.)

AR 40–3
Medical, Dental, and Veterinary Care. (Cited in para 3–1*c* and *k*.)

AR 40–7
Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances. (Cited in paras 1–4*c*, 2–9*c*(5), and 3–1*v*.)

AR 40–10
Health Hazard Assessment Program in Support of the Materiel Acquisition Decision Process. (Cited in para 2–8*d*.)

AR 70–10
Test and Evaluation During Development and Acquisition of Materiel. (Cited in para 2–8*d* and the glossary.)

AR 70–31
Standards for Technical Reporting. (Cited in para 3–2*l*(1).)

AR 71–3
User Testing. (Cited in para 3–1*t*.)

AR 335–15
Management Information Control System. (Cited in para 3–2*c*(1).)

AR 340–21
The Army Privacy Program. (Cited in paras 3–2*a*(4) and H–1.)

AR 360–5
Army Public Affairs, Public Information (Cited in paras 3–1*w* and 3–2*l*(2).)

AR 385–16
System Safety Engineering and Management. (Cited in para 2–8*d*.)

AR 600–46
Attitude and Opinion Survey Program. (Cited in paras 2–6, 2–9*c*(12), and 3–2*c*(5).)

AR 602–1
Human Factors Engineering Program. (Cited in para 2–8*d*.)

AR 602–2
Manpower and Personnel Integration (MANPRINT) in Materiel Acquisition Process. (Cited in para 2–8*d*.)

DA Pam 70–21
The Coordinated Test Program. (Cited in para 3–2*c*(1).)

DA Pam 71–3
Operational Testing and Evaluation Methodology and Procedures Guide. (Cited in para 3–2*c*(1).)

MIL–STD 847B
Format Requirements for Scientific and Technical Reports Prepared by or for the Department of Defense. (Cited in para 3–2*l*(1).) (This publication is available from the Naval Publications and Forms Center, 5801 Tabor Avenue, Philadelphia, PA 19120–5099, Attn: Code 3015 (Specifications and Standards Requisition).)

TB MED 525
Occupational and Environmental Health Control of Hazards to Health from Ionizing Radiation Used by the Army Medical Department. (Cited in para 3–2*c*(4).)

Section II
Related Publications

A related publication is merely a source of additional information. The user does not have to read it to understand this regulation.

AR 11–2
Internal Control Systems

AR 40–38
Clinical Investigation Program

AR 40–66
Medical Record and Quality Assurance Administration

AR 70–14
Publication and Reprints of Articles in Professional Journals

AR 70–65
Management of Controlled Substances, Ethyl Alcohol, and Hazardous Biological Substances in Army Research, Development, Test, and Evaluation Facilities

AR 600–50
Standards of Conduct for Department of the Army Personnel

AR 611–3
Army Occupational Survey Program (AOSP)

DODD 3216.2
Protection of Human Subjects in DOD-Supported Research. (To obtain this publication, see MIL–STD 847B, sec I, above.)

DODD 6465.2
Organ Disposition After Autopsy. (To obtain this publication, see MIL–STD 847B sec I, above.)

FM 3–9/AFR 355–7
Military Chemistry and Chemical Compounds

DHHS Regulation, 45 CFR 46
Protection of Human Subjects. (This publication is available from Commander, USAMRDC, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.)

FDA Regulation 21 CFR subchapters A, D, and H
Food and Drugs. (This publication is available for reference at the local installation staff judge advocate office.)

Memorandum of Understanding between the FDA and DOD
Investigational Use of Drugs by Department of Defense, May 21, 1987. (This publication is available from the Commander, USAMRDC, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012.)

10 USC 980
Limitation on the Use of Humans as Experimental Subjects. (This publication is available for reference at the local installation staff judge advocate office.)

10 USC 1102
Restriction on the Use of Information Obtained During Certain Epidemiologic-Assessment Interviews. (This publication is available for reference at the local installation staff judge advocate office.)

Unnumbered Publication
Convention on the Prohibition of the Development, Production, and Stockpile of Bacteriological (Biological) and Toxin Weapons and on their Destruction, Article I. (This article is printed as a part of the publication entitled "Arms Control and Disarmament Agreements: Text and Histories of Negotiations", and is available from the U.S. Arms Control and Disarmament Agency, Washington, D.C. 20451.)

Section III
Prescribed Form

DA Form 5303–R
Volunteer Agreement Affidavit. (Prescribed in para 3–2*c*(1).)

Section IV
Referenced Forms

DD Form 1425
Specifications and Standards Requisition

DHHS Form HHS 596
Protection of Human Subjects Assurance/Certification/Declaration. (Only the contractor or grantee will obtain and use this form. This form after approval, however, is shown to the contracting officer as proof of the contractor's or grantee's compliance with this regulation. See para 3–2*k*, fig 3–1, and the glossary.)

Appendix B
Guidelines for Preparation of Research Protocol and/or Test Plan

B–1. Project title
Enter complete project title. (If an amendment, the words "Amendment to. . . ." must precede the project title.)

B–2. Investigators
a. Principal investigator.
b. Associate investigators.

B–3. Location of study
List of facilities to be used.

B–4. Time required to complete
Give month and year of expected start and completion dates.

B–5. Introduction
a. Synopsis.
(1) One-page summary of proposed study similar to the abstract of a scientific paper.
(2) Major safety concerns for human subjects briefly highlighted.
b. Military relevancy. Explain briefly the medical importance and possible usefulness of the project.
c. Objectives. State briefly, but specifically, the objectives of the project. Include items below when applicable.
(1) Study design.
(2) Type of subject population observed.
d. Status. State what has been accomplished or published in the proposed area of study. Describe the way in which the project will relate to, or differ from, that which has been accomplished.
e. Bibliography. List all references used in preparing the protocol.

B–6. Plan
Outline expected accomplishments in enough detail to show a clear course of action. Include technological validity of procedures and chronological steps to be taken. The plan should include, as a minimum, the information shown below on the study subjects.
a. Number of subjects. Give the total number of subjects expected to complete the study.
b. Age range.
c. Sex.
d. Inclusion criteria. Specific and detailed reasons for inclusion should be presented.
e. Diagnostic criteria for entry.
f. Evaluations before entry. Entries should include x ray, physical examinations, medical history, hematology, chemistry, and urinalysis as deemed appropriate.
g. Exclusion criteria. Include a complete list detailing the subjects, diseases, and medications that are excluded from the study.
h. Source of subjects. Describe briefly where the subjects will be obtained.
i. Subject identification. Describe the code system used.
j. Analysis of risks and benefits to subjects; risks to those conducting research.
k. Precautions to be taken to minimize or eliminate risks to subjects and those conducting the research.
l. Corrective action necessary.
m. Special medical care or equipment needed for subjects admitted to the project.

B–7. Evaluations made during and following the project
An evaluation may also be represented by using a project schematic. It is very important to identify in the protocol the person who will perform the evaluations below.
a. Specimens to be collected.
(1) Amount and schedule of collections.
(2) Evaluations to be made on specimens.
(3) Storage. State where and if special conditions are required.
(4) Labeling and disposition.
(5) Laboratories performing evaluations.
(6) Special precautions for subject and investigators.
b. Clinical assessments. Include how adverse effects are to be recorded.
c. Vital signs. When desired and frequency.
d. Follow up procedures.
e. Disposition of data. State location and duration of storage.
f. Methods used for data collection. State critical measurements used as end points to characterize safety, efficacy, or equivalency.

B–8. Departure from protocol for individual patients
a. When allowed. Use flexible but definite criteria.
b. Who will be notified. (For example, patient, HUC, approving official.)

B–9. Incidents
a. Definition of incidents.
b. Immediate reporting.
c. Routine reporting.

B–10. Modification of protocol
Describe the procedure to be followed if the protocol is to be modified, terminated, or extended.

B–11. Examples of all forms to be used in the protocol

B–12. Use of information and publications arising from the study

B–13. Special or unusual funding implications

B–14. Name and telephone number of the medical monitor, when applicable

B–15. Human use committee

Brief explanation of which HUC will provide initial, continued, and annual review.

B–16. Signature of appropriate approving official and date

B–17. Documentation

a. Completed DA Form 5303–R.
b. Institutional review of scientific and human use issues.
c. HUC review with commander's approval.
d. Biographical sketch of principal and associate investigators.

Appendix C
Human Use Committees

C–1. Membership

a. Membership will include only full-time Federally employed persons.

b. Each HUC will have at least five members. Members will have diverse backgrounds to ensure thorough review of research studies involving human volunteers as research subjects. Members should be sufficiently qualified through experience and expertise. The racial and cultural backgrounds of members and their sensitivity to such issues as community attitudes should ensure respect for their advice and counsel in safeguarding the rights and welfare of human subjects.

c. Besides having the professional competency to review research studies, the HUC will be able to determine if the proposed research is acceptable. Acceptability will be in terms of Army Medical Department (AMEDD) commitments and regulations, applicable law, and standards of conduct and practice. A HUC may review research periodically that involves vulnerable categories of human subjects (for example, those individuals with acute or severe physical or mental illness; or those who are economically or educationally disadvantaged). Therefore, it will include one or more persons concerned primarily with the welfare of these subjects.

d. Normally, no HUC may consist entirely of men or women, or members of one profession. However, the approving official may waive this requirement in those cases in which compliance is impractical.

e. Each HUC will include at least one member whose primary concerns are nonscientific; for example, lawyers, ethicists, and members of the clergy. Should a given proposal include more than minimal risk, a physician will be included as an ad hoc member of the committee.

f. Each HUC will 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 affiliated with the institution. This requirement may be met by appointing a member of an institution or organizational unit not subject to the immediate authority of the approving official.

g. Except to provide information requested by the HUC, no HUC member may take part in a review of any project in which the member serves as the principal investigator or associate investigator.

h. The HUC may invite individuals with special competence to assist in the review of complex issues that require expertise beyond that available on the HUC. These persons may not vote with the HUC.

i. The approving official may not be a member. The approving official may not approve research for which he or she is also a principal or associate investigator. A higher echelon of command must review and approve such research projects.

C–2. Functions and operations

Each HUC—

a. Will observe written procedures for the following:

(1) Conducting the initial and continuing review of the research. Included are reporting findings and actions to the investigator and the approving official.

(2) Determining those projects that must be—

(a) Reviewed more often than yearly.

(b) Verified from sources other than the investigators, that no material changes have occurred since the previous HUC review.

(3) Ensuring prompt reporting to the HUC of proposed changes in the research. Each HUC will ensure that changes in approved projects (during the period for which approval has already been given) are not initiated without HUC review except to eliminate immediate hazards to the subject.

(4) Ensuring prompt reporting to the HUC and approving official of unexpected problems involving risks to the subjects or others.

b. Will review proposed protocols at meetings attended by a majority of members except when an expedited review is used (see C–3 below). For the protocol to be approved, it will receive the approval of a majority of those members present.

c. Will report to the approving official any serious or continuing noncompliance with HUC requirements and determinations found by investigators.

d. Will conduct continuing review of research studies at intervals proper to the degree of risk, but not less than once per year.

e. Will have the authority to observe or have a third party observe the consent process and the investigation.

f. Will maintain a current list of HUC members. Members will be identified by name, earned degrees, representative capacity and, experience such as board certificates and licenses. The information will be complete enough to describe each member's chief expected contributions to HUC reviews. Any employment or other relationship between members and the institution will be noted.

g. May recommend safeguards or special conditions to a protocol. If the HUC does so, the approving official may take the following action:

(1) Not reduce the safeguards or conditions if he or she approves the protocol.

(2) Require additional safeguards.

(3) Disapprove the protocol.

(4) Refer the protocol to a higher echelon approving authority and review committee.

C–3. Expedited review procedures

a. See appendix D for a list of categories of investigations that the HUC may review in an expedited review procedure.

b. See paragraph 3–2g for the expedited review procedure that the HUC will follow.

C–4. Criteria for HUC approval of activities/investigations requiring volunteers

a. In evaluating risks and benefits for research investigations, the HUC should consider only those that may result from the investigation.

b. To approve investigations covered by this regulation, the HUC will determine that all of the requirements below are met.

(1) Risks to subjects are minimized by using procedures that are—

(a) Consistent with sound investigation design and do not unnecessarily expose subjects to risk.

(b) Already being used on the subjects for diagnosis or treatment, when appropriate.

(2) Risks to subjects are reasonable in relation to anticipated benefits to subjects.

(3) In making an assessment for the selection of subjects, the HUC should take into account the—

(a) Purpose of the investigation.

(b) Setting in which the research investigation will be conducted.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative.

(5) Informed consent will be properly documented.

(6) The plan makes adequate provision for monitoring the data collected to ensure the safety of subjects when appropriate.

(7) Adequate provisions exist to protect the privacy of subjects and to maintain the confidentiality of data when appropriate.

c. Some or all of the subjects may be vulnerable to coercion or undue influence such as persons with acute or severe physical or mental illness, or those who are economically or educationally disadvantaged. If so, proper additional safeguards will be included in the study to protect the rights and welfare of these subjects.

C–5. Suspension or termination of approved research investigation

a. A HUC will have the authority to suspend or end an approved investigation that—

(1) Is not being conducted according to the HUC's requirements.

(2) Has been associated with unexpected serious harm to subjects.

b. Suspensions or terminations of research will include a statement of the reasons for the HUC's action. They will be reported promptly to the principal investigator and approval official.

C–6. HUC records

a. A HUC will prepare and maintain adequate documents on HUC activities, including—

(1) Copies of all protocols reviewed, scientific evaluations that accompany the proposals, approved sample consent documents, progress reports submitted by investigators and reports of injuries and adverse reactions.

(2) Minutes of HUC meetings showing attendance; actions taken by the HUC; the vote on these actions, including the number of members voting for, against, and abstaining on a decision; the basis for requiring changes or disapproving the investigation; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

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

(5) A list of HUC members.

(6) Written procedures for the HUC.

(7) Statements of significant new findings.

b. The records required by this regulation will be retained permanently (see AR 25–400–2). Such records will be reasonably accessible for inspection and copying by authorized DA personnel and representatives of the FDA.

C–7. Conflict of interest

a. It is essential that the members of the HUC continue to be perceived and, in fact, are free from conflict of interest in their daily duties and especially in regards to the protocols they review.

b. The issue of conflict of interest has been addressed by public law, DOD directive, and Army regulation. The situations discussed below are merely examples of the types of activities and relationships which may result in conflict or the appearance of conflicts of interest. They are by no means the only ways that conflicts arise.

(1) *The potential for personal or financial gain.* A committee member who is deliberating a protocol which is to be performed by a contractor, in which the member or a member of his or her immediate family is a corporate officer, stockholder, consultant or employee, could be accused of conflict of interest if he or she voted on the protocol, regardless of his or her vote.

(2) *The potential for personal reward.* A committee member who is affiliated with a protocol in the capacity of principal, associate or co-investigator, could be accused of conflict of interest if he or she voted on the protocol, regardless of his or her vote.

(3) *Command influence.* The mission (for example, the purpose of the research) should not override or obscure its methods. It is imperative that the committee, through its members, continue to be recognized as a reasonable, deliberative body, whose bias is the safety and welfare of the research subject. It is incumbent upon each committee member to assure his or her concerns regarding the moral, ethical, and legal issues of each protocol are answered to his or her satisfaction before voting according to his or her conscience.

c. Commanders and organizational heads will establish a method to ensure that each committee member is familiar with the pertinent laws and regulatory guidance regarding conflict of interest.

C–8. Legal review

Prior to establishing a HUC, the commander or organizational head will obtain legal counsel from the staff judge advocate.

Appendix D
Expedited Review Categories

D–1. Hair, nails, teeth

Collection of—

a. Hair and nail clippings in a nondisfiguring way.

b. Deciduous teeth.

c. Permanent teeth if patient care indicates a need for extraction.

D–2. Excreta and secretions

Collection of—

a. Excreta and external secretions including sweat and uncannulated saliva.

b. Placenta at delivery.

c. Amniotic fluid at the time of rupture of the membrane before or during labor.

D–3. Physical data

Recording of data from subjects who are 18 years of age or older, using noninvasive procedures routinely employed in clinical practice. This category—

a. Includes the use of physical sensors that are applied either to the surface of the body or at a distance and do not involve input of matter or significant amounts of energy into the subject or an invasion of the subject's privacy.

b. Includes such procedures as—

(1) Weighing.

(2) Electrocardiography.

(3) Electroencephalography.

(4) Thermography.

(5) Detection of naturally occurring radioactivity.

(6) Diagnostic echography.

(7) Electroretinography.

c. Does not include exposure to electromagnetic radiation outside the visible range (for example, x rays or microwaves).

D–4. Blood

Collection of blood samples by venipuncture, in amounts not exceeding 450 milliliters in an 8-week period and no more often than two times per week. Subjects will be 18 years of age or older, in good health, and not pregnant.

D–5. Dental plaque and calculus
Collection of both supragingival and subgingival dental plaque and calculus. The procedure must not be more invasive than routine prophylactic scaling of the teeth. The process must be accomplished according to accepted prophylactic techniques.

D–6. Voice records
Voice recordings made for research purposes such as investigations of speech defects.

D–7. Exercise
Moderate exercise by healthy volunteers.

D–8. Existing data
Study of existing data, documents, records, or pathological or diagnostic specimens.

D–9. Behavior
Research on individual or group behavior or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate the subject's behavior and research will not involve stress to subjects.

Appendix E
Instructions for the Completion of the Volunteer Agreement Affidavit

E–1. Title and location
The title of the study and place where it is to be conducted.

E–2. Principal investigator
The name of the principal investigator conducting the study.

E–3. Description of the study
A statement that the study involves research. An explanation of the purpose of the study and the expected duration of the subject's participation. A description of the procedures to be followed. An identification of any experimental procedures. A statement giving information about prior, similar, or related studies that provide the rationale for this study.

E–4. Risks
A description of any reasonably foreseeable risks or discomforts to the subject.

E–5. Benefits
A description of the benefits, if any, to the subject or to others that may reasonably be expected from the study. If there is no benefit to the subject, it should be so stated.

E–6. Alternative treatment
When applicable, a disclosure of proper alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

E–7. Confidentiality
A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained. Also, in the case of an investigational drug or medical device protocol, a statement noting that the FDA may inspect the records. If the study is being performed by a contractor, a statement noting that representatives of the DOD may inspect the records.

E–8. Points of contact
An explanation of whom to contact for answers to pertinent questions about the study and the study subject's rights, and whom to contact in the event of a study-related injury to the subject. This should include a name or office and the commercial and AUTOVON telephone numbers.

E–9. Subject's consent
A statement that—
a. Participation is voluntary.
b. Refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled.
c. The subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

E–10. Compensation
For a study involving more than minimal risk, an explanation as to whether any compensation and medical treatment are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

E–11. Cautions
When appropriate, one or more of the elements of information below will also be given to each subject.
a. A statement that a certain treatment or procedure may involve risks to the subject (or to the embryo or fetus if the subject is or may become pregnant) that are currently unforeseeable. (Possible genetic effects to the offspring of males should be addressed when applicable.)
b. The anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
c. Any additional costs to the subject that may result from participation in the study.
d. The consequences of a subject's decision to withdraw from the study and procedures for the orderly end of the subject's participation.
e. A statement that new findings developed during the course of the study which could affect the subject's willingness to continue will be given to the subject.
f. The approximate number of subjects involved in the study.
g. The precautions to be observed by the subject before and after the study.
h. If photographs are to be taken, the degree to which actions will be taken to protect the identity of the subject.
i. A statement as to whether the results of the research will be made known to the subject.

E–12. Disposition of the informed consent
The principal investigator will retain the original signed informed consent. A copy will be provided to the volunteer. If the volunteer consents, the investigator will provide a copy of the signed DA Form 5303–R to the medical records custodian for inclusion in the volunteer's medical treatment record (AR 40–66, para 6–2*f*.)

Appendix F
Exemptions

Activities in which human subjects are involved in one or more of the categories below are exempt from this regulation.
a. Routine epidemiological surveys that are of no more than minimal risk as set forth in the human protection regulations issued by the DHHS (45 CFR 46). (See the glossary for the definition of epidemiological survey.)
b. Research in educational settings which involves normal educational practices such as—
(1) Regular and special education strategies.
(2) The effectiveness of, or the comparison among, techniques of instruction, curricula, or classroom management methods.
c. Research that involves the use of educational tests when the data is recorded in such a way that subjects cannot be identified directly or indirectly.
d. Research that involves survey, interview procedures, or the observation of public behavior (including observation by participants) except where all the following exist:

(1) Responses or observations are recorded in such a way that subjects can be identified directly or indirectly.

(2) The subject's responses or recorded observations, if they become known outside the research, could reasonably place the subject at risk of criminal or civil liability, or would damage the subject's financial standing or employability.

(3) The research deals with sensitive aspects of the subject's behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol.

e. Research involving the collection or study of existing data, documents, records, or pathological or diagnostic specimens, if these sources are publicly available or if the information is recorded in such a way that subjects cannot be identified directly or indirectly.

f. Individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercise (for example, Army Training and Evaluation Program (ARTEP), Skill Qualification Test (SQT)). Evaluation of the training's effect on the individual participants may or may not be exempt depending on how the evaluation is made (for example, drawing of blood is not exempt).

g. Job related tasks of military or civilian personnel who are qualified to test by duty assignments that call specifically for such qualifications.

h. ~~Research involving deliberate exposure of human subjects to nuclear weapons effect, to chemical warfare agents, or to biological warfare agents.~~Inclusion of human subjects as the indirect object of research involving minimal risk or less in the development and testing of military weapon systems, vehicles, aircraft, and other material are exempt from the requirement for obtaining informed consent from the participants. The determination of whether a proposal is minimal risk or less is made by a HUC established in accordance with paragraph 3–2*b* of this regulation.

i. Other research which is exempted by future changes to DHHS regulations, and which is consistent with this regulation and DOD Directive 3216.2.

Appendix G
Legal Implications

G–1. Authority

The Secretary of the Army is authorized to conduct research and development programs including the procurement of services that are needed for these programs (10 USC 4503). The Secretary has the authority to "assign, detail and prescribe the duties" of the members of the Army and civilian personnel (10 USC 3013).

G–2. Military personnel and Department of the Army civilian employees

Compensation for the disability or death of a civilian employee resulting from personal injury or disease proximately caused by employment is payable under the Federal Employees Compensation Act (5 USC 8100 et seq.), regardless of whether employment was of a hazardous nature. The amount and type of disability compensation or other benefits payable by reason of the death or disability of a member of the Army resulting from injury or disease incident to service depends upon the individual status of each member, and is covered by various provisions of law. It may be stated generally that under present laws no additional rights against the government will result from the death or disability of military and civilian personnel participating in experiments by reason of the hazardous nature of the operations.

G–3. Private citizens

It is the policy of the United States to prohibit the acceptance of voluntary services (31 USC 1342). Individuals may, however, enter into an independent contractual relationship and participate for compensation as authorized by applicable directives (for example, volume 45 Decision of the Comptroller General, 1966, p. 649 (45 1966-649)). Accordingly, any such service should be accompanied by a statement to the effect that the individual will not receive or become entitled to any compensation other than that stated in the contract for these services.

G–4. Use of appropriated funds for the purchase of insurance

Since the payment of insurance premiums on the life of an officer or employee of the United States is a form of compensation which is not currently authorized, payment of those premiums is prohibited.

G–5. Contractor's employees

There appears to be no legal objection to the use of employees of contractors in research and development experiments. It is the responsibility of the contracting officer to determine whether the terms of the contract are sufficiently broad to permit the participation of these employees. Generally, benefits to which contract employees may become entitled by reason of death or disability resulting from their employment are payable under State Workmen's Compensation law, except persons covered by the survivor's insurance provisions of the Social Security Act (42 USC 402). Reimbursement of the employer for additional costs by reason of this liability for his or her employees will depend upon the terms of each contract. These employees are not disqualified from prosecuting claims against the government under the Federal Torts Claim Act (28 USC 2671 et seq.), if such a claim exists.

G–6. Irregular or fee-basis employees

Intermittent services of such employees are authorized. (Experts and consultants, 5 USC 3109(b) and Sec. 710 Defense Production Act of 1960 (64 Stat. 819, 50 USC App 2160); and for architects, engineers, and other technical and professional personnel on a fee-basis, 10 USC 4540.) Whether these employees can be detailed or assigned to the proposed experiments will depend upon the statutory authority for employment and the provisions of their employment agreement in each case. The Federal Employees Compensation Act, *supra*, in all probability applies with respect to these irregular and fee-basis employees for any injury or disease resulting from their employment, although a final determination in such cases will have to be made by the Federal agency responsible for deciding claims. Subject to such restrictions and limitations as may appear in the statutory authority under which he or she is employed, it would appear that the Government may legally bear the expense of premiums upon the life of an irregular or fee-basis employee whose rate of compensation is not fixed by law or regulations. In this regard, it may be advisable for the government to provide an additional allowance to the employee for financing such private insurance arrangements as he or she may wish to make rather than to undertake direct negotiations with insurance carriers for the desired coverage.

Appendix H
Volunteer Data Base

H–1. General

The intent of the data base is twofold: first, to readily answer questions concerning an individual's participation in research conducted or sponsored by the command; and second, to ensure that the command can exercise its "duty to warn." The data base must contain items of personal information, for example, name, social security number (SSN), etc., which subjects it to the provisions of The Privacy Act of 1974. AR 340–21 addresses the requirements for establishing such a system of records. For assistance in developing the systems notice for publication in the Federal Register, contact Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012, AUTOVON 343–2165.

H-2. Data elements

The elements listed below are representative of those items that could be found in such a data base. It is not meant to be all inclusive, and can be modified to meet individual command needs.

a. Records of the study. A copy of the—

(1) Approved test plan or protocol.

(2) Letter or other document approving the conduct of the test or protocol.

(3) Signed informed consent for each volunteer.

(4) Report generated by the results of the test or protocol.

b. Data elements—volunteer's personal information.

(1) Name.

(2) Rank (if applicable).

(3) SSN.

(4) Sex.

(5) Date of birth.

(6) MOS or AOC (if applicable).

(7) Local address and telephone number.

(8) Permanent address and telephone number.

(9) Unit (if applicable).

c. Data elements—test plan or protocol information.

(1) Test or protocol title.

(2) Principal investigator's name.

(3) Laboratory, unit, or facility conducting the test protocol.

(4) Location of the test.

(5) Test period.

(6) Challenge material data (if applicable).

(a) Name of the material used (both active and inert material).

(b) Manufacturer.

(c) Lot number.

(d) Expiration date.

(e) IND or IDE number.

(7) Date the volunteer completed or withdrew from the study.

(8) Reason for withdrawal (if applicable).

(9) Description of untoward reactions experienced by the volunteer (if none, so state).

H-3. Updating perishable data

Selected items of personal information are perishable; for example, local address and telephone number. A method should be established, which is consistent with the potential for long-term risks of the test or protocol, to update this information. For example, the risks associated with testing a new parachute will be readily apparent; whereas the risks associated with the testing of new, obscurant smoke may not be known for some time to come.

Section I
Abbreviations

AIDS
Acquired immune deficiency syndrome

AMEDD
Army Medical Department

AOC
area of concentration

ARNG
Army National Guard

ARTEP
Army Training and Evaluation Program

ASA (RDA)
Assistant Secretary of the Army (Research, Development, and Acquisition)

ASD (HA)
Assistant Secretary of Defense (Health Affairs)

CFR
Code of Federal Regulations

DA
Department of the Army

DCSPER
Deputy Chief of Staff for Personnel

DHHS
Department of Health and Human Services

DOD
Department of Defense

DTF
dental treatment facility

FDA
Food and Drug Administration

HIV
human immunodeficiency virus

HSRRB
Human Subjects Research Review Board

HUC
human use committee

HURRAO
Human Use Review and Regulatory Affairs Office

IDE
Investigational Device Exemption

IND
Notice of Claimed Investigational Exemption for a New Drug

IRB
institutional review board

MACOM
major Army command

MOS
military occupation specialty

MTF
medical treatment facility

NDA
New Drug Application

OTSG
Office of the Surgeon General

PCS
permanent change of station

PI
principal investigator

RDTE
research, development, test, and evaluation

SI
skill identifier

SSC–NCR
Soldier Support Center—National Capital Region

SSN
social security number

SQT
skill qualification test

TSG
The Surgeon General

USAMRDC
U.S. Army Medical Research and Development Command

USAR
U.S. Army Reserve

USD (A)
Under Secretary of Defense for Acquisition

USUHS
Uniformed Services University of the Health Sciences

Section II
Terms

Adverse personnel action
For the purposes of paragraph 3–11, this term includes—

a. A court martial.
b. Non-judicial punishment.
c. Involuntary separation (other than for medical reasons).
d. Administrative or punitive reduction in grade.
e. Denial of promotion.
f. Entry of unfavorable information in a personnel record.
g. A bar to reenlistment.
h. Any other action considered by the DA to be an adverse personnel action.

Approving official
A military commander or civilian director of an organizational element of a DA component who has been delegated authority to approve the use of human subjects in research.

Assent
A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Associate investigator
A person who may be involved in the execution of research, but does not have overall primary responsibility. The FDA refers to such an individual as a subinvestigator.

Certificate of Assurance
See Protection of Human Subjects Assurance/Certification/Declaration.

Chemical warfare agent (FM 3–9)
A chemical compound which, through its chemical properties, produces lethal or damaging effects on man. Excluded from consideration are riot control agents, anti-plant agents, and smoke and flame materials.

a. Chemical agents may be grouped according to use:

(1) *Toxic chemical agents.* Agents capable of producing incapacitation, serious injury, or death when used in field concentrations.

(2) *Incapacitating agents.* Agents that produce physiological or mental effects or both that may persist for hours or days after exposure, rendering individuals incapable of concerted efforts in the performance of their assigned duties. Complete recovery of incapacitating agent casualties is expected without medical treatment.

b. Nonchemical warfare agents may be grouped according to use as follows:

(1) Riot control agents. Compounds widely used by governments for domestic law purposes, and which produce transient effects on man that disappear minutes after removal from exposure.
(2) Training agents and compounds.
(3) Screening and signaling smokes.
(4) Anti-plant agents.

c. It should be noted that the Convention on the Prohibition of the Development, Production, and Stockpile of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, Article I, dated 26 March 1975, stipulates that—

"Each State Party to this Convention undertakes never in any circumstance to develop, produce, stockpile, or otherwise acquire or retain:

(1) Microbial and other biological agents or toxins whatever their origin or method of production, of types or in quantities that have no justification for prophylactic, protective or other peaceful purposes;

(2) Weapons, equipment, or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict."

Accordingly, chemical materials obtained from such sources or processes are considered biological, not chemical, weapons.

Clinical investigation
An organized inquiry into health problems for all conditions that are of concern in providing health care to beneficiaries of the military health care system, including active duty personnel, dependents, and retired personnel. The clinical investigation program is described in AR 40–38.

Consent
See informed consent.

Development
Systematic use of scientific knowledge, directed toward—

a. Significant improvements in or creation of useful products to meet specific performance requirements.

b. Development of components for incorporation in end items to meet specific performance requirements.

c. Construction of hardware for test purposes to determine feasibility of technical approaches.

d. Formulation and refinement of techniques and procedures which improve Army capabilities in nonmateriel areas.

Epidemiologic-assessment interview
For the purpose of paragraph 3–1*l*, this term means questioning of a serum positive member of the Armed Forces for the purposes of medical treatment or counseling, or for epidemiologic or statistical purposes.

Epidemiological surveys
For the purpose of this regulation, the term means studies of the distribution and determinants of disease frequency in humans, involving no more that minimal risk in which research data is not linked to personal identifiers. Epidemiological surveys focus on "ills" of a population rather than on persons.

Evaluation
The subjective determination of the military value of a hardware item or system, real or conceptual, to the user. There are three types of evaluation: Developer, technical, and operational. See 70–10 for more detail.

Expedited review procedures
Those procedures used in research involving no more than minimal risk and those used for minor changes in approved investigations (see app D). These procedures minimize time required for review.

Experimental subject
See Human subject.

Health care personnel
Military personnel, civilian employees, or contract personnel (including military and civilian staff members, assigned to, employed by, or appointed to the USUHS) who provide patient care or patient care support services in military MTFs and dental treatment facilities (DTFs).

Health care delivery study
Application of scientific methods to the study of availability, organization, administration, and management of health services. The efficiency and effectiveness with which such services are delivered are included.

Health and Human Services Certificate of Assurance
See Protection of Human Subjects Assurance/Certification/Declaration.

Human subject
a. 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 qualifications such as test pilots or test engineers.

b. Minor (child). A person who has not attained the legal age for consent to treatments or procedures involved in research, under the applicable laws and jurisdiction in which the research will be conducted.

c. Human subjects may be thought of as direct objects when the research is to determine the effects of a new system on humans (for example. the effects of a weapon's blast on hearing) as indirect objects when a test is conducted to determine how humans affect the ultimate performance of a system (doctrine concepts, training programs).

Human Subjects Research Review Board
The principal body of the Office of The Surgeon General (OTSG) for review of clinical investigation and research activities.

Human use committee
A body set up to provide initial and continuing review of research involving the use of human subjects. A HUC is fundamentally similar to an institutional review board (IRB) (45 CFR 46), but has somewhat different authority as compared to an IRB. Within DOD, authority to approve use of human subjects in research is vested in commanders. Commanders act on the recommendations of validly constituted HUCs. Outside DOD, IRBs tend to be vested with this authority. Appendix C describes the membership, functions, and operations of a HUC.

Informed consent
The legally effective agreement of the subject or subject's legally authorized representative for the subject to participate in research covered by this regulation. Informed consent includes, when appropriate, those elements listed in appendix E of this regulation.

a. Permission. The agreement of parent(s) or guardian to the participation of their child or ward in research.

b. Guardian. An individual who is authorized under applicable State or local law to consent on behalf of a minor (child) to general medical care.

c. Assent. A minor's (child's) affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Institution
Any public or private entity or agency (including Federal, State, or other agencies).

Investigational drug
A drug may be considered investigational when the composition is such that—

a. Its proposed use is not recognized for the use under the conditions prescribed; or its proposed use is not recommended or suggested in its approved labeling. Experts qualified by scientific training and experience evaluate the safety and effectiveness of drugs to make this determination.

b. Its use has become recognized as investigational, as a result of studies to determine its safety and effectiveness for use under such conditions.

Investigational medical device
a. A device that is not generally used in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans, and recognized as safe and effective.

b. Research is usually, but not necessarily, initiated to determine if the device is safe or effective.

Legally authorized representative
A person or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's taking apart in the procedures involved in the research.

Medical monitor
This person is a military or DA civilian physician qualified by the training and/or experience required to provide care to research subjects for conditions that may arise during the conduct of the research, and who monitors human subjects during the conduct of research. For the purpose of this regulation, the principal investigator may function as the medical monitor only in situations in which no other physician is available and approval for the principal investigator to function as medical monitor is granted by TSG. Requests for the principal investigator to function as the medical

monitor will be sent to the Assistant Surgeon General for Research and Development, c/o Headquarters, U.S. Army Medical Research and Development Command, ATTN: SGRD–HR, Fort Detrick, Frederick, MD 21701–5012. In contractor performed research, a military or DA civilian physician may be the medical monitor; however, this is usually a contractor provided resource.

Minimal risk
The proposed risks are not considered greater than these encountered in the subject's daily life or during routine physical or psychological examinations.

Non-U.S. citizens
Foreign nationals, excluding personnel on active duty.

Personal identifier
A method or system which links data to the individual from whom or about whom it pertains.

Principal investigator
A person, regardless of title, who is primarily responsible for the actual execution of the research.

Prisoner
Any person, (adult or minor) involuntarily confined or detained in a penal or correctional institution (for example, jail, workhouse, house of detention, prison, military stockade, or brig). The term is intended to encompass individuals detained pending arraignment, trial, or sentencing; and prisoners of war including detained personnel). The term does not include individuals voluntarily confined nor those persons subject to civil commitment procedures that are not alternatives to criminal prosecution.

Protection of Human Subjects Assurance/ Certification/Declaration
A document issued by the Office for Protection from Research risk, DHHS, in which that office acknowledges that a research institution has established policies and procedures consistent with 45 CFR 46.

Protocol
The written, detailed plan by which research is to be conducted. (See app B for an example of research protocol.) The plan contains, as a minimum—

a. The objectives of the project.
b. The information to be collected.
c. The means by which it will be collected and evaluated; an assessment of potential risk and benefits to subjects; safety measures, and other means to be used to reduce any risk to subjects.

Radioisotope/radiation control committee
A committee appointed by the commander to ensure that individual users of radioactive materiels within the medical facility and each radionuclide will be approved and controlled. The approval and control is in accordance with the requirements specified in the conditions of the Nuclear Regulatory Commission license and DA radioactive material authorization and appropriate Federal directives.

Research
A systematic investigation 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 (DODD 3216.2)

Research, development, test, and evaluation
Includes those categories of research and development included in Program 6, Research and Development, and operational systems development contained in the Five-Year Defense Program.

Schedule I controlled drug substances
Any drug or substance by whatever official name, common or usual name, chemical name or brand name listed in 21 CFR 1308, for example, heroin.

Serum positive member of the Armed Forces
For the purposes of paragraph 3–1*l*, this term means a member of the Armed Forces who has been identified as having been exposed to a virus associated with the acquired immune deficiency syndrome (AIDS).

Subinvestigator
See associate investigator.

Test
A process by which data are accumulated to serve as a basis for assessing the degree to which an item or system meets, exceeds or fails to meet the technical or operational properties required. AR 70–10 has a more detailed discussion of the RDTE type test.

VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 70-25 or AR 40-38; the proponent agency is OTSG

PRIVACY ACT OF 1974

Authority: 10 USC 3013, 44 USC 3101, and 10 USC 1071-1087.

Principle Purpose: To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.

Routine Uses: The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study; implementation of medical programs; adjudication of claims; and for the mandatory reporting of medical conditions as required by law. Information may be furnished to Federal, State and local agencies.

Disclosure: The furnishing of your SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A(1) - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, _____, SSN _____,

having full capacity to consent and having attained my _____ birthday, do hereby volunteer/give consent as legal

representative for _____ to participate in _____

_____

(Research study)

_____

under the direction of _____

conducted at _____.

(Name of Institution)

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

_____.

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the rights of the person I represent on study-related injury, I may contact

_____

at _____

(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, I/the person I represent may be required (military volunteer) or requested *(civilian volunteer)* to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well-being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

_____

PART A (2) - ASSENT VOLUNTEER AFFIDAVIT *(MINOR CHILD)*

I, _____, SSN _____ having full

capacity to assent and having attained my _____ birthday, do hereby volunteer for _____

_____ to participate in _____

_____

(Research Study)

_____

under the direction of _____

conducted at _____.

(Name of Institution)

(Continue on Reverse)

PART A(2) - ASSENT VOLUNTEER AFFIDAVIT (*MINOR CHILD*) (Cont'd.)

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

_____

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights I may contact

_____

at _____

(Name, Address, and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my assent and withdraw from the study without further penalty or loss of benefits; however, I may be requested to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

_____

PART B - TO BE COMPLETED BY INVESTIGATOR

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: *(Provide a detailed explanation in accordance with Appendix C, AR 40-38 or AR 70-25.)*

I do ☐ **do not** ☐ *(check one & initial)* consent to the inclusion of this form in my outpatient medical treatment record.

SIGNATURE OF VOLUNTEER	DATE	SIGNATURE OF LEGAL GUARDIAN *(If volunteer is a minor)*
PERMANENT ADDRESS OF VOLUNTEER	TYPED NAME OF WITNESS	
	SIGNATURE OF WITNESS	DATE

REVERSE OF DA FORM 5303-R, MAY 89

Approved For Release 2000/08/08 : CIA-RDP96-00788R001500140002-0

H.5. USE OF HUMAN SUBJECTS:

a. Definitions

1. Subject at Risk - means any individual who may be exposed to the possibility of injury, including physical, psychological or social injury, as a consequence of participation as a subject in any research, development or related activity which departs from the application of those established and accepted methods necessary to meet his needs, or which increases the ordinary risk of daily life, including the recognized risks inherent in a chosen occupation or field of service.

2. Investigational Drugs - means those new drugs restricted by the Federal Food, Drug and Cosmetic Act to be used by or under the supervision of an investigator pursuant to a notice of Claimed Investigational Exemption for the New Drug (IND).

3. Investigational Medical Devices - means those devices which are not generally recognized as safe and/or effective, intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in, or research on, humans where the research is usually (but not necessarily) for the purpose of determining whether or not the device is safe and/or effective.

b. Requirements for the Use of Humans

1. Safeguarding the rights and welfare of subjects at risk in activities supported by this contract is primarily the responsibility of the Contractor. Compliance with this contract will in no way render inapplicable pertinent federal, state, or local laws or regulations. In order to provide for the adequate discharge of this institutional responsibility, it is the policy of the DIA that no activity involving human subjects under this contract shall be undertaken unless a Contractor Human Use Review Board (CRB) has reviewed and approved such activity.

2. The contractor shall provide to DIA a written assurance that it will abide by the policy for the protection of human subjects as contained in title 45, Part 46, of the Code of Federal Regulations (CFR), as amended. When the contractor has a Health and Human Services (HHS) approved assurance, evidence of CRB approval of this study shall have been accomplished by submission to DIA of an executed HHS form 596. For a contractor without an HHS approved assurance, an assurance concerning the protection of human subjects shall have been negotiated with the DIA COTR, and CRB approval given. (Note: the CRB activity is referred to in the CFR as an Institutional Review Board (IRB) activity.)

3. In addition to the requirements of Title 45, Part 46 of the CFR, the following shall apply to all DIA contracts supporting research, development, and related activities:

a) Prisoners of war (POW) and detainees shall not be used under any circumstances.

b) Use of prisoners as research subjects shall have been specifically approved by the DIA Contracting Officer.

c) A mentally disabled or institutionalized mentally infirm person shall not participate as a research subject unless the nature of the research involved is such that it would be impossible or meaningless if mentally infirm were restricted from participation, or other considerations are involved. Specific approval for their use shall have been granted by the Contracting Officer. The research must be concerned with:

(i) The diagnosis, treatment, prevention, or etiology of the particular impairment with which the subject is afflicted, or

(ii) Any other condition from which the subject is suffering, providing there is a direct potential benefit to the subject and adequate prior testing has been accomplished to give assurance of acceptable risk, or

(iii) The effects of institutional life upon the institutionalized mentally infirm subject, and involves no appreciable risk to the subject, or

(iv) Information which cannot be obtained from any other class of subject.

d) Volunteers and/or research subjects, either contractor, consultant, or subcontractor, shall be the responsibility of the contractor who shall provide all necessary medical care for injury or disease that is the proximate result of taking part in the contract research.

e) New people entering this project for training purposes, or for participation as subjects of research, shall sign a statement that they will not use information attained during the course of participation to invade the privacy of US citizens.

f) Studies conducted outside the United States, its territories or possessions, shall be conducted in compliance with all laws, customs and practices of the country in which the study is to be conducted.

c. Requirements for the Use of Investigational Drugs
Investigational drugs of any kind shall not be used for this contract.

d. Requirements for Use of Investigational Medical Devices
The Contractor shall comply with Title 21, Part 812, of the CFR, as amended, for the study and evaluation of those devices which are not generally recognized as safe and/or effective intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in, or research on, humans. The contractor shall have to provide with his proposal a copy of FDA approval of, or grant of waiver for, use of investigational device exemption.

e. Requirements for Reporting and Documentation

1. Copies of all documents presented or required for initial and continuing review of the CRB, e.g., Board minutes pertaining only to the contract, record of subjects consent, transmittal on actions, instructions and conditions resulting from Board deliberations addressed to the activity director, are to be retained by the Contractor for at least three (3) years after completion of the research. All documents shall be accessible for inspection during normal working hours, by the DIA COTR or authorized representative.

2. Except as otherwise provided by law, information in the records or possession of the Contractor which refers to or can be identified with a particular subject may not be disclosed except:

a) With the consent of the subject or his legally authorized representative, or

b) As may be necessary for the DIA to carry out its legal responsibilities.

3. Upon expiration or termination of this contract, a list of all unused test material shall be provided to the DIA Contracting Officer.

4. The Contractor shall immediately notify the DIA Contracting Officer, by telephone, of inquiries outside the Department of Defense concerning the use of human subjects under this contract. In addition, the Contracting Officer shall be notified as soon as possible of inspections of the facility or contract protocols by the FDA.

§ 46.114 Cooperative research.

Cooperative research projects are those projects, normally supported through grants, contracts, or similar arrangements, which involve institutions in addition to the grantee or prime contractor (such as a contractor with the grantee, or a subcontractor with the prime contractor). In such instances, the grantee or prime contractor remains responsible to the Department for safeguarding the rights and welfare of human subjects. Also, when cooperating institutions conduct some or all of the research involving some or all of these subjects, each cooperating institution shall comply with these regulations as though it received funds for its participation in the project directly from the Department, except that in complying with these regulations institutions may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.

§ 46.115 IRB records.

(a) An institution, or where 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.

(3) Records of continuing review activities.

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

(5) A list of IRB members as required by § 46.103(b)(3).

(6) Written procedures for the IRB as required by § 46.103(b)(4).

(7) Statements of significant new findings provided to subjects, as required by § 46.116(b)(5).

(b) The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Department at reasonable times and in a reasonable manner.

§ 46.116 General requirements for informed consent.

Except as provided elsewhere in this or other subparts, no investigator may involve a human being as a subject in research covered by these regulations 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: