PROCEDURES FOR USE OF HUMANS AS RESEARCH SUBJECTS

IN THE EXTRAMURAL RESEARCH PROGRAM

I. Purpose: This is to establish uniform procedures and responsibility for review of the use of humans as research subjects, negotiation of provisions, and administration of research projects in the extramural program. Wherever the term "contractor" appears it shall also mean grantee and other Government agency.

II. References

1. 45 CFR 46 HHS Regulation on Protection of Human Subjects;

2. 10 U.S.C. Section 980 Limitations on Use of Humans as Experimental Subjects;

3. 21 CFR 312 Investigational Drugs and Vaccines;

4. 21 CFR 812 Investigational Medical Devices;

5. 21 CFR 56.111(a)(3) Advertisement Guidelines for the Recruiting of Research Subjects;

6. DOD Directive 6465.2 Organs and Tissues Obtained from Autopsy;

7. DOD Directive 3216.2 Protection of Human Subjects in DOD-Supported Research;

8. Federal Acquisition Regulation (FAR) 52.228-7 Insurance Liability to Third Persons and FAR 31.109 Advance Agreements;

9. USAMRDC Regulation 70-25 Use of Human Subjects in Research, Development, Testing and Evaluation;

10. USAMRDC Broad Agency Announcement (BAA);

11. Army Regulation 340-21 The Army Privacy Program; and

12. Federal Acquisition Regulations (FAR) Part 24 Protection of Privacy and Freedom of Information, 52.224-1 Privacy Act Notification, and 52.224-2 Privacy Act.

III. Objectives:

1. Safeguarding the rights and welfare of human subjects participating in research and development supported by contracts, grants and orders awarded by U.S. Army Medical Research and

Development Command (USAMRDC) is of utmost concern to the Command, and is primarily the responsibility of the contractor or recipient who receives or is accountable to USAMRDC for the funds awarded for the support of the project. However, the sensitivity of such research necessitates that the Command exercise prudence in its oversight responsibilities. The procedures employed shall be flexible and tailored to the requirements of the specific acquisition.

2. It is the policy of USAMRDC that the Department of Health and Human Services (HHS) Regulation on Protection of Human Subjects, Food and Drug Administration Regulations on Investigational Drugs and Vaccines and Investigational Medical Devices, and Advertisement Guidelines for the Recruiting of Research Subjects shall be adhered to by USAMRDC contractors and recipients, with the addition of the following specific DOD/USAMRDC requirements.

a. Informed consent must be obtained in advance from the subject, or in the case of research intended to be beneficial to the subject, the informed consent of the subject or a legal representative of the subject must be obtained in advance.

b. Contractors and recipients shall provide all necessary medical care to research subjects for injury or disease which is the proximate result of participation in the research.

c. Anatomical Substances (organs, tissues, or tissue fluids) obtained from autopsy shall not be used for research or investigational purposes without the expressed consent of the next of kin. It should be noted that a general autopsy consent may not, in itself, be sufficient. If autopsy tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

d. Anatomical Substances (organs, tissues, or tissue fluids) obtained from a surgical procedure shall not be used for research or investigational purposes without the expressed consent of the patient or patient's legal representative. It should be noted that a consent to perform surgery may not, in itself, be sufficient. If excised tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

e. Anatomical substances linked by identifiers to a particular person and used for research shall be donated for the purpose of research, and shall be lawfully acquired. The donor shall be the person from whom the substance is removed or, in the event of death or legal disability of the person from whom the substance is removed, the next of kin or legal representative of such person. Donation shall be made by written consent and the donor shall relinquish all ownership and/or rights to the substance. If excised or autopsy tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

f. Prisoners of war shall not be used as research subjects.

g. Use of prisoners as research subjects shall follow 45 CFR 46, Subpart C.

h. Studies conducted outside the U.S., its territories or possessions, which involve the use of non-U.S. citizens as subjects, in addition to compliance with 45 CFR 46 and above special DoD and USAMRDC requirements, shall comply with the laws, customs, and practices of the country in which the study is to be conducted. The minimum standards to be adhered to are contained in the Declaration of Helsinki (Tab D). The research proposal submitted for approval will document this action. In exceptional circumstances where laws, customs or practices of the country involved take exception to particular procedural requirements of this provision (as, for example, the documentation of informed consent or the procedures by which it is obtained), specific approval will be obtained from the Commander, U.S. Army Medical Research and Development Command as an integral part of the proposal review and approval process.

i. None of these provisions apply to epidemiological surveys involving no more than minimal risk.

j. The USAMRDC may inspect contractor records concerning human use.

IV. Goals:

1. The Human Use Review and Regulatory Affairs Office (SGRD-HR) shall be responsible for all aspects of the USAMRDC extramural program involving the use of humans in research and testing, and use of human anatomical substances. SGRD-HR is specifically responsible for:

a. Review of any proposal and consent form, contract, subcontract, grant, intragovernmental transfer of funds order, or modification which involve the use of humans or human anatomical substances. Review shall ensure:

(1) that applicable DOD directives, Army Regulations, FDA and HHS regulations, and public laws will be complied with;

(2) that appropriate validation of the human use process has occurred, and;

(3) that the recipient or contractor has an assurance of compliance with 45 CFR 46 satisfactory to the HHS, or has provided sufficient information for negotiation with the USAMRDC of a special assurance of compliance.

b. Development, in coordination with the U.S. Army Medical Research Acquisition Activity (SGRD-RMA), of special provisions to be included in RFPs, contracts, and grants. Development, in coordination with the Acquisition Management Office (SGRD-ACQ), of special provisions to be included in the BAA and intragovernmental transfer of fund orders.

c. Participating in negotiations (in conjunction with SGRD-RMA or SGRD-ACQ) with prospective contractors for the development of special assurance of compliance with HHS 45 CFR 46. The SGRD-HR shall be the final approval authority for special assurances.

d. Review and approval of proposals recommended for inclusion in the competitive range as a result of solicitations, and its accompanying consent form. Where applicable, advertisements used to recruit subjects will be reviewed.

e. Assuring that all parties (e.g., contracting officer's representative (COR), Project Manager and Product Manager (PM), SGRD-ACQ, AMLO, and SGRD-RMA) are kept informed regarding issues relative to the use of humans.

f. Monitoring contracts, grants, and orders funded by USAMRDC by means of documentation review or site survey (pre- and post-award) as required.

g. Receiving reports of research related illnesses or injuries from principal investigators.

2. The SGRD-RMA shall be responsible for the following concerning the use of humans as research subjects or the use of human anatomical substances:

a. Negotiation, in conjunction with SGRD-HR, of special assurances of compliance with regulations with prospective contractors.

b. Development, in coordination with SGRD-HR, of special provisions to be included in RFPs and contracts.

c. When assigned contract administration, assuring compliance with contract terms.

d. Approval of use of prisoners as research subjects, after review and approval of the Command Judge Advocate and SGRD-HR.

3. The SGRD-ACQ shall be responsible for the following concerning the use of humans as research subjects:

a. Issuing required changes to this procedure.

b. Negotiation, in conjunction with SGRD-HR, of special assurances of compliance with regulations with other Government agencies.

c. Development, in coordination with SGRD-HR, of special provisions to be included in intragovernmental transfer of fund orders.

d. Approval of use of prisoners as research subjects, after review and approval of the Command Judge Advocate and SGRD-HR.

e. Administration of intragovernmental orders to assure compliance with the order.

4. The U.S. Army Medical Materiel Development Activity shall assist and participate with SGRD-HR, SGRD-RMA, and SGRD-ACQ on all matters pertaining to the use of humans as research subjects in programs under their cognizance.

5. The Office of the Command Judge Advocate shall advise SGRD-HR, SGRD-RMA, and SGRD-ACQ on all legal matters pertaining to the use of humans as research subjects or the use of anatomical substances.

6. The appointed COR through the AMLO or PM shall assist and participate with SGRD-RMA, SGRD-HR, and SGRD-ACQ in administration of contracts, grants, and intragovernmental orders.

V. Procedures:

1. Proposed contracts, RFPs, and proposals received under the BAA, and proposals from other Government agencies which are recommended for funding shall be reviewed by SGRD-HR prior to submission to SGRD-RMA for procurement or to SGRD-ACQ for intra-government transfer of funds.

a. Clarifications or changes to proposals received in response to the BAA or from other Government agencies is the responsibility of SGRD-HR. Copies of all correspondence will be provided the affected AMLO.

b. Clarification or changes in RFPs and contracts is the responsibility of SGRD-HR. All communications with the contractor will be through SGRD-RMA.

2. To permit timely award of the contract, the USAMRDC Form 9 and documentation may be submitted by SGRD-HR to SGRD-RMA or SGRD-ACQ, even though all issues relating to the use of human subjects have not been resolved, on the condition that the Prohibition of Use of Human Subjects provision will be included in the contract, grant, or order.

a. Comments on proposals submitted in response to specific RFPs shall be provided by SGRD-HR to SGRD-RMA prior to negotiation by SGRD-RMA with organizations in the competitive range. SGRD-HR shall provide SGRD-RMA recommendations for negotiation of provisions to be included in contracts to be awarded as the result of other than full and open competition, and provisions for changes or tasks after contract award.

b. Upon receipt of required information, SGRD-HR shall review and approve the appropriate provision in the contract, grant, or order.

c. SGRD-HR will review and approve task order protocols in accordance with the provisions of the contract.

d. Upon resolution of all issues involving the use of humans in research, the clause entitled "Use of Human Subjects, Investigational Drugs, and Investigational Medical Devices" (TAB B) will be included in the contract.

3. Compliance by subcontractors with 45 CFR 46 and these procedures is the responsibility of the prime contractor, subject to the following:

a. Subcontracts shall contain the prime contract clause Prohibition of Use of Human Subjects (Tab A) or Use of Human Subjects, Investigational Drugs, and Investigational Medical Devices (Tab B). The proposed subcontract and assurance of compliance with 45 CFR 46 satisfactory to the HHS, or sufficient information for negotiation with USAMRDC of a special assurance of compliance, shall be submitted to SGRD-RMA for review and approval by SGRD-HR prior to award of the subcontract, or use of humans as research subjects.

b. The SGRD-RMA will obtain comments and approval of SGRD-HR prior to SGRD-RMA approval of the subcontract or use of humans, or negotiation of a special assurance with the subcontractor.

c. The prime contractor shall be involved with and participate in all discussions and negotiation. Responsibility for compliance with 45 CFR 46 and this procedure shall be the responsibility of the prime contractor and subcontractor(s) utilizing humans as research subjects. Subcontractors shall have Institutional Review Boards and follow 45 CFR 46, except under unusual circumstances where SGRD-HR and SGRD-RMA (or SGRD-ACQ) approve the prime's assuming responsibility for the subcontractor in this regard.

4. The requirement for site visits, extent of examination of records, and discussions with researchers and research subjects

shall, except under unusual circumstances, be coordinated between SGRD-HR, the assigned administrative contracting office (ACO) (or SGRD-ACQ), AMLO, and the COR or PM. Copies of correspondence and telephone memoranda shall be exchanged between SGRD-HR, ACO (or SGRD-ACQ) and the COR and AMLO or PM to assure awareness of human use issues. If the ACO, in consultation with SGRD-HR, determines that the contractor is not in compliance with the requirements of the provisions in Tab B, the ACO may suspend work and further payment until corrections are made by the contractor.

5. All contracts, grants, and intragovernmental orders which involve the use of humans shall:

a. Contain the provision (Tab A) to prohibit the use of humans as research subjects, or

b. Contain the provision (Tab B) governing the use of human subjects, investigational drugs or vaccines, and investigational medical devices, and/or

c. Contain the provision (Tab C) governing the use of donated anatomical substances,

d. Be reviewed and approved by SGRD-JA prior to award,

e. Be reviewed and approved by SGRD-HR prior to award.

6. Due to the fact that DA policy requires the contractor to provide necessary medical care of research subjects, requests may be made by prospective contractors for assurance of future funding for certain liabilities, as set out in FAR 52.228-7(c)(2). Since the Government's liability is subject to the availability of funds at the time the contingency occurs, to cover such a contingency, an advance agreement (pursuant to FAR 31.109) may be negotiated to recognize costs, associated with such medical care, which exceed those covered by the contractor's insurance required by the contract. Such allowable costs, however, may not exceed the total amount of funds obligated by the Government to the contract. It is the responsibility of the contractor to initiate a specific request for funds to pay premiums for additional insurance coverage, or the costs of medical care required as a result of research performed under the contract. Approval of the Secretary of the Army to indemnify a contractor against unusually hazardous risks may be requested pursuant to DOD FARS 235.070. Such requests shall only be made after receipt of proof the risk cannot be compensated by insurance or otherwise.

7. a. It is the policy of the USAMRDC that whenever the use of volunteers exists in USAMRDC sponsored research, data sheets are to be completed on <u>all</u> volunteers for entry in the USAMRDC's Volunteer Registry data base. SGRD-HR may, on request, exempt this requirement for studies which the IRB has determined to be minimal risk. The intent of the data base is two fold: first, to readily

answer questions concerning an individual's participation in research conducted or sponsored by the USAMRDC; and second, to ensure that the USAMRDC can exercise its "duty to warn." The "duty to warn" is 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 volunteer has completed his or her participation in research. To accomplish this, a system must be established which will permit the identification of volunteers who have participated in research conducted or sponsored by the USAMRDC. The data base must contain items of personal information, for example, name, Social Security number, etc., which subjects it to the provision of the Privacy Act of 1974 (Reference 11.).

b. For each subject enrolled in a study a Volunteer Registry Data Sheet (USAMRDC Form 60-R), TAB E, is to be completed. The principal investigator is to complete Part A of Form 60-R; after which, Form 60-R is to be provided to volunteers for completion at the time of consent. The information collected is then sent to SGRD-HR upon completion of the research or upon expiration/ termination of the contract, whichever occurs first. Data sheets collected on volunteers participating in task orders are to be submitted to SGRD-HR upon completion of each task order. The information is stored in the USAMRDC Headquarters data base for a minimum of 75 years.

c. Information stored in the Volunteer Registry data base will be disclosed in accordance with Reference 10, and the privacy Act of 1974. Upon written or oral requests, persons on whom data is collected, or his or her designated agent or legal guardian may have access to the record pertaining to that individual contained in the Volunteer Registry data base. Only authorized staff of the HURRAO may have access to information entered in and information selected from the Volunteer Registry data base.

d. The record system name and notice number for the Volunteer Registry data base is Medical Research Volunteer Registry, AD 1304-22a DASG, as published in the Federal Register/VOL. 51, No. 125/Monday, June 30, 1986.

8. Research and development conducted outside the U.S. utilizing investigational drugs, vaccines, and devices is subject to the same safety reviews and regulatory procedures as research and development conducted within the U.S. Initial dose ranging, toxicity and safety studies (Phase I studies) will only be conducted within the U.S.

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Prohibition of Use of Human Subjects

Notwithstanding any other provisions contained in this contract or incorporated by reference herein, the contractor is expressly forbidden to use or subcontract for the use of human subjects in any manner whatsoever. In the performance of this contract, the contractor agrees not to come into contact with, use or employ, or subcontract for the use or employ of any human subjects for research, experimentation, tests or other treatment under the scope of work as set out in the contract without express written approval from the contracting officer.

Tab A

Use of Human Subjects, Investigational Drugs and Vaccines, and Investigational Medical Devices

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 risks of daily life, including the recognized risks inherent in a chosen occupation or field of service.

(2) **Investigational drugs and vaccines** means a drug or vaccine that 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 and vaccines 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 (21 CFR 312).

(3) **Investigational medical devices** means 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. Research is usually, but not necessarily, initiated to determine if the device is safe or effective (21 CFR 812).

b. None of these provisions applies to epidemiological surveys which involve no more than minimal risk.

c. 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 U.S. Army Medical Research and Development Command (USAMRDC) that no activity involving human subjects under this contract shall be undertaken unless an Institutional Review Board (IRB) has reviewed and approved such activity.

TAB B

(2) The institution shall have provided to USAMRDC a written assurance that it will abide by the policy for the protection of human subjects as contained in 45 CFR 46. When an institution has an assurance of compliance satisfactory to the Department of Health and Human Services (HHS), evidence of IRB approval of the study shall have been accomplished by submission to USAMRDC of an executed HHS Form 596. For an institution without a HHS approved assurance of compliance, an assurance concerning the protection of human subjects shall have been negotiated with the USAMRDC contracting officer, and IRB approval given.

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

(a) Informed consent must be obtained in advance from a subject at risk, or in the case of research intended to be beneficial to the subject, a legal representative of the subject may give informed consent in advance of the research.

(b) The contractor shall provide for all necessary medical care of subjects at risk for injury or disease which is the proximate result of participation in the research.

(c) Prisoners of war shall not be used under any circumstances.

(d) Use of prisoners as research subjects shall have been specifically approved by the USAMRDC contracting officer.

(e) Studies conducted outside the United States, its territories or possessions, which involve the use of non-U.S. citizens as subjects, in addition to compliance with 45 CFR 46 and special DOD requirements, shall comply with all laws, customs, and practices of the country in which the study is to be conducted. The minimum standards to be adhered to are contained in The Declaration of Helsinki. The research proposal submitted for approval will document this action. In exceptional circumstances where laws, customs or practices of the country involved take exception to particular procedural requirements of this provision (as, for example, the documentation of informed consent or the procedures by which it is obtained), specific approval will be obtained from the Commander, U.S. Army Medical Research and Development Command as an integral part of the proposal review and approval process.

(4) In accordance with 21 CFR 56.111(a)(3), IRBs are responsible for reviewing the methods used by investigators to recruit subjects. One method of recruiting subjects is through advertisements which should be seen as an extension of the informed consent. IRB review of advertisements is necessary to ensure that the information is not misleading to subjects. The FDA has established guidelines on advertisement for research subjects.

Generally, the FDA believes that any advertisement to recruit subjects should be limited to:

(a) The name and address of the principal investigator;

(b) The purpose of the research and, in summary form, the eligibility criteria that will be used to admit subjects into the study;

(c) A straightforward and truthful description of the benefits (e.g., payments or free treatment) to the subject from participation in the study;

(d) The location of the research and the person to contact for further information.

(5) In addition to the requirements noted above, a copy of the protocol and informed consent for each phase of a study will be forwarded to the Commander, U.S. Army Medical Research and Development Command, ATTN: SGRD-HR, Fort Detrick, Frederick, MD 21701-5012. If available, a copy of the local IRB review and approval should be provided. Research involving the use of human subjects may not commence until approved by the contracting officer.

d. Requirements for the Use of Investigational Drugs and Vaccines

The contractor shall comply with 21 CFR 312 for the study and evaluation of those new drugs restricted by the Federal Food, Drug, and Cosmetic Act. The drug shall be used by, or under the supervision of an investigator pursuant to an Investigational New Drug Application (IND). A copy of the current applicable forms as related under Part 312 shall have been provided with the contractor's proposal.

e. Requirements for the Use of Investigational Medical Devices

The contractor shall comply with 21 CFR 812 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. Should the contractor propose to use an investigational device in the research, he shall provide with his proposal a copy of Food and Drug Administration (FDA) approval of, or grant of waiver for, use of an investigational device exemption (IDE).

f. Requirements for Reporting and Documentation:

(1) Immediate telephone notification shall be given to the USAMRDC Human Use Review and Regulatory Affairs Office of any significant adverse reactions. (Telephone weekdays, Area

Code 301/663-2165; nights, weekends, and holidays, the Duty Officer Telephone Area Code 301/ 663-7114.)

(2) Copies of all documents presented or required for initial and continuing review by the IRB, e.g., Board minutes pertaining only to the contract, record of subject's consent, transmittals on actions, instructions, and conditions resulting from IRB deliberations addressed to the activity director, are to be retained by the contractor for at least three years after completion of the research. All documents shall be accessible for inspection during normal working hours, by the USAMRDC contracting officer or authorized representative.

(3) Information on volunteers used in research sponsored by USAMRDC will be entered in the USAMRDC Volunteer Registry data base. The data base is required to ensure that USAMRDC can readily exercise its "duty to warn" individuals of any newly acquired information which may affect their well-being, even after participation in the research. The SGRD-HR may, on request of the contractor, exempt the research from this requirement; such exemption may only be granted for studies which the local IRB has determined to be minimal risk. The Volunteer Registry Data Sheet USAMRDC Form 60-R (Tab E) is to be completed at the time the subject consents to participate and is entered into the study. The forms shall be submitted to the HURRAO upon completion of the research project or upon expiration/termination of the contract, whichever occurs first. The USAMRDC will retain information in the data base for 75 years. Persons on whom data is collected, or a designated representative or legal guardian, may have access to the record pertaining to that individual.

(4) 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 USAMRDC to carry out its legal responsibilities.

(5) Upon expiration or termination of this contract, a list of all unused test material shall be provided to the USAMRDC contracting officer.

(6) The contractor shall immediately notify the USAMRDC 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.

g. Subcontracts. Compliance by subcontractors with Code of Federal Regulations 45 CFR 46 and this contract provision is the responsibility of the prime contractor. All subcontracts which contain this contract provision shall be approved by the contracting officer prior to award. The requirements of paragraph c(2) above shall apply to subcontractors.

h. If at any time during performance of this contract, the contracting officer determines, in consultation with the USAMRDC Human Use Review and Regulatory Affairs Office, that the contractor is not in compliance with any of the requirements and/or standards stated in paragraphs c, d, and e above, the contracting officer may immediately suspend, in whole or in part, work and further payments under this contract until the contractor corrects such noncompliance. Notice of the suspension may be communicated by telephone and confirmed in writing. If the contractor fails to complete corrective action within the period of time designated in the contracting officer's written notice of suspension, the contracting officer may terminate this contract in whole or in part, and the contractor's name may be removed from the list of those contractors with approved policies on the use of human subjects.

Use of Anatomical Substances 25 JUN 1990

Any anatomical substance (organs, tissues, or tissue fluids) linked by identifiers to a particular person and used for research under this contract shall be donated for the purpose of research or investigation. The donor shall be the person from whom the substance is removed or, in the event of death or legal disability of the person from whom the substance is removed, the next of kin or legal representative of such person. Donation shall be made by written consent and shall relinquish all ownership and/or rights to the substance. All human anatomical substance used in research under this contract shall be lawfully acquired. It should be noted that a general autopsy consent form or a consent to perform surgery in and of themselves, may not be adequate. If excised or autopsy tissue is to be used, the protocol should include a copy of the consent form used to obtain the tissue.

Tab C

25 JUN 1990

THE DECLARATION OF HELSINKI

1. BASIC PRINCIPLES

a. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

b. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a specially appointed independent committee for consideration, comment, and guidance.

c. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.

d. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

e. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

f. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

g. Doctors should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Doctors should cease any investigation if the hazards are found to outweigh the potential benefits.

h. In publication of the results of his or her research, the doctor is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

Tab D

i. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The doctor should then obtain the subject's given informed consent, preferably in writing.

j. When obtaining informed consent for the research project, the doctor should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a doctor who is not engaged in the investigation and who is completely independent of this official relationship.

k. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.

l. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

2. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE (CLINICAL RESEARCH)

a. In the treatment of the sick person, the doctor must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health, or alleviating suffering.

b. The potential benefits, hazards and discomforts of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.

c. In any medical study, every patient--including those of a control group, if any--should be assured of the best proven diagnostic and therapeutic methods.

d. The refusal of the patient to participate in a study must never interfere with the doctor-patient relationship.

e. If the doctor considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee.

f. The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

3. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (NON-CLINICAL BIOMEDICAL RESEARCH)

a. In the purely scientific application of medical research carried out on a human being, it is the duty of the doctor to remain the protector of the life and health of that person on whom biomedical research is being carried out.

b. The subjects should be volunteers--either healthy persons or patients for whom the experimental design is not related to the patient's illness.

c. The investigator or the investigating team should discontinue the research if in his or her or their judgment it may, if continued, be harmful to the individual.

d. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

VOLUNTEER REGISTRY DATA SHEET

25 JUN 1990

THIS FORM IS AFFECTED BY THE PRIVACY ACT OF 1974

1. AUTHORITY: 5 USC 301; 10 USC 1071-1090; 44 USC 3101; EO 9397

2. Principal and Routine Purposes: To document participation in research conducted or sponsored by the U.S. Army Medical Research and Development Command. Personal information will be used for identification and location of participants.

3. Mandatory or Voluntary Disclosure: The furnishing of the SSN 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 participation in the research study.

PART A-INVESTIGATOR INFORMATION

(To Be Completed By Investigator)

PLEASE PRINT, USING INK OR BALLPOINT PEN

1. Study NR: _____ 2. Protocol Title:

3. Contractor (Laboratory/Institute Conducting Study):

4. Study Period: From: 01/___/___ To: 15/___/___
(DA/MO/YR) *(DA/MO/YR)*

5. Principal/Other Investigator(s) Names(s) 6. Location/Laboratory

(1) _____ _____/_____
(Last) *(First)* *(MI)*

(2) _____ _____/_____

(3) _____ _____/_____

PART B-VOLUNTEER INFORMATION

(To Be Completed By Volunteer)

PLEASE PRINT, USING INK OR BALLPOINT PEN

7. SSN:____/___/_____ 8. Name: _____
(Last) *(First)* *(MI)*

9. Sex: M__F__ 10. Date of Birth: ___/___/___ 11. *MOS/Job Series:___ 12. *Rank/Grade:____

13. Permanent Home Address (Home of Record) or Study Location Address:

_____
(Street) *(P.O. Box/Apartment No.)*

_____
(City) *(Country)* *(State)* *(Zip Code)*

( ) -
(Perm Home Phone No)

14. *Local Address (If Different From Permanent Address):

_____
(Street) *(P.O. Box/Apartment No.)*

_____
(City) *(Country)* *(State)* *(Zip Code)*

( ) -
(Local Phone No)

5.*Military Unit: _____ Zip Code: _____

Organization: _____ Post: _____ Duty Phone No. ( ) -

PART C-ADDITIONAL INFORMATION

(To Be Completed By Investigator)

PLEASE PRINT, USING INK OR BALLPOINT PEN

16. Location of Study:

17. Is Study Completed: Y___ N___

Did volunteer finish participation: Y___ N___ If YES, Date finished: ___/___/___ *(DA/MO/YR)*

If NO, Date withdrawn: ___/___/___ *(DA/MO/YR)* Reason withdrawn:

18. Did Any Serious or Unexpected Adverse Incident or Reaction Occur: Y___N___ If YES, Explain:

19.*Volunteer Followup: _____

Purpose: _____

Date: ___/___/___ *(DA/MO/YR)* Was contact made: Y___N___ If No action taken, explain:

20.*Hard Copy Records Retired: Place: _____ File NR: _____

21.*Product Information:

Product: _____

Manufacturer: _____

Lot NR: _____ Expiration Date: _____

NDA NR: _____ IND/IDE NR: _____

*Indicates that item may be left blank if information is unavailable or does not apply.
Entries must be made for all other items.

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