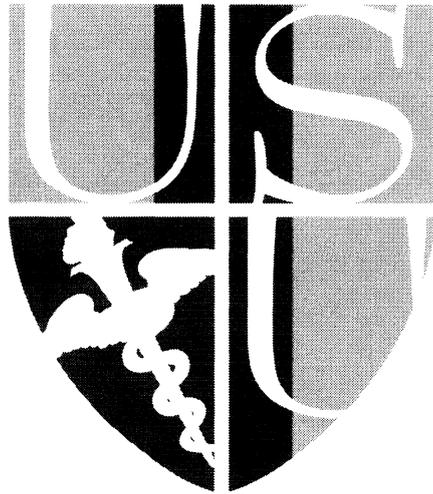


**USUHS  
INSTRUCTION  
3201**





# UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES



## SUBJECT: The Use of Human Volunteers in Research at the Uniformed Services University of the Health Sciences

Instruction 3201

MAR 25 1999

(REA)

### ABSTRACT

This Instruction prescribes Uniformed Services University of the Health Sciences (USUHS) policies and procedures for the use of human volunteers as research subjects.

**A. Purpose.** This Instruction reissues USUHS Instruction 3201<sup>a</sup> and prescribes USUHS policies and procedures for the use of human volunteers as research subjects.

**B. References.** See *Enclosure 1*.

**C. Applicability.**

This Instruction applies to the following as specified within:

1. Studies conducted at the USUHS (regardless of source of funding);
2. Studies conducted by the Henry M. Jackson Foundation for the Advancement of Military Medicine (HMJF) on behalf of the USUHS or USUHS billeted faculty;
3. Studies conducted at sites other than the USUHS by billeted faculty if they are:
  - a. funded through the USUHS,
  - b. conducted by or designate a USUHS billeted faculty member or student as Principal Investigator (PI), or
  - c. involved with the records or other materials of the USUHS; and

4. Studies conducted at sites other than the USUHS if they:

- a. use USUHS faculty, students, or employees to identify and/or contact volunteers, or
- b. advertise and/or solicit on the USUHS campus for recruitment of human volunteers, including protocols that are not otherwise associated with the USUHS.

**D. Definitions.** See *Enclosure 2*.

**E. Policy.**

1. Initiation of Studies
  - a. The USUHS Institutional Review Board (IRB) and, if applicable, the comparable committee of a Department of Defense Medical Treatment Facility (MTF), or other U.S. Government health care facilities, as well as the President or designee, USUHS, will approve all USUHS studies involving human subjects before their enrollment can begin. Investigators will submit their studies to the USUHS IRB if the study is located at

the USUHS and/or any clinical centers for which the USUHS has direct responsibility. If the study of a billeted investigator utilizes human subjects at an MTF, the proposal must first be submitted to the MTF Human Subjects Use (or functionally similar) Committee. Following MTF approval, the study must be submitted to the USUHS IRB for final approval. This subsequent review may simply take the form of an approval by concurrence by the IRB Chair. In this case, the Chair acts as a representative of the entire IRB. However, the Chair may decide that the study will be reviewed by the full IRB. The IRB can also request full IRB review when the expedited review and approval by concurrence is presented to the IRB at its meeting. No research involving human subjects may be conducted until the PI receives written confirmation of the USUHS IRB approval. After all applicable IRBs approve studies, the President or designee, USUHS, will review and approve or disapprove all proposed studies in accordance with 32 CFR, Chapter 1, Part 219<sup>e</sup>. Approval may consist of approving the final version of the IRB minutes.

(1) The President or designee, USUHS, may not approve human subject research if it has not been approved by the appropriate IRB.

(2) The President may delegate all or part of the review and approval authority.

(3) The President or designee, USUHS, may require additional review by the USUHS IRB when the initial review is at an MTF or other institution with which the USUHS is performing cooperative research.

b. Studies involving other institutions may be subject to additional requirements of the other institutions.

## 2. Department of Health and Human Services and Department of Defense Policies

The regulations adopted by the Department of Defense (DoD) and other Federal agencies for the protection of human subjects set forth in 45 CFR, Part 46<sup>b</sup>; 32 CFR, Chapter 1, Part 219<sup>e</sup>; 21 CFR<sup>d</sup>; USUHS Instruction 3200<sup>e</sup>; and DoD Directive 3216.2<sup>f</sup>, as they may be amended from time to time, are followed by the USUHS.

## 3. Consent Standards

a. Consent to participate in a USUHS study will be the consent of a competent person or that person's legally authorized representative and will meet the requirements set forth in 45 CFR, Part 46<sup>b</sup> and 21 CFR<sup>d</sup>. (See Appendix A for general informed consent document guidelines.)

b. The investigator will document the consent process by assuring that:

(1) The consent is obtained in writing on a consent form stamped with the USUHS IRB approval;

(2) The consent form is initialed on each page by the volunteer and a witness, and signed on the last page by the volunteer, the witness, and the principal investigator or, via a letter of request by the investigator, an IRB-approved designee;

(3) The fully initialed and signed informed consent document is filed and maintained in accordance with the provisions on Maintenance of Research Records; and

(4) Is initialed or signed by all parties in duplicate so that a copy of the consent document is provided to the volunteer.

c. Consent documents will not contain exculpatory language in which the volunteer waives, or appears to waive, any

of his or her legal rights, including any release of the USUHS from liability for negligence.

d. Per 45 CFR, Part 46<sup>b</sup> and 32 CFR, Chapter 1, Part 219<sup>c</sup>, a written consent may be waived under special circumstances.

#### 4. Contacting Volunteers

a. The investigator will contact volunteers in a way that will not embarrass or inconvenience them or otherwise intrude on their privacy.

b. If the study involves patients, the IRB will determine if it is necessary for the patient's physician or other health care provider to be consulted before the investigator contacts the patient.

#### 5. Study Criteria

According to 45 CFR, Part 46<sup>b</sup> and 32 CFR, Chapter 1, Part 219<sup>c</sup>, the IRB will examine proposed studies to determine whether they meet the criteria for Office for Protection from Research Risks (OPRR) and DoD approval of research. These criteria consist of the following:

a. Risks to subjects are minimized;  
b. Potential benefits to subjects will be maximized;

c. Risks to subjects are reasonable in relation to anticipated benefits;

d. Selection of subjects is equitable to include volunteer recruitment procedures;

e. Unless waived, informed consent is sought from each prospective subject or subject's legally authorized representative;

f. Informed consent is appropriately documented;

g. Where appropriate, the research plan makes adequate provision for monitoring data that are collected to ensure safety of subjects; and

h. Where appropriate, the research plan makes adequate provision for protecting the privacy of subjects and subjects' family, and maintaining confidentiality of the data.

#### 6. Double-Blind Studies/Use of Placebos/Deception

No experimental design will include the use of "double-blind" studies, placebos, deception or less than full disclosure unless this use is explained in the consent process or is given explicit IRB approval. If the study involves deception or less than full disclosure, a statement must be provided in the informed consent document that some of the information is being withheld because of the study design.

#### 7. Debriefing of Volunteers

Volunteers will normally be debriefed after a study involving less than full disclosure or deception. Debriefing will concentrate on the nature of the subjects' participation and the results obtained. Debriefing may be omitted if the procedure is risk free, or if the IRB finds it is not in the volunteers' best interest. Whether deception is necessary and acceptable and what safeguards, if any, are necessary will be determined by the IRB during the review process.

#### 8. Studies Using Hospitalized Patients

Studies involving hospitalized patients or studies requiring in-hospital testing or care of volunteers will be conducted at and approved by a DoD MTF or other United States government hospital on patients who are eligible for admission to these hospitals. When studies are proposed for non-government hospitals, approval may be granted if the IRB is satisfied that volunteers' rights are

adequately protected, and if the President or designee, USUHS, approves the use of the non-government hospital.

## 9. Employees and Students as Volunteers

### a. Employees

(1) When civilian employees of the DoD volunteer to participate, the following provisions will apply:

(a) Any duty as a volunteer performed during the employee's regularly scheduled duty will be considered constructive duty for which straight time rates apply. Employees must have the approval of their immediate supervisor to participate during duty time;

(b) Participation outside an employee's regularly scheduled duty or during leave is not considered duty time. If compensated, the employee must take leave or participate in the study at a normally scheduled break. Off duty employment qualifications must be followed.

(c) The employee will be informed of the above.

(2) Solicitation and selection of employees or students will not suggest coercion or preferential treatment.

(3) Generally, investigators should not use employees under their supervision as research subjects. However, if an employee wishes to participate in his or her supervisor's study, the employee may seek the approval of the IRB Chair or IRB Executive Secretary. A special form is available from the Office of Research that must be completed by the employee before his/her participation in the study.

### b. Students

(1) Upon request by the principal investigator, the USUHS IRB will specifically review the issue of

acceptability of participation of uniformed students as research subjects. This request may be considered at the same time that the protocol is first reviewed by the IRB. For protocols previously approved for conduct at the USUHS, an affiliate MTF, or at another site, the USUHS IRB will consider the request for uniformed student participation per guidelines below. The USUHS IRB will provide a recommendation to the appropriate Dean and Commandant as to the acceptability for USUHS uniformed students to serve as research subjects.

(2) Approval of student participation: Uniformed students are not permitted to participate as human subjects in any form of research being conducted at USUHS or at any other institution unless all of the following approvals are obtained:

(a) Concurrence with the USUHS IRB recommendation by the Dean, School of Medicine (DEN) or the Dean, Graduate School of Nursing (DSN), as appropriate;

(b) Concurrence with the USUHS IRB recommendation by the Commandant, SOM or the Commandant, GSN, as appropriate;

(c) Approval of the USUHS IRB recommendation by the President or designee, USUHS, who serves as approval authority for USUHS on all matters regarding the protection of human subjects.

Approval for uniformed student participation will be based upon a number of factors including evaluation of benefits versus risks, requirements of time and effort for participation, and conflicts of interest with the goals and objectives of students. Those offices from which concurrence approval is required may seek the advice of the USUHS General Counsel

and appropriate subject matter experts, as required, prior to rendering a decision.

(3) Recruitment of uniformed students as research subjects. No principal investigator, regardless of his/her service affiliation, is permitted to use academic (teaching classroom) settings or mandatory military assemblies or formations to inform or recruit students for a human subject use protocol. If recruitment is conducted in an assembly apart from those that are academic or military, for the purpose of obtaining uniformed students as volunteers, then the recruitment must be in accordance with DoD Directive 3216.2<sup>f</sup>. This directive is intended to reduce the possibility of coercion through the normal command and control hierarchical structure of the military. This directive is incorporated into the following provisions for this Instruction.

(a) Recruitment will be divided into two separate and distinct phases:

1 An informational briefing in which the purpose, methods, risks, benefits, issues of confidentiality, time commitment, and other pertinent issues regarding the specific research project and human subject volunteers are discussed; and

2 An enrollment session in which human subjects volunteer to participate by reading and signing an informed consent document.

(b) Unit officers and senior noncommissioned officers (NCOs) in the chain-of-command shall not be present during research subject enrollment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. Officers

and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate enrollment session.

(c) Civilian or military faculty who may exercise authority over or influence grades, class standing, or future assignments of students may not be present during enrollment sessions for students.

(d) At all recruitment sessions, including informational briefings and enrollment, an ombudsman not connected in any way with the proposed research shall be present to monitor that the voluntary nature of participation is adequately stressed and that the information provided about the research is adequate and accurate.

(e) At all recruitment sessions, the Commandant or his/her representative will reiterate the requirement and the rationale for removing even the perception of influence by the chain-of-command and for the policy that faculty absent themselves during enrollment to re-enforce the principle of non-coercion.

(f) Following any informational briefing, there must be time allowed for questions to occur from potential participants when officers and NCOs in the chain-of-command and faculty are not present. If the principal investigator is within the chain-of-command and/or a faculty member, then that officer or faculty member may stay to answer general questions, but then must exit the meeting to allow students to ask specific questions that they might consider sensitive or subject to coercion. In these cases, the principal investigator may wait outside the room to serve as a resource and allow another person associated with the protocol to remain in the room specifically to answer these types of questions.

(g) Sufficient time must be given between the informational briefing and enrollment session to allow students to thoughtfully consider their participation.

(4) The above procedures would permit students to sign up for a study in which one of their professors is the principal investigator. A concern this possibility raises is that students could be influenced by this awareness. The USUHS IRB should evaluate this concern carefully if it is germane to a protocol that it is reviewing.

#### 10. Advertisements, Commercials, Flyers, etc. for On-Campus Subject Recruitment

Before recruitment of human subjects sponsored by any IRB is permitted on campus, whether these subjects are military students, nonmilitary students or staff, the USUHS IRB must review and approve all human subject use studies and all advertisements seeking volunteers. Advertisements without a USUHS IRB stamp of approval will be removed from USUHS property.

#### 11. Active Duty, Non-Student, Military Volunteers

Active duty military personnel may participate as human subjects, but generally may not be compensated for participation while in active status. However, per Title 24, USCA, Chapter 30<sup>e</sup>, at present, active duty personnel may be compensated up to \$50 for each blood withdrawal done for scientific or research purposes. If no more than minimal time away from work is required (one hour or less), no additional approval is necessary. Compensation of

active duty military personnel for participation in studies other than blood draws (as indicated above) must receive approval through the appropriate military chain-of-command. In the case of USUHS military personnel, approval must be obtained from the Brigade Commander and the Office of General Counsel.

#### 12. Retired Military and Dependents as Volunteers

Retired military personnel, dependents, and others entitled to medical care in military facilities may participate as human subjects. Per 45 Comptroller General Opinions 649<sup>h</sup>, these persons may be compensated as authorized by applicable directive, except that retired officers of a regular component are subject to the 30-day limitation of 5 USC, Section 5532(c)(2)<sup>i</sup>.

#### 13. Use of Private Citizens as Volunteers

It is the policy of the United States not to accept voluntary services from private citizens when the services may provide a basis for a future claim against the government for their value. Accordingly, a statement that the individual will not be entitled to any compensation for these services will accompany such services. However, per 45 comptroller General Opinions 649<sup>h</sup>, private citizens may enter into an independent contractor relationship and participate for compensation as authorized by applicable directives. A third party payer may be responsible for extra costs incurred by the volunteer during his or her participation in the study.

14. Waiver of Provisions of the Instruction

a. Certain circumstances may require exceptions to provisions of this Instruction. In these cases, the investigator must provide justification for waiver.

b. The IRB will follow the procedures set forth in 45 CFR, Part 46<sup>b</sup> when it waives the requirement for informed consent, or approves a procedure which does not include or alters some or all of the elements of informed consent, and when it waives the requirement for a signed consent form.

15. Patient Care

All research involving physical intervention/manipulation of human subjects will generally be conducted in an approved Medical Treatment Facility (MTF). The committee, or the Chair acting on behalf of the IRB, may determine that the physical intervention is such that it may be conducted outside an MTF. Physical intervention/manipulation includes for example: drawing blood, treadmill testing, and giving injections. It does not include administering pen and pencil tests or conducting class exercises.

16. Medical Monitor Policy

DoD Directive on Medical Monitors for Human Subject Use Research

For any research involving human subjects, an independent medical monitor shall be appointed by name if the IRB determines that the research risk is more than minimal. Medical monitors shall be physicians capable of overseeing the progress of research protocols, especially issues of individual patient management and safety.<sup>1</sup> Medical monitors shall be independent of the investigative team and shall possess sufficient educational and

professional experience to serve as the patient/subject advocate. Medical monitors shall discuss research progress with the principal investigators, shall interview and consult on individual cases and shall report discrepancies or problems to the IRB. They shall have the authority to suspend a research study in progress, remove individual subjects from a study, and take whatever steps are necessary to protect the safety and well being of research subjects.

17. Genetic Research Policy

a. Considerations of genetic research extend to all research protocols involving the analysis of human DNA and chromosomes when the intent of the research with biochemical analysis of proteins and metabolites is to collect and evaluate information about heritable traits, conditions, diseases, and/or characteristics within a family.

b. When genetic research poses risk of psychosocial harm to subjects and/or their families, the IRB will provide a higher level of scrutiny to these research protocols. The IRB will carefully evaluate whether the proposed study affords sufficient protections to the rights and welfare of the subjects.

c. When non-genetic research poses the same or similar levels and types of risk as genetic research, the IRB may apply the same principles and analysis described below in paragraph D.19.

18. Use of Human Tissue and/or Specimens in Research

a. Biological specimens (e.g. tissue, blood, urine) from human subjects may be collected either retrospectively or prospectively.

(1) Retrospective collection refers to existing specimens (i.e. tissue, blood, urine, etc.) which have been collected, are "on the shelf," and have previously been stored at the time that the protocol is submitted for review to the IRB.

(a) The specimens were collected for research but for a different project to that which is being proposed.

(b) The specimens were obtained for clinical assessment for routine examination, for diagnosis, during the course of treatment, or at autopsy.

(2) Prospective collection consists of specimens which have not yet been collected at the time the protocol is submitted for review to the IRB.

(a) The procedures to be performed are specifically for research purposes (e.g., additional blood at time of clinical venipuncture, additional biopsy material collected, normal control blood drawing).

(b) The specimens are to be obtained from future discarded samples obtained in the routine course examination, diagnosis and/or treatment (e.g., tumor tissue from newly diagnosed patients, left over urine/blood after clinical tests, etc.).

b. When specimens are collected retrospectively the following rules apply:

(1) Generally, specimens that are anonymous and cannot be linked to the subject in any way are considered exempt or may be given expedited review. In special cases where the research poses foreseeable risks to certain classes of subjects, full review by the IRB may be required;

(2) Specimens linked to identifiers to which the investigator has open access will be given full IRB review or will be reviewed by expedited procedures if criteria for expedited review

are met. Consent or, in the case of tissue previously collected for research purposes, re-consent is required if the project poses significant risk as stipulated by the IRB;

(3) Protocols utilizing specimens that have been collected retrospectively, but identifiers are known only to a third party or intermediate entity and are unknown to the investigator, may be given expedited review provided that:

(a) the specimen procurement and storage procedures are acceptable,

(b) the original consent document is consistent with the proposed research, and

(c) the IRB is satisfied that sufficient safeguards are in place to establish a sound "firewall" between the subject and the investigator;

(4) In protocols utilizing specimens that are identifiable either directly or through the use of codes, consent/re-consent may be waived by the IRB if the study meets all of the following requirements:

(a) the research presents no more than minimal risk,

(b) conducting the research without a waiver is impractical,

(c) the waiver will not adversely affect the subjects' rights or welfare,

(d) the subject has waived re-consent in the original consent document, and

(e) pertinent information will be provided to volunteers if deemed appropriate by the IRB.

c. In studies that use specimens that are collected prospectively and obtained expressly and specifically for research purposes, the protocol will be reviewed by full committee or by expedited procedures if criteria are met for expedited review.

Consent is required for specimens collected prospectively for research whether they are:

- (1) identifiable directly or through the use of coded identifiers known to the investigator; or
- (2) linked by identifiers unknown to the investigator; or
- (3) linked by identifiers known only to a third party or intermediate entity and unknown by the investigator such that a sound "fire wall" exists between the coded information and the investigator.

d. The following pertains to specimens that are collected prospectively for clinical assessment during routine examination, for diagnosis, or during the course of treatment, and that become future discarded clinical samples:

(1) Generally, specimens that are anonymous and cannot be linked to the subject in any way are considered exempt or may be given expedited review. In special cases where the research poses risks to certain classes of subjects, full review by the IRB may be required.

(2) Protocols utilizing specimens that are tied to identifiers known to the investigator will be given full review or reviewed by expedited procedures if criteria for expedited review are met. Generally, informed consent is necessary.

(3) Protocols utilizing specimens that are tied to identifiers known only to a third party or intermediate entity will be given full review but need for consent process may be waived by the IRB. If the principal investigator later needs additional information from the chart, the IRB will again review the proposed process to be used to ensure patient privacy.

e. Generally, recontact of a subject is prohibited whether the purpose for the recontact is for recontact for future

research or because of research results unless:

- (1) The subject has consented to recontact and/or recontact; or
- (2) An unexpected epidemiological finding of importance is identified after the specimen was collected; or
- (3) The original diagnosis is found to be incorrect and the results suggest that a different course of treatment is appropriate.

f. For secondary use of specimens, if subsequent investigators may be given access to the samples with direct or indirect identifiers, the consent document should state this and should give the subject the option of consenting to future use in other future research. The consent process should inform subjects that they may be recontacted or give subjects the option of not being recontacted. The consent should also give the subject the option of limiting or specifying the future use of the sample.

g. In addition to the policy, rules and guidelines concerning informed consent contained elsewhere in the body of this Instruction or in the Appendix, consent documents for genetic research will inform subjects of:

(1) the possible commercial value arising out of the research, and if applicable, whether the subject will retain any proprietary interest in the sample and/or whether the subject will receive any share in profits from commercial development;

(2) the information the subject is entitled to receive, if any. If there is to be no or limited disclosure, the consent should explain the reasons. If some or all findings are to be disclosed, the consent should set forth disclosure procedures.

h. As to matters concerning genetic research, if any of the provisions contained above, that is, in paragraph D.16, are in conflict with other provisions contained in this Instruction, the provisions of paragraph D.16 will be deemed controlling.

## **F. Institutional Review Board (IRB).**

### **1. Composition and Organization**

The constitution of the IRB will conform to the requirements of this Instruction, 45 CFR, Part 46<sup>b</sup>; 32 CFR, Chapter 1, Part 219<sup>c</sup>; 21 CFR<sup>d</sup>; and DoD Directive 3216.2<sup>f</sup>.

a. The IRB will have a minimum of nine members and may have alternates.

b. The IRB will be composed of persons with varying backgrounds to assure a complete review of proposed studies involving human volunteers.

(1) The IRB will be qualified through the maturity, experience, expertise, and diversity of racial and cultural background of its members and sensitivity to such issues as community attitudes to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

(2) Consideration will be given to include diversity of gender, ethnic or racial group, and profession.

(3) In addition to possessing professional competence, the IRB must be able to evaluate proposals in terms of organizational commitments and regulations, applicable law, and standards of professional conduct and practice. Therefore, the IRB will include persons knowledgeable in these areas.

c. The IRB will include at least one non-DoD member who is not otherwise affiliated with USUHS, or part of the immediate family of a person affiliated with USUHS.

d. The IRB may have up to 20% of its members, but at least one member whose primary concern is non-scientific, for example, a lawyer, ethicist, member of the clergy, or member of the community.

e. An IRB member will not participate in initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

f. The IRB may invite individuals with competence in special areas to assist the IRB or its subcommittees. These individuals may not vote with the IRB.

g. The IRB may have individuals who serve in more than one capacity, thus a lawyer may serve as a non-scientific member as well as an unaffiliated member.

### **2. Appointments**

#### **a. Method of Appointment**

The President of USUHS or designee, USUHS, will appoint members with the concurrence of the Commander or appropriate institutional official for nominated members from organizations outside the USUHS.

#### **b. Alternates**

(1) The President of USUHS or designee, USUHS, may appoint an alternate for any or all members of the IRB.

(2) Alternates serve in the absence of the IRB member.

(3) The alternate will have qualifications similar to the respective IRB member for whom he or she will serve.

(4) An alternate will vote only on proposals he or she has personally reviewed.

#### **c. Attendance**

(1) All IRB members shall give reasonable notice to the Executive Secretary of an anticipated absence.

(2) If an absence cannot reasonably be anticipated, such as illness or family emergency, the IRB member shall give notice as quickly as possible.

(3) The failure to attend three or more meetings without reasonable notice as described in E.2.c.(1) and (2) above, may be considered cause for removal.

d. The President or designee, USUHS, will designate a member of the IRB as Chair. A Vice-Chair will also be appointed to serve in the Chair's absence. If neither Chair nor Vice-Chair is available, the Executive Secretary may chair the meeting.

e. Term

(1) The Chair shall serve no less than three years. The President or designee, USUHS, may extend his or her term.

(2) IRB members shall serve for a period of three years and may be re-appointed.

f. Removal

The President or designee, USUHS, may remove the Chair, Vice Chair or an IRB member for cause for the following reasons:

(1) misconduct;

(2) negligence or dereliction of his or her duties;

(3) chronic absenteeism as defined in E.2.c, above; or

(4) disclosure of confidential material or information.

g. Vacancies on the IRB

The President or designee, USUHS, may appoint a replacement for any member of the IRB.

h. Training or Continuing Education

USUHS will provide appropriate training for new and returning IRB members and officers in the form of local

and national meetings, seminars and conferences, as institutional funding allows.

3. Voting

a. Quorum

(1) At each meeting, the IRB will consist of:

(a) a majority of the members including the Chair or Vice Chair, or his/her representative;

(b) one member whose background and primary concern is non-scientific;

(c) members sufficiently diverse to have sufficient knowledge to review proposals from diverse research fields, (e.g. requiring that there be at least one physician when reviewing studies of FDA regulated articles);

(d) appropriate representation to properly review proposals, as determined by the Chair and/or Executive Secretary.

(e) when reviewing studies of FDA regulated test articles the presence of a physician will be required.

(2) Voting will be in accordance with paragraph F.8;

(3) IRB members must be present to vote; and, when reviewing studies of FDA regulated test articles:

(a) proxy vote is not permitted.

(b) telephone or other electronic voting is not permitted unless members participate in the discussion via speakerphone or videoteleconferencing.

(4) Members will vote only on proposals that they have personally reviewed.

b. Consultants to the IRB. The IRB may consult any concerned person or group within or outside USUHS. These individuals may not vote with the IRB.

#### 4. Reports of Noncompliance to the President

The IRB will report to the President or designee, USUHS, any serious or continuing noncompliance by investigators with the requirements and determinations of the IRB.

#### 5. Duties of the Chair, IRB

The Chair will:

- a. convene meetings;
- b. request that the investigator be present to answer questions during the meeting, if this is determined to be necessary;
- c. perform expedited review of studies involving no more than minimal risk, per the categories for expedited review contained in the Expedited Review Procedure appendix in 45 CFR, Part 45<sup>b</sup>, or for protocol changes that are considered to reduce, or have no effect, on risk to the subjects in approved research and:
  - (1) delegate, at his or her discretion, part or all of such expedited review to experienced IRB members;
  - (2) exercise all of the IRB's authority during expedited review except that of disapproval of a study, which may only be done by the full IRB;
- d. hold in abeyance an ongoing study until full committee review can concur in cases where harm to human subjects, noncompliance with Federal regulations and/or this policy, or misconduct is suspected; and
- e. if applicable, perform concurrent review on USUHS studies that have received prior approval by an IRB at another institution, e.g., MTF, NIH.

#### 6. Duties of the Executive Secretary

The Director, Research Programs, will function as the Executive Secretary of the IRB and will:

- a. perform initial review of all protocols involving human subjects research and determine the level of IRB review with concurrence of the IRB chair;
- b. prepare the agenda and distribute supporting written material;
- c. forward a copy of each proposal to receive full review to each member of the IRB at least 5 working days prior to the meeting, or where appropriate, forward proposals to the Chair or designated member for expedited or concurrence reviews;
- d. request that the investigator be present to answer questions during the meeting if this is determined necessary.
- e. prepare minutes of the meeting showing:
  - (1) actions taken by the IRB
  - (2) the number voting for/against or abstaining on each action
  - (3) the basis for requiring changes in or disapproving research
  - (4) a written summary of the discussion of controversial issues and their resolution;
- f. record IRB member attendance;
- g. report all research proposals given expedited review to the IRB;
- h. report to the IRB any inquiries or expedited protocol changes concerning research that is being conducted;
- i. notify investigators in writing of IRB recommendations that apply to them, including all specific actions that must be completed prior to approval (e.g., project assurances requirements, written approvals from all IRBs involved, approved informed consent form, written approval of all modifications);

j. notify investigators prior to the time that an annual human use review is required;

k. furnish Federal regulations, copies of references, journal articles, and other relevant material to the IRB;

l. meet periodically with the IRB Chair or the IRB itself to discuss possible changes in IRB procedures and prepare such revisions for approval of the President or designee, USUHS;

m. make available to the President or designee, USUHS, proposals which have been approved by the IRB;

n. for five years after completion of the research maintain records of:

(1) continuing review activities

(2) all correspondence between

the IRB and the investigators

(3) a list of IRB members as required by 45 CFR, Part 46<sup>b</sup>

(4) statements of significant new findings provided to subjects as required by 45 CFR, Part 46<sup>b</sup>.

#### 7. Duties of the IRB Members

The IRB members will:

a. comprehend the relevant regulations, instructions, and directives dealing with human subject research;

b. examine the proposals with respect to human subjects issues, be prepared to point out the deficiencies in the proposals, and suggest possible modifications to correct them;

c. weigh the potential benefits of the study involved against the risk undertaken by the subject;

d. obtain clarification from the investigator or consult appropriate literature or experts if a proposal is unclear or raises questions;

e. evaluate the research design employed in the study to assure scientific

validity so that the risk to subjects is justified and minimized;

f. vote for approval, disapproval, deferral, or modification of proposals, or call for full reviews of proposals slated for expedited review;

g. make site visits and perform continuing/annual reviews when requested by the Chair and/or the Executive Secretary;

h. meet in subcommittees to devise policy and procedures, on particular issues (e.g. student inclusion as research subjects, genetic testing, etc.); and

i. determine whether studies of medical drugs, devices, or biologics pose significant or non-significant subject/patient risks.

#### 8. Conduct of IRB Deliberations

a. New, competing, and non-competing continuation intramural proposals are reviewed by the IRB only after they have been reviewed and recommended for funding by the USUHS Merit Review Committee and the Office of Research.

b. Extramural projects are reviewed upon notification by Director, Grants Administration.

c. All decisions of the IRB will be made with a quorum present and with at least one member whose primary concern is non-scientific, as defined in Section D.3.a, consistent with 45 CFR, Part 46<sup>b</sup>. Decisions will be based upon the majority of those members at the meeting.

d. Each member must review the proposal to participate in IRB decisions except for reviews where the expedited or concurrence review procedure applies.

e. If any additional information is needed, the investigator may be called into the room or contacted by telephone. The

investigator may only be present to give information and will be excused before the IRB resumes its deliberations.

f. The IRB will make one of several determinations:

(1) Approval:

(a) approved, as submitted;

(b) conditionally approved,

contingent upon specific modifications being made.

(2) Deferral:

(a) cannot be approved without additional information (the IRB will specify the information needed and who will be responsible for gathering it). Providing the additional information does not guarantee approval;

(b) cannot be approved at this time because major modifications are needed.

(3) Disapproval:

(a) The IRB through the Executive Secretary will provide written notice to the investigator.

(b) If the IRB disapproves or defers the research study, the notice will include reasons for the decision.

(c) The investigator may respond in person or in writing to a notice of deferral or disapproval.

#### 9. Suspension or Termination

a. The IRB has the authority to hold in abeyance, suspend, or terminate approval of research that is not being conducted in accordance with the requirements or that has been associated with unexpected harm to subjects.

b. If the IRB suspends or terminates approval, it will notify the investigator, the President or designee, USUHS, and the Secretary DHHS or DoD and state the reasons for its actions, as appropriate.

c. The Chair has the authority to hold in abeyance the accrual of subjects in an approved research study that is not being conducted in accordance with regulatory requirements or that has been associated with unexpected harm to subjects until the issue(s) can be considered by the IRB at its next meeting.

#### 10. Studies Requiring IRB Review

The IRB will review all research involving humans conducted by the USUHS or by the HMJFAMM at USUHS or by USUHS billeted faculty whether it is conducted or funded in whole or in part by USUHS except as provided in 45 CFR, Part 46<sup>b</sup>; 21 CFR<sup>d</sup>; and USUHS Instruction 3200<sup>e</sup>.

#### 11. Studies Not Requiring IRB Review

Those studies not requiring IRB review are listed in 45 CFR, Part 46<sup>b</sup> (Sec. 46.101(b)) and consist of the following:

a. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

(1) Research on regular and special education instructional strategies, or

(2) Research on the effectiveness of, or the comparison among, instructional techniques, curricula, or classroom management methods.

b. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), if information taken from these sources is recorded in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

c. Research involving survey or interview procedures, except where the following conditions exist:

(1) Responses are recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects;

(2) The subject's responses, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing or employability; or

(3) The research deals with sensitive aspects of the subject's own behavior, such as illegal conduct, drug use, sexual behavior, or use of alcohol. All research involving survey or interview procedures is exempt, without exception, when the respondents are elected or appointed public officials or candidates for public office.

d. Research involving the observation (including observation by participants) of public behavior, except where all of the following conditions exist:

(1) Observations are recorded in such a manner that the human subjects can be identified, directly or through identifiers linked to the subjects, (ii) the observations recorded about the individual, if they became known outside the research, could reasonably place the subject at risk of criminal or civil liability or be damaging to the subject's financial standing or employability, or

(2) The research deals with sensitive aspects of the subject's own 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, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a

manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

12. Studies Which may be Reviewed through Expedited Review Procedures

a. The studies involving minimal risk that may be given expedited review are listed in Expedited Review Procedures appendix in 45 CFR, Part 46<sup>b</sup>, unless such samples are to be used for DNA analysis or testing.

b. These regulations consist of the following:

(1) Clinical studies of drugs and medical devices only when conditions (a) or (b) are met:

(a) Research on drugs or devices for which an investigational device exemption is not required.

(b) Research on medical devices for which (i) an investigational device exemption application is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

(a) From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amount drawn may not exceed 550 ml in an 8 week period and no more than 2 times per week, or

(b) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amounts drawn may not exceed the lesser

of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

(3) Prospective collection of biological specimens for research purposes by noninvasive means:

(a) Hair and nail clippings in a non-disfiguring manner.

(b) Deciduous teeth at the time of exfoliation, or if routine patient care indicates a need for extraction.

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

(d) Excreta and external secretions (including sweat).

(e) Uncannulated saliva collected either in an unstimulated fashion or simulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue.

(f) Placenta removed at delivery.

(g) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor.

(h) Supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.

(i) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.

(j) Sputum collected after saline mist nebulization.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. When medical devices are employed, they must be cleared/approved for marketing.

Examples include:

(a) physical sensors that are applied either to the surface of the body, or at a distance, and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;

(b) weighing or testing sensory acuity;

(c) magnetic resonance imaging;

(d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;

(e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

(6) Collection of data from voice, video, or image recordings made for research purposes.

(7) Research on individual or group characteristics or behavior (including but not limited to research involving perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

(8) Continuing review of research previously approved by the convened IRB as follows:

(a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or

(b) where the research remains active only for the purposes of data analysis; or

(c) where no subjects have been enrolled and no additional risks have been identified.

(9) Continuing review of research, not conducted under an investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

13. Funds appropriated to the DoD may not be used for research involving a human being as an experimental subject unless:

a. The informed consent of the subject is obtained in advance; or,

b. Per 10, USC, Chapter 980<sup>j</sup>, in the case of research intended to be beneficial to the subject, the informed consent of the legal representative of the subject is obtained in advance.

c. Generally, there is no exception for emergency use providing retrospective approval applicable to USUHS. Absent pre-approval by the USUHS Office of General Counsel, these studies will not be considered by the IRB. (21 CFR, Part 50, Section 23<sup>k</sup> is not applicable.)

#### 14. Scope of IRB Review

a. The IRB will review and approve, require modifications in, or

disapprove all USUHS human research activities covered by this Instruction.

b. The IRB will require that information given to volunteers as part of informed consent is in accordance with 45 CFR, Part 46<sup>b</sup>; 32 CFR, Chapter 1, Part 219<sup>c</sup>; and 21 CFR<sup>d</sup>. The IRB may require that the volunteer receive additional information if the IRB determines it would add meaningfully to the information provided to the volunteer.

c. The IRB will require documentation of informed consent or may waive documentation in accordance with 45 CFR, Part 46<sup>b</sup>.

d. The IRB will provide investigators with notice of its decisions.

#### 15. Submission of the Proposal

a. Investigators will complete proposals and consent forms in accordance with this Instruction. The documents become part of the permanent records of the IRB and may be inspected and reviewed by various government agencies. The IRB does not act on incomplete proposals; these will be returned to the investigator for completion.

b. The completed proposal showing the required review and approval will be submitted to the Executive Secretary of the IRB, who will process the proposal for IRB review and determine the type of review required (i.e. full, expedited, or exempt) with concurrence of the Chair.

c. The completed proposal should contain documents as described herein under Sections F and G.

#### 16. Review Timetable

The IRB meets at the call of the Chair or Executive Secretary. Proposals generally are reviewed within 45 days of submission. Proposals submitted for

expedited review or approval by concurrence generally are reviewed within 30 days of submission.

17. Questioning the Investigator on the Submitted Proposal

a. The Chair or Executive Secretary of the IRB may request that the investigator attend part of the IRB meeting to provide information and answer questions.

b. The investigator will be excused before the IRB resumes deliberations concerning the proposal.

c. Even if not requested to attend, the investigator should try to be available when his/her proposal is on the IRB agenda in case the IRB raises questions.

18. Period of Approval

a. IRB approval for human use is granted for a specific period of time, not to exceed one year.

b. The IRB may decide that more frequent review is necessary and recommend approval for a shorter period.

19. Changes in the Proposal after USUHS Approval

a. IRB approval is only for the described study. If the investigator modifies the study, he or she must have the modification approved by the IRB before involving volunteers.

b. If any part of the investigation is to be conducted at another institution, its appropriate approving authority also must approve the proposal. Any and all changes in the protocol or consent form required by the facility off site must be submitted to the USUHS IRB for review prior to accrual of research subjects.

c. Unexpected situations may require the investigator to modify the

consent form or modify or suspend the study.

(1) If the investigator encounters unanticipated injuries or inconveniences to subjects, he/she will immediately notify the IRB.

(2) The IRB, or designee, may observe the consent process and research in progress, and will have unlimited access to research records.

**G. Proposal Format.**

1. All proposals will be completed in accordance with USUHS Instruction 3200<sup>e</sup>. Information provided about human use will meet the minimum requirements provided in Public Health Service (PHS) grant application requirements (PHS Form 398).

2. If an interview or questionnaire is used in the study, a copy will be appended to the proposal.

3. The proposed consent form(s) will be attached. A description of how and by whom the informed consent is obtained will be included.

4. Other information. The following items will be set forth in this section:

a. If other review boards have reviewed the study, the current status of their determinations, (e.g., pending, approved, or disapproved) will be provided to the IRB in writing by the investigator or by the review board(s). The investigator will explain any disapproval.

b. Proposals should contain detailed explanations of subject exclusion and inclusion criteria.

c. It is expected that women and minorities will be included per NIH or DoD guidelines unless there is adequate justification for exclusion.

d. When a study seeks the participation of a vulnerable population, such as children, prisoners, mentally impaired or economically disadvantaged, the protocol should contain justification for their use and state specific protections that will be used.

e. When a field study will be done within a particular racial, religious, or geographic community, the investigator will explain the nature and extent of any preliminary contacts with community representatives to determine acceptance of the study by the community. If the study will be done within a school, business, or other institution that does not have a review board, the investigator will outline any preliminary contacts with appropriate officials. This will be documented by correspondence with the community representatives or officials.

f. When a new drug, an old drug or device will be used for a new (nonapproved) purpose, the investigator will document the filing of appropriate forms and information with the Food and Drug Administration (FDA), or that the FDA has waived jurisdiction for the specific study.

#### **H. Informed Consent Document.**

A written consent form is required and will include the basic elements of consent as specified in 45 CFR, Part 46<sup>b</sup>, Sec. 46.116. (See also Appendix A for consent guidelines and a model consent form).

#### **I. Records and Reports.**

##### **1. Annual Progress Reports**

Annual continuation proposals for each approved project will be submitted to the Director, Research Programs, in accordance with USUHS Instruction 3200<sup>e</sup>.

##### **2. Final Reports**

A final human use report following completion or termination of the research project will be submitted to the IRB for each approved protocol.

##### **3. Additional Reports Required for Investigational New Drugs**

The IRB requires that investigators using applicable investigational new drugs comply with all FDA requirements.

##### **4. Reports to Pharmaceutical Companies**

To procure investigational drugs not yet released by FDA, the FDA requires that a report (FD Form 1573) be sent to the drug company (see 21 CFR<sup>d</sup>). The investigator is responsible for directing reports to the drug company.

##### **5. Maintenance of Research Records**

a. The following will be filed in the volunteer's record: a copy of the signed consent form; documentation or code identifying any drugs administered, investigational or not; investigational procedures performed; significant observations, including effects, physical and mental state of the subject; and tests and laboratory procedures performed. The record may contain any additional material the investigator believes is relevant.

b. The investigator will retain all research records for the period governing retention of medical records in the jurisdiction (state or county) where the research is conducted.

c. For all research records pertaining to clinical trials of a compound to be considered for FDA approval, the FDA regulations will be followed (21 CFR).

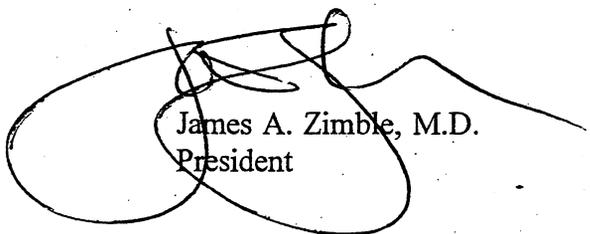
**J. Investigational New Drug and Device Requirements.**

1. Proposals involving an investigational new drug or device will be completed in accordance with Section E, above. The drug or device and the investigator requesting its use will be identified.

2. The investigator's application will include whether the 30-day interval required for investigational new drugs by USUHS Instruction 3200<sup>c</sup> and for significant risk devices by 21 CFR<sup>d</sup> has elapsed, or whether the FDA has waived that requirement. If the 30-day interval has expired, the institution will state whether the FDA has requested that the

sponsor continue to withhold or restrict the use of the drug or device in human subjects. If the 30-day interval has not expired and a waiver has not been received, the investigator will send a statement to DHHS upon expiration of the interval. DHHS will not consider a certification acceptable until the institution has submitted a statement that the 30-day interval has elapsed, and the FDA has not requested it to limit the use of the drug or device, or that the FDA has waived the 30-day interval.

3. For off-site research supported by non-DoD sources, an appropriate reimbursement will be collected for IRB review.



James A. Zimble, M.D.  
President

Enclosures:

1. References
2. Definitions

REFERENCES

- (a) USUHS Instruction 3201, "The Use of Human Volunteers in Research at the Uniformed Services University of the Health Sciences," dated November 2, 1989 (hereby cancelled)
- (b) 45 Code of Federal Regulations, Part 46, Department of Health and Human Services Regulation, "Protection of Human Subjects," including the Appendix on "Categories of Research That May Be Reviewed by the Institutional Review Board (IRB) through an Expedited Review Procedure"
- (c) 32 Code of Federal Regulations, Chapter 1, Part 219, Department of Defense Policy, "Protection of Human Subjects"
- (d) 21 Code of Federal Regulations, Food and Drug Administration Regulation, Subchapters A, D, and H
- (e) USUHS Instruction 3200, "Research and Clinical Investigation," dated September 30, 1997
- (f) DoD Directive 3216.2, "Protection of Human Subjects in DoD-Supported Research," dated January 7, 1983
- (g) Title 24, United States Code Annotated, Chapter 30, "Payments to Donors of Blood of Persons Undergoing Treatment at Government Expense"
- (h) 45 Comptroller General Opinions 649
- (i) Title 5, United States Code, Section 5532, (c)(2)
- (j) Title 10, United States Code, Section 980, "Limitation on Use of Humans as Experimental Subjects"
- (k) 21 Code of Federal Regulations, Part 50, Section 23

**DEFINITIONS**

Definitions of terms used in this document are defined in 45 CFR, Part 46<sup>b</sup>; 32 CFR, Chapter 1, Part 219<sup>c</sup>; 21 CFR<sup>d</sup>; and USUHS Instruction 3200<sup>e</sup>.