OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

JUN 1 3 2005

MEMORANDUM FOR DEPUTY DIRECTOR, TRICARE MANAGEMENT ACTIVITY

SUBJECT: Approval of TMA Multiple Project Human Research Subject Protection Assurance

REFERENCES: (a) "Assurance of Compliance with DoD and DHHS Regulations for Protection of Human Research Subjects," signed by Deputy Director TMA on May 11, 2005
(b) Director, Defense Research and Engineering Memorandum, "Delegation of Authority to Approve and Accept Assurances," April 28, 2005
(c) Director, Defense Research and Engineering Memorandum, "Review of DoD Components' Human Subject Research Protection Programs," January 23, 2004
(d) Memorandum of Agreement, "Institutional Review Board Review of Human Subject Research," March 3, 2005

DDR&E has granted me the authority, as the USD(P&R) Component Designated Official (CDO), to approve and accept federal assurances of compliance with human subjects research statutes, regulations and policies (Reference (b)). DDR&E has determined (reference (c)) that the TRICARE Management Activity (TMA) is or may be an agency that conducts activities meeting the regulatory definition of human subjects research and, therefore, TMA requires its own human subject protection program within the USD(P&R) component.

You have provided me with your plan to implement applicable laws, regulations, and policies through a human research subject protection program and provided me (reference (a)) a TMA Multiple Project Assurance of compliance for my approval.

We have reviewed your Multiple Project Assurance, and I approve it as comporting with guidance for an effective human subjects protection program. Your Assurance Number is DoD-P60002. Attached is your signed Assurance memorandum with my signed endorsement. This Assurance will expire on June 1, 2010, unless earlier revoked, renewed, or renegotiated, and should be updated and resubmitted for CDO review at least four months before expiration.

TMA's designated IRB of record is the U.S. Army Medical Research and Materiel Command's Human Subject Research Review Board (HSRRB) as specified in the

memorandum of agreement (reference (d)). Please advise me should there be any serious or continuing non-compliance including: investigators' failure to adhere to the requirements of the IRB; restriction, suspension, or termination of IRB approval of research; serious, unexpected adverse events involving human subject(s); or unanticipated problems involving risks to subjects or others. You have recognized that TMA will be responsible for funding any significant costs associated with HSRRB review of TMA's human subject research beyond routine costs associated with supporting other organizations.

Ellen P. Embrey
Deputy Assistant Secretary of Defense
Force Health Protection and Readiness

Attachment:
As stated

# Attachment 1

"Assurance of Compliance with DoD Regulations for Protection of Human Research Subjects," signed by Deputy Director TMA on May 11, 2005

**ASSURANCE OF COMPLIANCE WITH DOD AND DHHS REGULATIONS FOR PROTECTION OF HUMAN RESEARCH SUBJECTS**

**PART 1**

The TRICARE Management Activity, hereinafter known as the "institution", hereby gives assurance that it will comply with the Department of Defense (DoD) regulations for the Protection of Human Research Subjects (Title 32 Code of Federal Regulations (CFR) Part 219 as specified below.

## I. Statement of Principles, Policies and Applicability

A. Ethical Principles

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

B. Institutional Policy

1. This institution acknowledges and accepts its responsibilities for protecting the rights and welfare of human subjects of research covered by the policy set forth in this assurance.

2. This institution assures that before human subjects are involved in research covered by this policy, proper consideration will be given to:

   a. the risks to the subjects;

   b. the anticipated benefits to the subjects and others;

   c. the importance of the knowledge that may reasonably be expected to result; and

   d. the informed consent procedures to be employed.

3. This institution acknowledges that it bears responsibility for the performance of all research involving human subjects, covered by this policy, including continuing review of the research.

4. This institution acknowledges its responsibility for complying with federal, state and local laws as they may relate to research covered by this policy.

5. This institution encourages and promotes constructive communication among the staff, human subjects, and institutional officials as a means of maintaining a high level of awareness regarding the safeguarding of the rights and welfare of human subjects in activities carried out under this assurance.

6. This institution will exercise appropriate administrative overview carried out least annually, to ensure that its practices and procedures designed for the protection of the rights and welfare of human subjects are being effectively applied.

7. This institution will consider additional safeguards in research when that research involves prisoners, fetuses, pregnant women, children, individuals institutionalized as mentally disabled, other potentially vulnerable groups and human *in vitro* fertilization.

8. This institution provide to each individual at the institution conducting human subject research (e.g., research investigators, department heads, research administrators, research reviewers) with a copy of this statement of ethical principles and policy (Part 1, I.a., b, and c).

C. Applicability

1. Except for research in which the only involvement of human subjects is in one or more of the categories exempted or waived under 32 CFR 219.101 (b)(1-6) or 219.119 of DoD regulations. This policy is applicable to all research involving human subjects and all other activities which even in part involve such research, if any of the following conditions are met:

   a. the research is sponsored by this institution; or

   b. the research is conducted by or under the direction of any employee or agent of this institution in connection with his or her institutional responsibilities; or

   c. the research is conducted by or under the direction of any facility of this institution; or

   d. the research involves the use of the institution's nonpublic information to identify or contact human research subjects or prospective subjects.

## PART 2

In regard to all research activities conducted at this institution, this institution has complied and will continue to comply with the requirements of 32 CFR 219 as specified below.

### II. Institutional Review Board Review

A. Before human subjects may be involved in research carried out through protocols authorized under this assurance, the protocols must be reviewed and approved by the appropriate Institutional Review Board (IRB) and certification filed with the Principal Investigator. The IRB is established in accordance with the compositional requirements of 32 CFR 219.107. The IRB is responsible for the initial and continuing review of the cooperative group protocols regardless of the site at which the research activity is conducted. The IRB will observe the quorum requirements of 32 CFR 219.108.

B. In light of the information provided in the research plan of the protocols, the IRB is to determine, in accordance with the following criteria (32 CFR 219.111), if human research subjects' protection is adequate.

1. Risks to subjects are minimized:

   a. by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk and

   b. whenever appropriate by using procedures already being performed on the subjects for diagnostic or treatment purposes.

2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB shall not consider long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable. In making this assignment, the IRB shall take into account the purpose of the research, the setting in which the research will be conducted, and the population from which subjects will be recruited.

4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 32 CFR 219.116.

5. Informed consent will be appropriately documented, in accordance with, and to the extent required by, 32 CFR 219.117.

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

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

8. Where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with acute or severe physical or mental illness, or persons who are economically disadvantaged, appropriate additional safeguards have been included in the study to protect the rights and welfare of these subjects.

9. Where some or all of the subjects are uniformed military personnel and the research is judged to involve more than minimal risk, unit officers and noncommissioned officers (NCOs) shall not influence the decisions of their subordinates to participate or not to participate as research subjects. Unit officers and senior NCOs (E-7 and above) in the chain of command shall not be present at the time of research subject solicitation and consent during any research recruitment sessions in which members of units under their command are afforded the opportunity to participate as research subjects. When applicable, officers and NCOs so excluded shall be afforded the opportunity to participate as research subjects in a separate recruitment session. During recruitment briefings to a unit for research with greater than minimal risk where a percentage of the unit is being recruited to participate as a group, an ombudsman not connected in any way with the proposed research or the unit shall be present to monitor that the voluntary nature of individual participants is adequately stressed and that the information provided about the research is adequate and accurate.

C. The IRB will determine that legally effective informed consent will be obtained in a manner and method which meets the requirements of 32 CFR 219.116 and 219.117. The basic elements of informed consent are:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

2. A description of any reasonably foreseeable risks and discomforts to the subject.

3. A description of any benefits to the subject or to others that reasonably may be expected from the research.

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.

6. For research involving more than minimal risk, an explanation as to whether any

compensation or any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.

7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

9. Additional elements of informed consent are required when, in the judgment of the IRB, they are appropriate. They are as follows:

   (a) a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;

   (b) anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

   (c) any additional costs to the subject that may result from participation in the research;

   (d) the consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

   (e) a statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject; and

   (f) the approximate number of subjects involved in the study.

D. The IRB shall review, and have the authority to approve, require modification in, or disapprove changes proposed in this research activity.

E. Each protocol reviewed and approved under this assurance will be reviewed on a continuing basis at intervals appropriate to the degree of risk as determined by the IRB, but not less than once per year. The IRB may be called into an interim review session by the chairperson at the request of any IRB member or any participating institutional official, to consider any matter concerned with the rights and welfare of any subject.

F. The IRB shall prepare and maintain adequate documentation of its activities in accordance with 32 CFR 219.115.

G. The IRB shall report the following promptly to the members, Principal Investigator, any

cooperative group operations office, the DoD component office accepting this assurance:

1. any serious or continuing noncompliance by investigators with the requirements of the responsible IRB and

2. any suspension or termination of IRB approval.

H. The IRB shall report promptly to the members, principal investigator, and any cooperative group operation office, and the DoD component office accepting this assurance any information received concerning:

1. injuries to human subjects,

2. unanticipated problems involving risks to subjects or others

3. any changes in this research activity which are reviewed and approved by the IRB.

The principal Institutional Review Board of record for this institution is the Human Subjects Research Review Board. A current membership roster of this IRB is appended to the implementing Memorandum of Agreement on IRB support maintained in the office of the USD(P&R) Component Designated Official.

**IV. Research Investigator Reporting Responsibilities**

A. Research investigators shall report promptly to the appropriate IRB proposed changes in this research activity. Significant changes shall not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the subjects.

B. Research investigators shall report promptly to the appropriate IRB any unanticipated problems involving risks to the subjects and others.

**V. Responsibilities of Affiliating Institution**

A. The requirements of 32 CFR 219.103 (b)(2) regarding establishment of the IRB(s) and provision for meeting space and sufficient staff have been met.

B. The participating institution responsible for the functions of the IRB shall report promptly to the DoD component office accepting this assurance and or appropriate, to the National Cancer Institute (NCI), DHHS OPRR, and appropriate cooperative group headquarters providing the protocol any injuries to human subjects, unanticipated problems involving risks to subjects or others, and any changes in this research activity which are reviewed and approved by the IRB.

**VI. Other Requirements**

The institution and research investigators and IRBs must comply with certain additional requirements of the Food and Drug Administration (FDA) when the activity involves investigational new drugs (IND) or devices (IDE).

## PART 3

### I. Endorsements and Approval

The official(s) signing below agrees that all research activities at this institution will be conducted in accordance with DoD and DHHS policies, procedures, and regulations for the protection of human research subjects (32 CFR 219 and 45 CFR 46), this assurance, and stipulations of the designated DoD- or OPRR-approved IRB.

A dated roster listing the current membership of the designated IRB is attached. The institution with the IRB will report promptly to the institution providing this assurance, changes in IRB membership via submission of a revised and dated roster. Such changes are subject to approval. As required at 32 CFR 219.103 and 45 CFR 46.103, provisions have been made for meeting space and sufficient staff to support the IRB's review and record-keeping duties.

A. Authorized Official of the Institution Providing This Assurance

Signature:  Date: 11 May 2005

Name: RADM Richard A. Mayo, USN

Title: Deputy Director, TRICARE Management Activity

Address: Skyline Place Five
5111 Leesburg Pike, Suite 810
Falls Church, VA 22041

B. Institutional Review Board Chairperson

(Available for review in the CDO's office)

II. **DoD Approving Official**

All parts of this assurance are in compliance with the requirements of appropriate sections of the Code of Federal Regulations. This assurance is valid only for the above-mentioned participating institution(s) and physicians/investigators participating on the protocols covered by this assurance.

DoD Approving Official

Signature: Ellen P. Embrey Date: 6/13/05

Name: Ellen P. Embrey

Title: Deputy Assistant Secretary of Defense (Force Health Protection and Readiness)

Address: Skyline Place Four
5113 Leesburg Pike, Suite 901
Falls Church, VA 22041

This assurance expires April 30, 2010, and must be renegotiated with the appropriate DoD oversight office

# Attachment 2

DDR&E memorandum, "Delegation of Authority to Approve and Accept Assurances," April 28, 2005

DIRECTOR OF DEFENSE RESEARCH AND ENGINEERING
3030 DEFENSE PENTAGON
WASHINGTON D C. 20301-3030

MEMORANDUM FOR UNDER SECRETARY OF DEFENSE FOR PERSONNEL AND READINESS

SUBJECT: Delegation of Authority to Approve and Accept Assurances

I have reviewed your "Component Management Plan" (attached) to protect human subjects in research, development, test, and evaluation (RDT&E) and find your policies to be compliant with the federal and DoD policies (32 Code of Federal Regulations 219 and the DoD implementing policy, DoD Directive 3216.2). Therefore, I delegate to you the authority to approve and accept a federal assurance for RDT&E sponsored or conducted by your Component. Assurances shall be coded in accordance with the unique range of alpha-numeric characters assigned to each Component (attached). You can further delegate this authority only as described in your "Component Management Plan." This plan will be reviewed and resubmitted to the Director, Defense Research & Engineering three years from the date of this memorandum or upon any significant changes in the plan, delegation of authority, policies, or procedures.

If you receive funding from another DoD Component or non-DoD organization, you are obligated to ensure your Component is in compliance with federal and DoD policies. You are required to notify my office of any significant changes to your Component's policies and procedures for protecting human subjects. Dr. Robert Foster, Director, BioSystems, is the Senior Executive responsible to me for these matters and his Action Officer is Mrs. Patty Decot (703-588-7402). I have asked them to review your implementation of key aspects of your "Management Plan" at the end of your first year of execution.

Ronald M. Sega

Attachment:
1. USD(P&R) "Management Plan"
2. DoD Assurance Identification

cc: DASD(FHP&R)

# Attachment 3

DDR&E memorandum, "Review of DoD Components' Human Subject Research Protection Programs," January 23, 2004

DIRECTOR OF DEFENSE RESEARCH AND ENGINEERING
3030 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-3030

JAN 23 2004

MEMORANDUM FOR SECRETARIES OF THE MILITARY DEPARTMENTS
UNDER SECRETARY OF DEFENSE FOR ACQUISITION, TECHNOLOGY AND LOGISTICS
UNDER SECRETARY OF DEFENSE FOR PERSONNEL AND READINESS
DIRECTOR, OPERATIONAL TEST AND EVALUATION
PRESIDENT, UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
DIRECTOR, DEFENSE ADVANCED RESEARCH PROJECTS AGENCY
DIRECTOR, DEFENSE THREAT REDUCTION AGENCY
DIRECTOR, NATIONAL SECURITY AGENCY
DIRECTOR, DEPARTMENT OF DEFENSE EDUCATIONAL ACTIVITY
DEPUTY UNDER SECRETARY OF DEFENSE (ADVANCED SYSTEMS AND CONCEPTS)

SUBJECT: Review of DoD Components' Human Subject Research Protection Programs

I have the responsibility for ensuring DoD's compliance with federal policy for the ethical conduct of RDT&E using human subjects (DoD Directive 3216.2, paragraph 5.1). As Head of a Component, you have been delegated the responsibility to develop, issue, and monitor implementing policies to comply with the Directive (paragraph 5.3). By this memorandum I am initiating a formal process to periodically review and assess compliance with the Directive. In addition, this memorandum terminates all current DoD Assurances as of December 31, 2004 to allow for reissuance following completion of the reviews and assessments.

I have tasked my Director, BioSystems, to conduct oversight visits to all Components that are conducting or sponsoring human - subject RDT&E subject to DoDD 3216.2. I have asked that these visits be conducted between February and May 2004 with a final report delivered to me by the end of July 2004. I hope that the preparation for and exchanges during these visits will strengthen human subject protection programs throughout the DoD. These visits will generate information necessary to reissue authority to relevant DoD organizations to grant DoD "Assurances" so that they can continue to sponsor and conduct RDT&E using human subjects after December 31, 2004.

Dr. Robert Foster, Director, BioSystems, is the Senior Executive responsible to me for these matters and his Action Officer is Patty Decot. If you have any questions, you can reach them through patty.decot@osd.mil or at 703-588-7420. Mrs. Decot will be contacting each Component to schedule the necessary meetings.

Ronald M. Sega

Attachment:
Information Paper

cc:
Office of the General Counsel (ATTN: Mr. John Casciotti)
Assistant Secretary of Defense (Health Affairs)
Deputy Assistant Secretary of Defense Force Health Protection and Readiness
Director of Policy Integration, OUSD(P&R)
Director, Defense Manpower Data Center East (ATTN: Mr. Ken Scheflen)
Acting Director, Defense Sciences Office, DARPA
DTRA (ATTN: LTC Keith Vesely)
USUHS (ATTN: CAPT Robert Bienvenu)
NSA (ATTN: Dr. Julie Sasscer-Bigos)
Surgeon General of the Army
Surgeon General of the Navy
Surgeon General of the Air Force

# Attachment 4

Memorandum of Agreement, "Institutional Review Board Review of Human Subject Research," March 3, 2005

MEMORANDUM OF AGREEMENT

# INSTITUTIONAL REVIEW BOARD REVIEW OF HUMAN SUBJECTS RESEARCH

**March 3, 2005**

## References

(a) Department of Defense Directive 3216.2, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research," March 25, 2002

(b) Title 32, Code of Federal Regulations, Part 219, "Protection of Human Subjects," July 1, 2000

(c) Title 10, United States Code, Section 980, "Limitation on Use of Humans as Experimental Subjects"

## Purpose

This agreement among the parties listed below sets out mutually agreed provisions whereby organizational activities under the purview of the Under Secretary of Defense (Personnel and Readiness) (USD(P&R)) that may conduct research on human subjects (as defined by reference (a), Enclosure 2) will carry out such research subject to the review and approval of the U.S. Army Medical Research and Materiel Command (USAMRMC), Human Subjects Research Review Board (HSRRB).

## Authority

This agreement is entered into under the authority of the Economy Act, 31 U.S.C. 1535.

## Parties to Agreement

The parties to this agreement are:

- The Deputy Assistant Secretary of Defense (Force Health Protection and Readiness), hereafter referred to as the Component Designated Official (CDO), who has been delegated the authority and responsibility from the USD(P&R) for directing and overseeing the P&R component's human research subjects protection program and for granting and accepting assurances of compliance.

- The USAMRMC Office of Research Protections (OPR) provides support to the HSRRB, which is constituted to perform the duties of an Institutional Review Board (IRB) as specified by reference (b), including review, approval, and monitoring of research involving human subjects.

- The TRICARE Management Activity (TMA), which conducts and supports studies and surveys that may constitute human subject research and which is not expected to but may engage in, support, or sponsor clinical research.

- The Defense Manpower Data Center (DMDC), which conducts and supports studies and surveys that may constitute human subject research and which is not expected to but may engage in, support, or sponsor clinical research.

- The Department of Defense Education Activity (DoDEA), which conducts and supports studies and surveys that may constitute human subject research and which is not expected to but may engage in, support, or sponsor clinical research.

The Uniformed Services University of the Health Sciences (USUHS), which also is under the purview of the USD(P&R), does conduct, sponsor, and support clinical research projects and is already subject to review by the USUHS and other IRBs.

**General Provisions**

The officials signing below agree that all undertakings within the definition of human subject research will be conducted in accordance with DoD policies, procedures, and regulations for the protection of human subjects as referenced above.

The Director, Defense Research and Engineering (DDR&E) has overall responsibility for oversight of DoD human subjects research and will take any action that requires communication on compliance-related issues with entities outside DoD. Such communication with DDR&E will be accomplished by, or pass through, the CDO.

Undertakings in which the only involvement of human subjects will be in areas specified in section 219.101(b) of reference (b) are exempt from the provisions of references (a), (b), and (c) and need not be reviewed by an IRB.

Per section 219.110 of reference (b), an IRB may use the expedited review procedure to review either or both of the following: a) some or all of the research appearing on the referenced list and found by the reviewer(s) to involve no more than minimal risk; and b) minor changes in previously approved research during the period (of one year or less), for which approval is authorized.

**Responsibilities of USD(P&R) Research Sponsoring Parties**

The TMA, DMDC, and DoDEA, hereafter "sponsoring parties," shall fulfill the following responsibilities under this agreement:

- Oversee conduct of initial and annual training on protection of human research subjects, commensurate with individuals' duties and responsibilities, covering the governing laws, regulations, and policies. The CDO's staff will arrange for conduct of initial and annual training.

- Assure that any collaborating or supporting organization engaged with a sponsoring party in human subject research is independently covered by an IRB or agrees to compliance with all provisions of this agreement relating to sponsoring parties.

- Propose to the CDO research that may be either not human subject research or exempt from the provisions of the references as permitted under section 219.101 of reference (b). The CDO will make a final determination on these types of undertakings.

- Develop human subject research plans or protocols that incorporate human subject protection measures in sufficient detail to permit thorough review by the HSRRB.

- Develop human subject research informed consent scripts or documents in accordance with reference (b).

- Advise the CDO of anticipated human subject research undertakings that may require HSRRB review at least 45 calendar days prior to required potential HSRRB review.

- At least four weeks prior to an initial HSRRB research review and two weeks prior to subsequent HSRRB reviews, forward complete electronic copies of research material and documentation to the HSRRB at hsrrb@amedd.army.mil for distribution to all HSRRB members. Also provide documentation to the CDO.

- Where research risk to human subjects is minimal and the nature of the research is covered under section 219.110 of reference (b), request expedited HSRRB review as appropriate after initial approval of the request by the CDO.

- In the event of adverse research outcomes resulting in injury or compromised privacy of human research subjects, promptly notify the HSRRB and the CDO in writing (e-mail).

- Maintain adequate documentation on human subject research including research plans and protocols, modifications to research plans or protocols, informed consent, results, analysis, and publication or distribution of results or analysis.

- Provide the HSRRB with progress reports on a schedule determined by the HSRRB based on perceived risk (but no less than once per year).

- Provide the HSRRB copies of informed consent documents.

- Participate in and support HSRRB continuing reviews of each reviewable project on a schedule determined by the HSRRB but at least annually.

- Host, participate in, and support CDO on-site audits of human subject research plans, procedures, guidelines, documentation, and protection training at least once every three years upon notification by the CDO. These audits may include individual human subject protection knowledge tests of those sponsoring party staff directly involved in designing and conducting human subject research.

- When required by the HSRRB, participate in and support independent verification that there has been no material change in the research since the last HSRRB review.

- Promptly advise the HSRRB of any desired material change in the research effort and do not implement such changes without HSRRB approval except to protect the health of human subjects in emergencies.

**Responsibilities of HSRRB**

The HSRRB shall fulfill the following responsibilities under this agreement:

- Follow standard guidance regarding the board's membership composition including scientific/non-scientific backgrounds, multiple professions, outside representation, and avoidance of potential conflicts of interest.

- A dated roster listing the current membership of the HSRRB is at Attachment 1. Upon request, updated rosters will be available from the Acting Chair, HSRRB throughout the course of this agreement.

- In the event the HSRRB or its chairperson considers inadequate HSRRB membership expertise relative to particular research submitted for review by sponsoring parties, notify the CDO and the sponsoring party to provide an opportunity for them to suggest to the HSRRB participation of qualified subject matter expert consultants having no conflict of interest.

- Distribute to HSRRB members documentation and requests from a sponsoring party in sufficient time for their review prior to decisions addressing research covered by this agreement.

- Make every effort to conduct reviews of sponsoring party research and report decisions within 45 calendar days of receiving complete and adequate sponsoring party documentation. Results will be reported to the CDO as well as to the sponsoring party and any other institution involved in collaborative research. In the event that this 45-day condition cannot be met, the HSRRB will notify these aforementioned institutions in writing of the reason for the delay and a projected time for an HSRRB decision.

- In the event an HSRRB decision calls for submission of additional information, modifications or restrictions to research protocols/plans, or suspension or termination of research, the HSRRB will provide their determination and stipulations in writing.

- Consider using expedited review procedures in all cases covered by this agreement that involve minimum risk to human subjects and where the nature of the research permits expedited review under section 219.110 of reference (b).

- Maintain for at least three years after reviewed research ends complete review documentation in accordance with accepted IRB standards and government regulations.

**Responsibilities of the USD(P&R) CDO**

The CDO shall fulfill the following responsibilities under this agreement:

- Arrange for on-site training in human subject protection for all sponsoring parties' staff involved in human subjects research prior to initial HSRRB reviews and prior to or as soon as practicable after this agreement enters into effect.

- Provide or arrange for providing to sponsoring parties educational courses thoroughly covering human subject protection laws, policies, regulations, procedures, and reviews in support of their continuing/annual training.

- Review all documentation forwarded by sponsoring parties to the HSRRB. Request changes or additions as necessary.

- Arrange scheduling of HSRRB reviews of research covered by this agreement.

- Make initial judgment on appropriateness of sponsoring party requests for expedited review.

- Determine whether sponsoring party research is exempt from IRB review.

- Provide to the sponsoring parties expert determinations regarding whether certain research is or is not human subject research.

- Review and approve sponsoring parties' informed consent scripts, documents, and procedures and ensure sufficient protections including for vulnerable classes of subjects.

- If human subjects research results in adverse outcomes, notify the HSRRB, USD (P&R), and DDR&E as appropriate.

- Monitor and maintain status of sponsoring party reporting and HSRRB schedules and actions.

- Perform on-site audits of sponsoring party human research subject protections, knowledge, and compliance with applicable policies, laws, and regulations. Such audits may include written human research subject protection knowledge tests.

- In collaboration with the sponsoring parties, identify temporary/intermittent subject matter consultants to participate in HSRRB reviews when requested by the HSRRB.

- When and if required, take the P&R lead in renegotiating this agreement.

**Agreement Modification Procedures**

This agreement remains in effect indefinitely until and unless any of the parties to the agreement notifies in writing the CDO that the notifying party desires to have the agreement modified or to withdraw from the agreement. Such notifications shall be submitted at least 30 days before the

requested action shall take effect. All remaining parties to the agreement must approve any proposed modifications to the agreement.

**Pricing, Billing, and Payment Terms**

The USAMRMC Office of Research Protections will apply its available funds to support this agreement so long as such support requires no significant expenditures (greater than $100 per month) over and above that required to fulfill its other requirements not covered in this agreement.

In cases where appropriate ORP-supported HSRRB review of research covered under this agreement requires significant expenditures over and above that required to fulfill its other requirements not covered in this agreement (e.g., consultants with special expertise on matters for which the HSRRB was not constituted), the HSRRB will notify in writing the CDO and sponsoring party to this agreement of the estimated funds required before incurring such expenses. The CDO and the sponsoring party to this agreement will either approve the expenditures, arrange to fulfill the requirement in kind, or withdraw the request to review research. Fulfillment in kind is subject to HSRRB approval.

The ORP will bill expenditures approved by the CDO and sponsoring party to the sponsoring party within 30 calendar days of the HSRRB activity generating the expenses. The sponsoring party within 30 calendar days of receiving a statement of expenses incurred will transfer funds to the USAMRMC in a manner specified by the USAMRMC Comptroller to fully cover the billed expenses.

In the event that the ORP determines that the workload or special expertise involved in implementing this MOA requires addition of permanent staff, paid HSRRB membership, or other substantial continuing support resources, they promptly will so notify the CDO of the nature and estimated recurring costs of such action. If the ORP and/or HSRRB takes action to expand its membership, staff, or support resources to fulfill requirements specified in this agreement, it will not review USD(P&R) plans or protocols pending renegotiation or termination of this agreement. A flat fee per protocol reviewed is possible, but the fee must be detailed and accepted by the CDO and sponsoring activity.

**Endorsements and Approval**

The authorized officials whose signatures appear below accept and expressly agree to the terms and conditions specified herein, confirm that no verbal agreements of any kind shall be binding or recognized, and hereby commit their respective organizations to the terms of this agreement.

**Attachment 1**

*INSTITUTIONAL REVIEW BOARD (IRB) MEMBERSHIP*

NAME OF IRB AGENCY OR COMMAND: **U.S. Army Medical Research and Materiel Command, Human Subjects Research Review Board**

Name, Address, and Phone Number of the Acting Chairperson:
**Laura R. Brosch, COL, AN**
**Acting Chair, Human Subjects Research Review Board**
**Commanding General**
**U.S. Army Medical Research and Materiel Command**
**ATTN: MCMR-RCQ**
**504 Scott Street**
**Fort Detrick, Maryland 21702-5012**

***Human Subjects Research Review Board (HSRRB) Membership***
***March 1, 2005***

| Rank/Title | Name (Last, First, MI) | Sex | Affiliated | Degrees | Expertise |
|---|---|---|---|---|---|
| 1. *MG | Martinez-Lopez, Lester | M | Yes | M.D. | Family Practice, Acrospace Medicine, Preventive Medicin |
| 2. **COL | Brosch, Laura R. | F | Yes | Ph.D.; R.N. | Nursing, Health Services Research |
| 3. COL | Babcock, Janiine | F | Yes | M.D. | Pediatrics, Hematology, Oncology |
| 4. COL | Kester, Kent E. | M | Yes | M.D. | Internal Medicine, Infectious Disease |
| 5. COL | Longfield, Jenice N. | F | Yes | M.D.; M.P.H. | Preventative Medicine, Internal Medicine, Epidemiology |
| 6. LTC | Styles, Jennifer R. | F | Yes | Pharm.D. | Pharmacist |
| 7. CH (MAJ) | Hollenbeck, Jon N. | M | Yes | M. of Divinity | Non-Scientist, Clergy, Layperson |
| 8. SFC | Floyd, Karon L. | F | Yes | M.S.A. | Non-Scientist, Enlisted, Layperson |
| 9. Dr. | Boyd, Ann | F | No | Ph.D.; M.S. | Biology |
| 10. Dr. | Creekmore, Stephen P. | M | No | M.D.; Ph.D. | Physics, Oncology, Internal Medicine |
| 11. Dr. | English, Charles K. | M | Yes | Ph.D.; M.S. | Pathology |
| 12. Dr. | Gifford, Robert K. | M | Yes | Ph.D. | Research Psychology |
| 13. Dr. | Krosnick, Steven H. | M | No | M.D. | Radiology-Oncology, Diagnostic Radiology |
| 14. Mr. | Maleson, Stephen E. | M | Yes | J.D. | Non-Scientist, Lawyer |
| 15. Mr. | Mood, Stephen G. | M | No | M.S.W. | Non-Scientist, Certified Social Worker, Layperson |
| 16. Dr. | Rock, Paul B. | M | No | D.O.; Ph.D. | Osteopathic Medicine, Environmental Medicine, Internal Medicine |
| 17. Dr. | Sever, John L. | M | No | M.D. | Pediatrics, Microbiology, Obstetrics, Gynecology, Infectious Disease |

***Alternates for Primary Members***

| Rank/Title | Name (Last, First, MI) | Sex | Affiliated | Degrees | Expertise | Alternate for Member (Name/Number) |
|---|---|---|---|---|---|---|
| 18. ***Ms. | Duchesneau, Caryn L. | F | Yes | B.S. | Biology | COL Brosch (2) |
| 19. COL | Grabenstein, John D. | M | Yes | Ph.D. | Pharmacist, Pharmaco-Epidemiology | LTC Styles (6) |
| 20. COL | Martin, Scott C. | M | Yes | Pharm.D.; M.A. Health Service | Pharmacist | LTC Styles (6) |

| Rank/Title | Name (Last, First, MI) | Sex | Affiliated | Degrees | Expertise | Alternate for Member (Name/Number) |
|---|---|---|---|---|---|---|
| 21. COL | Pittman, Phillip R. | M | Yes | M.D. | Internal Medicine, Infectious Disease | COL Babcock (3); COL Kester (4); COL Longfield (5); Dr. Rock (16) |
| 22. LTC | Altman, Ann M. | F | Yes | M.S.N.; R.N. | Nurse, Critical Care | Alternate Nurse (2) |
| 23. LTC | Caouette, Marc L. | M | Yes | Pharm.D.; M.S. | Pharmacist | LTC Styles (6) |
| 24. LTC | Wortman, Glenn W. | M | Yes | M.D. | Internal Medicine, Infectious Disease | COL Kester (4) |
| 25. CH (MAJ) | Sager, William A. | M | Yes | M. of Divinity; M.A. | Non-Scientist, Chaplain, Clinical Ethicist | CH (MAJ) Hollenbeck (7) |
| 26. CPT | Jennings, William | M | Yes | J.D. | Non-Scientist, Lawyer | Mr. Maleson (14) |
| 27. SFC | Ball, Ludlow | M | Yes | M.B.A.; M.H.A. | Non-Scientist, Layperson, Enlisted | SFC Floyd (8) |
| 29. Ms. | Arwine, Elizabeth A. | F | Yes | J.D. | Non-Scientist, Lawyer | Mr. Maleson (14) |
| 29. Dr. | Nussbaum, George F. | M | Yes | Ph.D.; R.N.; B.S.N. | Nurse | Alternate Nurse (2) |
| 30. Mr. | Winchester, Jay B. | M | Yes | J.D. | Non-Scientist, Lawyer | Mr. Maleson (14) |

*Chair **Acting Chair ***Vice Acting Chair

***Authorized Official of the U.S. Army Medical Research and Materiel Command***

Signature: _____ Date: 15 Mar 2005

Name: MG Lester Martinez-Lopez,
Title: Commander, U.S. Army Medical Research and Materiel Command
Address: Commanding General
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ
504 Scott Street
Fort Detrick, Maryland 21702-5012

***Authorized Official of the U.S. Army Medical Research and Materiel Command, Human Subjects Research Review Board***

Signature: Laura R. Brosch Date: 15 Mar 05

Name: Laura R. Brosch, COL, AN
Title: Deputy, Office of Research Protections
Acting Chair, Human Subjects Research Review Board
Address: Commanding General
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ
504 Scott Street
Fort Detrick, Maryland 21702-5012

***Authorized Official of the TRICARE Management Activity***

Name: Rear Admiral Richard A. Mayo
Title: ~~Executive~~ Deputy Director, TMA
Address: TRICARE Management Activity
Skyline 5, Suite 810
5111 Leesburg Pike
Falls Church, VA 22041-3206

Signature _____

Date: 23 Mar 05

***Authorized Official of the Defense Manpower Data Center***

Signature: _____ Date: 31 March 05

Name: Robert J. Brandewie
Title: Director, DMDC
Address: Defense Manpower Data Center
400 Gigling Road
Seaside, CA 93955-6771

***Authorized Official of the Department of Defense Education Activity***

Signature: Joseph D Tafoya Date: 3/25/05

Name: Dr. Joseph D. Tafoya
Title: Director, DoDEA
Address: Department of Defense Education Activity
4040 North Fairfax Drive
Arlington, VA 22203-1635

***Component Designated Official***

Signature: Ellen P. Embrey Date: 03/21/05

Name: Ellen P. Embrey
Title: Deputy Assistant Secretary of Defense (Force Health Protection and Readiness)
Address: Office of the Assistant Secretary of Defense (Health Affairs)
Deputy Assistant Secretary of Defense (Force Health Protection and Readiness)
Washington, DC 20301-1200