

AWARD NUMBER: W81XWH-07-1-0283

Á  
ÁTITLE: Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure

Á  
Á  
PRINCIPAL INVESTIGATOR: ÁJaul B. Hicks, M.D., Ph.D.  
Michael L. Adams, Ph.D.,  
LTC Brett Litz, Ph.D.  
Keith Young, Ph.D.  
Jed Goldart, M.D.  
Tom Velez, Ph.D.  
Walter Penk, Ph.D.  
Kathryn Kotrla, M.D.

Á  
CONTRACTING ORGANIZATION: TEMPVA Research Group, Inc.  
Temple, TX 76504

Á  
REPORT DATE: July 2009

Á  
TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and not those of the U.S. Army Medical Research and Materiel Command. Distribution is unlimited. This report is available to the public without restriction.

Á  
Á  
Á  
Á  
Á  
Á  
Á  
Á  
Á  
Á  
Á

# REPORT DOCUMENTATION PAGE

*Form Approved*  
*OMB No. 0704-0188*

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

<b>1. REPORT DATE</b> 1 July 2009			<b>2. REPORT TYPE</b> Annual		<b>3. DATES COVERED</b> 1 Jul 2008 – 30 Jun 2009	
<b>4. TITLE AND SUBTITLE</b>  Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure					<b>5a. CONTRACT NUMBER</b>	
					<b>5b. GRANT NUMBER</b> W81XWH-07-1-0283	
					<b>5c. PROGRAM ELEMENT NUMBER</b>	
<b>6. AUTHOR(S)</b>  Paul B. Hicks, M.D., Ph.D.; Michael L. Adams, Ph.D.; Brett Litz, Ph.D.; Keith Young, Ph.D.; Jed Goldart, M.D.; Tom Velez, Ph.D.; Walter Penk, Ph.D.; Kathryn Kotrola, M.D.  E-Mail: paul.hicks@va.gov					<b>5d. PROJECT NUMBER</b>	
					<b>5e. TASK NUMBER</b>	
					<b>5f. WORK UNIT NUMBER</b>	
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b>  TEMPVA Research Group, Inc. Temple, TX 76504					<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b>	
<b>9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b> U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012					<b>10. SPONSOR/MONITOR'S ACRONYM(S)</b>	
					<b>11. SPONSOR/MONITOR'S REPORT NUMBER(S)</b>	
<b>12. DISTRIBUTION / AVAILABILITY STATEMENT</b> Approved for Public Release; Distribution Unlimited						
<b>13. SUPPLEMENTARY NOTES</b>						
<b>14. ABSTRACT</b> T:Although selective serotonin reuptake inhibitors (SSRIs) are routinely prescribed for acute stress disorder and early PTSD and recommended in the VA-DoD best practice guidelines, the efficacy of SSRIs as an early intervention for PTSD in service members returning from war-zone duty has still not been determined. Consequently, this study was designed to conduct a controlled trial of fluoxetine as an early intervention for recently redeployed soldiers, as well as to develop methodologies for understanding the multiple factors that may predict outcome. The Brooke Army Medical Center IRB, the regional IRB for the Carl R. Darnall Army Medical Center, has given full approval. A CRADA between TEMPVA Research Group, Inc and the Carl R. Darnall Army Medical Center has been executed. The protocol has now also been approved by the Central Texas Veterans Health Care System (CTVHCS) IRB and the Research and Development Committee. The review by Kristen R. Katopol, MS, CIM, Human Subjects Protection Scientist (AMDEX Corp.) Human Research Protection Office (HRPO) Office of Research Protections (ORP) U.S. Army Medical Research and Materiel Command (USAMRMC) Fort Detrick has been completed and the BAMC IRB is reviewing the documents revised to comply with her audit. No subjects have been enrolled and will not be enrolled until final approval is obtained from USAMRMC.						
<b>15. SUBJECT TERMS</b> Fluoxetine, Posttraumatic Stress Disorder, Antidepressants						
<b>16. SECURITY CLASSIFICATION OF:</b>				<b>17. LIMITATION OF ABSTRACT</b>	<b>18. NUMBER OF PAGES</b>	<b>19a. NAME OF RESPONSIBLE PERSON</b> USAMRMC
<b>a. REPORT</b> U	<b>b. ABSTRACT</b> U	<b>c. THIS PAGE</b> U	<b>19b. TELEPHONE NUMBER</b> (include area code)			
				UU	66	

## Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	6
Reportable Outcomes.....	6
Conclusions.....	7
References.....	7
Appendices.....	8
Supporting Data.....	

**INTRODUCTION:**

Although selective serotonin reuptake inhibitors (SSRIs) are routinely prescribed for acute stress disorder and early PTSD and recommended in the VA-DoD best practice guidelines, the efficacy of SSRIs as an early intervention for PTSD in service members returning from war-zone duty has still not been determined. Consequently, this study was designed to conduct a controlled trial of fluoxetine as an early intervention for recently redeployed soldiers, as well as to develop methodologies for understanding the multiple risk factors that may predict outcome. Fluoxetine was selected as the psychopharmacologic agent for this study because it is well tolerated, it has a very favorable cost-benefit advantage as a generic drug, and the fact that it is the only SSRI with at least preliminary studies demonstrating its efficacy in recent-onset, war-related PTSD. Studies focusing on targeting chronic combat-related PTSD with SSRIs have shown mixed results with some small open-label studies suggesting efficacy, while two controlled trials with Vietnam veterans were negative. In a recent study of survivors of war violence in Europe, Israel, and South Africa, fluoxetine was shown to significantly reduce PTSD symptoms. Because in all prior trials there is considerable variability of response to fluoxetine, we plan to examine several predictors of efficacy. We argue that the efficacy of SSRIs for recently redeployed soldiers at risk for chronic PTSD is moderated by multiple personal, deployment, and environmental factors. It is expected that not all subjects will respond to fluoxetine. For those that do not respond to fluoxetine alone, augmentation with either buspirone or bupropion will be offered based on their reasonable tolerability, low cost and the recent findings documenting their utility as adjunctive treatments for depression.

**BODY:**

The approval letter has been received from the Brooke Army Medical Center IRB, the regional IRB for the Carl R. Darnall Army Medical Center. The IRB has approved the protocol with the caveat that a CRADA must be completed between TEMPVA Research Group, Inc and the Carl R. Darnall Army Medical Center. The protocol has now also been approved by the Central Texas Veterans Health Care System IRB and the Research and Development Committee. The review by Kristen R. Katopol, MS, CIM, Human Subjects Protection Scientist (AMDEX Corp.) Human Research Protection Office (HRPO) Office of Research Protections (ORP) U.S. Army Medical Research and Materiel Command (USAMRMC) Fort Detrick suggested multiple changes to the informed consent document and protocol for full compliance. We have prepared appropriate responses that Ms. Katopol agreed were acceptable. The CTVHCS IRB has accepted these changes, and the BAMC IRB will review them at their August 5, 2009 meeting. The CTVHCS IRB agreed to accept the BAMC Informed Consent Document as approved by the BAMC IRB. The CRADA between TEMPVA Research Group, Inc. and CRDAMC has been executed. No subjects have been enrolled and will not be enrolled until final approval is obtained from USAMRMC.

Two research assistants have been hired. Both have master's degrees in counseling psychology and have considerable clinical experience, as well as some research experience. They have been trained on the administration of the psychological tests associated with this project and have developed the casebooks used in data collection, as well as been trained on the use of the CRDAMC electronic medical record system. Not all of the offices we had been assigned at the Carl R. Darnall Army Medical Center Resilience and Restoration Center, Bldg. 36009 have

remained available. To accommodate our space needs, we have made arrangements to have a 12'X52' office trailer moved to the site of the Resilience and Restoration Center.

Credentialing and privileging of Drs. Peggy Pazzaglia and Paul Hicks at the Carl R. Darnall Army Medical Center has been completed.

The second continuing review from the BAMC IRB has been approved (see Appendix). PR064845 is now registered in ClinicalTrials.gov, No. NCT00633685.

#### Project Tasks:

##### Task 1: Submission of the Proposal to the IRBs

- The proposal must be approved by both the Brooke Army Medical Center IRB and the Central Texas Veterans Health Care System Human Subjects Subcommittee.
- **Completed**

##### Task 2: Recruitment and Training of Study Personnel

- Hire two master's prepared research assistants
- Training on recruitment procedures and research assessments (SCID, CAPS, etc.)
- **Completed**

##### Task 3: Preparation of Over-Encapsulated Blinded Medications for the First Phase of the Clinical Trial

- Purchase of the fluoxetine and gelatin capsules from VA pharmacy suppliers (purchased each 3 months throughout the first 15 months of the study)
- Over-encapsulation of fluoxetine and empty gelatin capsules by CTVHCS Pharmacy staff
- Transfer of medications prepared by the CTVHCS Pharmacy directly to the Carl R. Darnall Medical Center Pharmacy
- **The Fluoxetine and placebo capsules have been prepared and will be transferred to the CRDAMC Pharmacy as soon as final approval to begin the study has been given.**

##### Task 4: Recruitment/Clinical Trial

- Enrollment of a minimum 20 subjects per month for 15 months
- Double-blind, placebo-controlled trial of fluoxetine + usual psychological care for 12 weeks
- Open-label extension of the fluoxetine trial for 20 weeks

##### Task 4: Data Collection and Transfer to the Boston VA National PTSD Research Center

- Data will be stored on compact discs for storage
- Compact discs will be sent on a monthly basis to the National PTSD Research Center for database development
- The post-doctoral fellow working with Dr. Brett Litz will maintain the database under the oversight of Dr. Litz

Task 5: Data Analysis at the Boston VA National PTSD Research Center

**KEY RESEARCH ACCOMPLISHMENTS:** Not applicable

**REPORTABLE OUTCOMES:** Not applicable.

**CONCLUSIONS:** Not applicable.

**REFERENCES:** Not applicable.

**APPENDICES:**

Appendix A: BAMC IRB Continuing Review Approval letter

Appendix B: BAMC IRB Approved Informed Consent Document

Appendix C: CTVHCS IRB Approval letters

1. Continuing Review Approval Letter of March 23, 2009

2. Letter Granting Cooperative Research Status of June 12, 2009

Appendix D: CTVHCS R&D Committee Continuing Review Approval letter

Appendix E: Fully Executed CRADA

**SUPPORTING DATA:** Not applicable



# Appendix A:

## Hicks, Paul B.

---

**From:** Adams, Michael L Dr CIV USA MEDCOM CRDAMC [Michael.Adams@AMEDD.ARMY.MIL]  
**Sent:** Friday, February 20, 2009 5:01 PM  
**To:** Hicks, Paul B.  
**Subject:** FW: February IRB subcommittee - Continuing Review Outcome (UNCLASSIFIED)  
**Signed By:** michael.adams6@us.army.mil

Classification: UNCLASSIFIED  
Caveats: NONE

-----Original Message-----

**From:** King, Ileana Ms CIV USA MEDCOM BAMC  
**Sent:** Friday, February 20, 2009 9:00 AM  
**To:** Adams, Michael L Dr CIV USA MEDCOM CRDAMC  
**Subject:** February IRB subcommittee - Continuing Review Outcome (UNCLASSIFIED)

Classification: UNCLASSIFIED  
Caveats: NONE

### Clinical Studies Requiring Expedited Continuing Review:

The intent of this review is to identify unrecognized risks to the participants; to ensure the Benefit:Risk potential to the participants is reasonable and that they are clearly informed of all Risks and Procedures. All protocols were discussed with this guidance in mind. The IRB reviewed these specific areas of performance for each protocol being reviewed, with discussion of any concerns or possible discrepancies: verification of the names and dates of CITI certification of all listed investigators; the name of the medical monitor, if one is appointed; the current status of the study; proof of a review of related scientific literature since the last continuing review; a description of the progress made since the last continuing review; a table of the number of subjects enrolled in the last year and previously, and the total authorized to enroll; the number of reports of local adverse events and total IND safety reports, when appropriate. The IRB also reviewed the current Informed Consent Document and HIPAA Authorization for each active protocol, identifying any required changes to the documents. Unless noted, the IRB felt the investigator had undertaken every effort to minimize risk to the participants and the IRB judged the risk to participants reasonable in relation to potential benefit. The IRB members were satisfied with the investigator's provision for participant privacy and confidentiality. Recruitment of potential participants was judged to be equitable. The Board felt the investigator's method safeguarded the rights of vulnerable participants. The following protocol which has been approved for Continuing Review is required to submit the next Continuing Review in January 2010.

A subcommittee consisting of Dr. Morris, MAJ Cabrera, CPT Livezey and Rick Wolf, all IRB members, expeditiously approved for continuing review the following protocol.

The study was either expedited (No Greater Than minimal Risk), CTNPA or have zero patients enrolled:



C.2007.145

LTC Michael Adams, MS

C. R. Darnall Army Medical Center

"Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure." PI reports this study has zero patients enrolled. The study was reviewed and approved for continuation by a vote of 4 For; 0 Against.

Please retain this correspondence in your records.

Ileana King

---

HIPAA Compliance, Quality Assurance and Training Coordinator Department of Clinical Investigation Brooke Army Medical Center, 3400 Rawley E. Chambers Ave, Suite A, Fort Sam Houston, TX 78234-6315

[www.sammc.amedd.army.mil/staff/research/dci/index.asp](http://www.sammc.amedd.army.mil/staff/research/dci/index.asp)

phone (210) 916-2000, DSN 429

facsimile (210) 916-1650

email: [ileana.king@amedd.army.mil](mailto:ileana.king@amedd.army.mil)

Confidentiality Notice: This email message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review, use, disclosure, or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply email and destroy all copies of the original message and / or attachments. Thank you for your compliance in this matter

Classification: UNCLASSIFIED

Caveats: NONE

Classification: UNCLASSIFIED

Caveats: NONE

# Appendix B:

MCHE-CI

MEMORANDUM FOR Principal Investigator

SUBJECT: Latest Approved Informed Consent Form

1. Attached please find the reviewed Consent Form with approval stamp date. You must begin using a copy of this Consent Form with the approved stamp to document informed consent of all subjects.
2. Any future changes to Consent Form must be submitted and approved by the Institutional Review Board (IRB) before use.

Brooke Army Medical Center  
Protocol Office

**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

**Site Principal Investigator:** Michael L. Adams, Ph.D., LTC

**Overall Principal Investigator:** Paul B. Hicks, M.D., Ph.D. (Central Texas Veterans Health Care System, Waco, Texas)

**We are asking you to volunteer to take part in a research study at the Carl R. Darnall Army Medical Center. It is important that you read and understand the information on this form. If you choose not to participate in this research study, your decision will not affect your eligibility for care or any other benefits to which you are entitled.**

**DESCRIPTION/PURPOSE OF RESEARCH:**

You are being asked to consider participation in this research study. The purpose of this study is to determine whether the medication fluoxetine, often used to treat depression, is an effective treatment for posttraumatic stress disorder (PTSD) and associated conditions in soldiers with recent war-zone exposure, as well as determine whether any response to fluoxetine is related to the degree of trauma exposure, the severity of PTSD symptoms, resistance to psychological trauma, adequacy of social supports (family, outside the military and military), the degree of post-deployment stressors and life problems, or the degree of any loss of memory. Many soldiers exposed to war-zone stress do not appear to have subsequent problems, however, as many as 20% (or one in five) will develop significant mental health problems because of their war exposure. The fact that such a significant number of soldiers have difficulty adapting to life after war exposure suggests that we need to have well-defined, affordable treatments that are effective. Currently, recommendations for medications to manage PTSD focus on the use of commonly prescribed antidepressants such as fluoxetine. Despite this recommendation by the Department of Defense (DoD)/Veterans Administration (VA) Clinical Practice Guidelines, there have not been any studies evaluating the effectiveness of these medications in patients that have recently been exposed to war-zone stressors. In fact, studies in Vietnam-Era veterans have shown limited effectiveness of these medications for PTSD. Also, there is very limited information available to understand the factors that influence whether a particular soldier will respond to treatment with these antidepressants. The procedures of this study will help identify which individuals with PTSD are likely to benefit from these medications.

This study will enroll approximately 300 subjects at the Carl R. Darnall Army Medical Center, over a period of three years. During your participation in this study, you will be asked to make approximately 11 one to two hour outpatient visits with Dr. Paul Hicks, LTC Michael Adams or other supporting staff at the Resilience and Restoration Center of the Carl R. Darnall Army Medical Center. This study involves the investigational (research) use of a drug called fluoxetine



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

(the generic equivalent of Prozac). The Food & Drug Administration (FDA) has not yet approved this drug for treating PTSD. However, the FDA has not objected to its use to study its safety and effectiveness. The safety of fluoxetine (Prozac) in humans has been tested in prior research studies. Fluoxetine has been prescribed to millions of patients experiencing depression.

**INCLUSION AND EXCLUSION CRITERIA:**

To qualify for this study you must:

1. Be a veteran of the Operation Enduring Freedom/Operation Iraqi Freedom war campaigns with trauma exposure sufficient to qualify for a diagnosis of PTSD.
2. Meet criteria for a diagnosis of PTSD as determined by a standard questionnaire of symptoms, and have a minimum score on that questionnaire.
3. If you are female, you must have a negative blood pregnancy test and agree not to become pregnant for the duration of the study.

You will not be allowed to participate in this study if:

1. It is known that you are not able to tolerate fluoxetine.
2. It is known that you do not respond to fluoxetine at 60 mg daily.
3. You have a history of a significant mental disorder other than PTSD.
4. You have a significant history of suicidal or homicidal behavior/thoughts.
5. You have a history of dependence on any substances in the past 6 months.
6. You have a serious general medical condition that would prevent you from completing the study.
7. You have been using medications for depression or other mental health conditions except for zolpidem (Ambien) for the two weeks prior to beginning the study.
8. You are female and are found to be pregnant.
9. You have participated in another research drug trial within 30 days of enrollment.

**PROCEDURES:**

If you volunteer to participate in this study, we will ask you to do the following things:

1. If you are a qualified candidate and you agree to take part, the doctor will obtain your written informed consent to participate in this study. If you do participate, you must agree to carefully follow all the instructions that you are given.



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

2. Your medical history will be obtained and you will be physically examined by a physician associated with the study. For your own safety, it is your responsibility to tell the doctor all of your past and present diseases, allergies and medical conditions that you are aware of and all drugs and medications that you currently take.
3. Your height, weight, and blood pressure will be recorded.
4. A tablespoon (15 ml) of blood will be obtained at the first visit and at the sixth visit to estimate the degree of effect fluoxetine is producing on your brain chemistry.
5. Since this research may have bad effects on an unborn child and should not be performed during pregnancy, it is necessary that a pregnancy test be done first. If you are female a blood pregnancy test will be performed. To your knowledge, you are not pregnant at the present time. You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study.
6. As a participant, you will be asked to participate in two phases of this study. In the first phase, you will be randomly assigned to one of two treatments. Randomization is a process like flipping a coin and means you will have an equal chance of being assigned to either of the treatments. One of the two treatments will require you to take the study medication, fluoxetine (150 subjects), in increasing doses from 20 to 60 mg daily for a 12-week period. A second group will be assigned to receive placebo (150 subjects). A placebo is an inactive, harmless substance, like a sugar pill, that looks like the other study medications. You will have a one in two chance of being in the placebo group. The first phase of this study is a double-blind study, which means that neither you nor the study investigators will know whether you are receiving the study medication or a placebo. In the event of an emergency, however, there is a way to determine which you are receiving. **All subjects will continue to receive psychological treatments from their providers in the Resilience and Restoration Center at the Carl R. Darnall Army Medical Center throughout the study.**
7. In the second phase of this study you will be given fluoxetine in increasing doses, as needed, up to 80 mg daily for an additional 20 weeks. If you do not have significant improvement (greater than 50%) after being given 80 mg daily of fluoxetine for 4 weeks, then you will be assigned to also receive either bupropion (generic equivalent of Wellbutrin at 150 mg daily) or buspirone (generic equivalent of Buspar at up to 40 mg daily) for the remainder of the 20-week period in an attempt to improve your response to fluoxetine.



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT**

**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

8. The total participation time, including both phases of the study, will be 8 months duration.
9. The use of other prescription or over-the-counter medicines will not be allowed without your study doctor's approval. You will need to take part in regular outpatient visits while taking the study medication and must tell the study doctor of any side effects that you experience. During the study you should continue your normal dietary habits and vitamin intake. The use of tobacco will also be allowed during the study.
10. You will be asked to complete questionnaires and answer questions about your symptoms and feelings at the beginning of the study and also at weeks 2, 4, 6, 8, 12, 16, 20, 24, 28 and 32. The tests will normally be completed in about 30-45 minutes. The testing will take longer (up to 2 1/2 hours long) before the start of the 1<sup>st</sup>, after the 12<sup>th</sup> week of treatment, and after the 32<sup>nd</sup> week. Approximately 25% (one-fourth) of the interviews will have audio recordings made so that reliability of the questionnaire measurements can be assessed. After reliability measurements are completed, the audiotapes will be destroyed. The questionnaires will require you to answer questions about:
  - Your demographic information (e.g., age, race, education, etc.) and military service (e.g., rank, the number of years in the Service, etc.)
  - Any trauma you have experienced during your life
  - The amount of your combat exposure
  - Your symptoms and feelings, including anxiety, depression and PTSD symptoms
  - The stress and adversity your family has experienced since your deployment
  - The quality of your family relationships and social supports
  - The quality of your peer and leader supports
  - The quality of your physical health, activities of daily living, and overall life satisfaction
  - Your ability to withstand stressful events
  - Your memory, attention, and ability to use language
  - Whether there are any bad side effects to your study medications
  - Which medications you are taking
  - Your current use of alcoholic beverages
  - Your guess as to which treatment you are receiving
  - Your treatment expectations
11. Study personnel will also regularly assess your response to treatment and will ask detailed questions about the treatment effects and side effects. If your condition gets worse, the



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT**

**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

study medication may be stopped and you will be given other medication instead. If your condition improves you must still return for further visits until the study has finished.

12. If you need a procedure requiring additional informed consent, a separate consent form will be given to you before that procedure.
13. We will obtain information from your medical records concerning laboratory test results, medical diagnoses, pharmacy records, clinic and hospital visits, and any procedures performed.
14. Your name will not be mentioned in research publications that result from this study.
15. We cannot guarantee that you will be able to continue receiving fluoxetine after this study is over, but fluoxetine may be available through your family doctor.

**RISKS, STRESS OR DISCOMFORT:**

The potential side effects associated with the administration of fluoxetine include:

- nausea
- diarrhea
- restlessness
- headache
- sleeplessness
- inability to perform sexually (e.g. impotence, inability to have an orgasm, decreased sex drive)
- drowsiness
- tremors (shaking). If you receive placebo there may be less benefit and therefore the symptoms of PTSD may be present for a longer time.

Zolpidem may cause:

- drowsiness, the intended benefit
- diarrhea
- nausea
- dry mouth
- muscle aches
- dizziness
- headaches
- confusion



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT**

**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

- depression

Bupirone may cause:

- nausea
- dizziness
- headache
- blurred vision
- agitation

Bupropion may cause:

- elevated blood pressure (hypertension)
- increased heart rate (tachycardia)
- rash
- sweating
- constipation
- nausea
- dry mouth
- confusion
- dizziness
- sleeplessness
- hostility
- trembling, shaking
- seizures (convulsions)

Other side effects may occur, some of which are not known and cannot be predicted. If you follow instructions and help the staff perform the appropriate examinations and laboratory tests, the chance of these unwanted side effects happening can be kept to a minimum. If side effects occur, you should contact the staff so that appropriate step to reduce them can be taken.

Some clients may experience some disruption of daily activities due to scheduling of the evaluation sessions. Also, answering questions that evoke painful memories will likely be uncomfortable for many subjects. Although you are free to decline to answer any questions you find objectionable, it is important for the purpose of this study that you try to answer all questions.

It is possible that the study medication may not be effective and that your condition may worsen. If, in the opinion of your study doctor, there are any problems caused by the study medication





**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER**  
**INFORMED CONSENT DOCUMENT**  
**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of**  
**War Zone Stress Exposure**

that make it unwise for you to continue taking it, you will be withdrawn from the study and appropriately treated by your doctor.

If you are a FEMALE OF CHILD BEARING POTENTIAL wishing to volunteer for this project, you must understand that fluoxetine, bupropion, zolpidem or buspirone might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding. Studies evaluating the capability of the medication under investigation to produce birth defects in an unborn child have not been conducted. Therefore, you must not be pregnant during the study and will be required to take a pregnancy test before you participate in this study. You must also agree to take precautions to prevent pregnancy during the course of this study due to the possible severe harm the drug/procedure may cause your unborn child. The only completely reliable methods of birth control are total abstinence or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products may not be totally effective in preventing pregnancy. Also, you must not breast-feed and participate in this study.

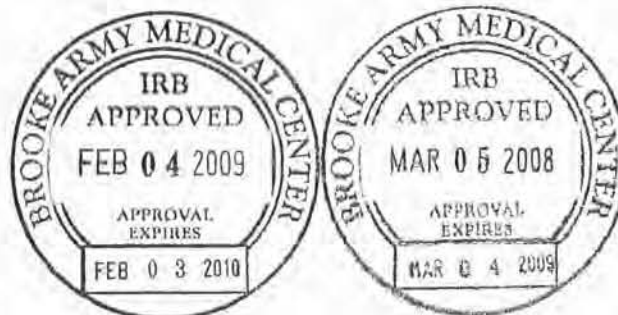
If you become pregnant or feel you might be pregnant, contact your provider and the study investigator listed in the voluntary participation section.

You will be kept informed of any significant new findings occurring during the course of the research that may influence your willingness to continue to participate in the study.

If you have any questions regarding the research, your participation, or suspect any research-related illness or injury, contact: **Dr. Michael Adams** at (254) 553-0921 or **Dr. Paul B. Hicks** at (254) 743-2643. After hours you may contact Dr. Paul B. Hicks, at (254) 760-8309.

**BENEFITS:**

The investigators have designed this study to learn if the new treatment is as good as or better than or worse than the most commonly accepted treatments. However, there is no guarantee or promise that you will receive any benefit from this study. The possible benefit of your participation in this study is that you are likely to receive some symptomatic improvement with the combination of psychological and pharmacological interventions offered in this study. If response is experienced, you will have symptomatic improvement and will likely be able to better adapt to current stressors in your life.



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT**

**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

There is no guarantee you will receive any benefit from this study other than knowing that the information may help future patients.

**PAYMENT (COMPENSATION):**

You will be paid \$50 for each blood draw for a maximum of \$100 for two blood draws.

**ALTERNATIVES TO PARTICIPATION:**

Participation in this study is entirely voluntary. **You may refuse to participate or may withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled.** If you decide to withdraw from the research study, notify the staff and/or study doctor of your intention to do so. The study doctor may stop your participation if it is determined to be in your best interest or if you fail to follow the directions of the study doctor.

You do not have to participate in this study to receive treatment for your condition. The medication involved in this study may also be available through your family doctor without the need for you to volunteer to participate in this study. Other drugs are available as alternatives to the drugs being tested in this study. These alternative medications include sertraline (Zoloft®), citalopram (Celexa® or Lexapro®), which are approved for the treatment of PTSD.

**RESEARCH RESULTS**

1. During the course of the study, you will be informed of any significant new findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation that might cause you to change your mind about continuing in the study. If new information is provided to you, your consent to continue participating in this study will be re-obtained.
2. All questionnaires and study materials will remain in the possession of the investigators at the Carl R. Darnall Army Medical Center. Only the investigators and their research associates will have access to these materials. They will be stored in a secured, locked location for three years after the completion of the study.
3. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. Your medical records will be maintained according to Department of Defense (DoD) requirements.



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

**CONFIDENTIALITY OF RECORDS OF STUDY PARTICIPATION:**

Records of your participation in this study may only be disclosed in accordance with federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. Your records may be reviewed by the U.S. Food & Drug Administration (FDA), other U.S. government agencies, as part of their official duties, the Brooke Army Medical Center Institutional Review Board, the Central Texas Veterans Health Care System (CTVHCS) and the Institutional Review Board. As a result, they may see your name; but they are bound by rules of confidentiality not to reveal your identity to others. Complete confidentiality cannot be promised, particularly for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities.

By signing this consent document, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.

**ENTITLEMENT TO CARE:**

In the event of injury resulting from this study, the extent of medical care provided is limited and will be within the scope authorized for Department of Defense (DoD) health care beneficiaries.

Your entitlement to medical and dental care and/or compensation in the event of injury is governed by federal laws and regulations, and if you have questions about your rights as a research subject or if you believe you have received a research-related injury, you may contact the Brooke Army Medical Center Protocol Coordinator at (210) 916-2598 or the Brooke Army Medical Center Judge Advocate General at (210) 916-2031 or the Carl R. Darnall Army Medical Center, Judge Advocate General, (254) 286-7339.

**SPECIAL INFORMATION:**

1. You are not required to take part in this study: your participation is entirely voluntary.
2. You can refuse to participate now or you can withdraw from the study at any time after giving your consent. This will not interfere with your regular medical treatment, if you are a patient.



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

3. There will be no costs to you for any of the treatment or testing done as part of this research study.
4. If you have questions about your rights as a research participant, you may contact **LTC Adams, Ph.D.** at (254) 553-0921.
5. If you are a patient, this consent form will be placed in your medical record and a copy will be kept in the research office.

**VOLUNTARY PARTICIPATION:**

The decision to participate in this study is completely voluntary on your part. No one has coerced or intimidated you into participating in this project. You are participating because you want to. The Principal Investigator or one of his associates has adequately answered any and all questions you have about this study, your participation, and the procedures involved. If significant new findings develop during the course of this study that may relate to your decision to continue participation you will be informed.

You may withdraw this consent at any time and discontinue further participation in this study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must contact Dr. Paul Hicks or a member of the study staff at the following number (254) 743-2643 or **LTC Michael Adams** at (254) 553-0921. You will be asked to complete end of study procedures. There are no consequences if you do not complete these procedures. Your condition will continue to be treated in accordance with acceptable standards of medical treatment.

The investigator of this study may terminate your participation in this study at any time if he/she feels this to be in your best interest. If you become ill during the research, you may have to drop out, even if you would like to continue. The investigator will make the decision and let you know if it is not possible for you to continue. The decision may be made either to protect your health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

**CONTACT INFORMATION:**

Site Principal Investigator (PI)

The Site Principal Investigator or a member of the research staff will be available to answer any of your questions concerning procedures throughout this study.



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL CENTER  
INFORMED CONSENT DOCUMENT  
Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of  
War Zone Stress Exposure**

Site Principal Investigator: **Dr. Michael Adams** at (254) 553-0921.

In addition, the Principal Investigator will also be available to answer any of your questions concerning procedures throughout this study.

Principal Investigator: **Dr. Paul B. Hicks** at (254) 743-2643.

You have read the information provided above. You have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction. You have been given a copy of this form. You agree to participate in this study on a voluntary basis. All oral and written information and discussions about this study have been in English, a language in which you are fluent.

A copy of this signed and dated form will be given to you.

\_\_\_\_\_  
**Volunteer's Signature**

\_\_\_\_\_  
**Volunteer's SSN**

\_\_\_\_\_  
**Phone #**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Volunteer's Printed Name**

\_\_\_\_\_  
**FMP Sponsor's SSN**

\_\_\_\_\_  
**Date of Birth**

\_\_\_\_\_  
**Volunteer's Address (street, city, state & zip code)**

\_\_\_\_\_  
**Advising Investigator's Signature**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Phone Number**

*(can only be signed by an investigator whose name is listed in the protocol)*



**BROOKE ARMY MEDICAL CENTER/CARL R. DARNALL ARMY MEDICAL  
CENTER  
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH  
INFORMATION FOR RESEARCH  
(APHI Template Version 3, February 04)**

You are being asked for permission to use or disclose your protected health information for research purposes in the research study entitled "Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure".

The Health Insurance Portability & Accountability Act of 1996, Public Law 104-109 (also known as HIPAA), establishes privacy standards to protect your health information. This law requires the researchers to obtain your authorization (by signing this form) before they use or disclose your protected health information for research purposes in the study listed above.

**Your protected health information that may be used and disclosed in this study includes:**

- Demographic information (e.g., age, race, education, etc.) and military service (e.g., rank, the number of years in the Service, etc.)
- Medical History/Surgical History
- Laboratory Results
- Responses to questionnaires

**Your protected health information will be used for:**

The purpose of this study is to determine whether the medication fluoxetine, often used to treat depression, is an effective treatment for posttraumatic stress disorder (PTSD) and associated conditions in soldiers with recent war-zone exposure, as well as determine whether any response to fluoxetine is related to the degree of trauma exposure, the severity of PTSD symptoms, resistance to psychological trauma, adequacy of social supports (family, extra-military and military), the degree of post-deployment stressors and life problems, or the degree of any loss of memory.

The disclosure of your protected health information is necessary in order to be able to conduct the research project described. Records of your participation in this study may only be disclosed in accordance with state and federal law, including the Privacy Act (5 U.S.C. 552a) and the Health Insurance Portability and Accountability Act of 1996 and its implementing regulations (45 CFR 160 & 164). Note: Protected health information of military service members may be used or disclosed for activities deemed necessary by appropriate military command authorities to ensure the proper execution of the military mission.



## Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure 2

By signing this authorization, you give your permission for information gained from your participation in this study to be published in medical literature, discussed for educational purposes, and used generally to further medical science. You will not be personally identified; all information will be presented as anonymous data.

### The Principal Investigator may use and share your health information with:

- The Brooke Army Medical Center/Carl R. Darnall Army Medical Center Institutional Review Board and the Central Texas Veterans Health Care System Institutional Review Board
- State and Federal Government representatives, when required by law
- Brooke Army Medical Center/Carl R. Darnall Army Medical Center Department of Defense representatives
- Other collaborating investigators:
  - Paul B. Hicks, M.D., Ph.D.  
Central Texas Veterans Health Care System

Brett Litz, Ph.D.  
VA Boston Health Care System

Keith Young, Ph.D.  
Central Texas Veterans Health Care System

Walter Penk, Ph.D.  
Texas A&M University HSC College of Medicine

Kathryn Kotrla, M.D.  
Texas A&M University HSC College of Medicine

Jed Goldart, M.D.  
Computer Technology Associates, Inc.

Tom Velez, Ph.D.  
Computer Technology Associates, Inc

The researchers and those listed above agree to protect your health information by using and disclosing it only as permitted by you in this Authorization and as directed by state and federal law.

You need to be aware that some parties receiving your protected health information may not have the same obligations to protect your protected health information and may re-disclose your



**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure** 3

protected health information to parties not named here. If your protected health information is re-disclosed, it may no longer be protected by state or federal privacy laws.

**You do not have to sign this Authorization. If you decide not to sign the Authorization:**

- It will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.
- You may not be allowed to participate in the research study.

**After signing the Authorization, you can change your mind and:**

- Notify the researcher that you have withdrawn your permission to disclose or use your protected health information (revoke the Authorization).

If you revoke the Authorization, you will send a written letter to:

Michael L. Adams, LTC  
Carl R. Darnall Army Medical Center  
Department of Psychology  
6000 Darnall Loop  
Fort Hood, Texas 76544-4752

to inform him/her of your decision.

- If you revoke this Authorization, researchers may only use and disclose the protected health information already collected for this research study.
- If you revoke this Authorization your protected health information may still be used and disclosed should you have an adverse event (a bad effect).
- If you withdraw the Authorization, you may not be allowed to continue to participate in the study.

During your participation in this study, you will not be able to access your research records. This is done to ensure the study results are reliable. After the completion of the study, you have the right to see or copy your research records related to the study listed above. A Request for Access must be made in writing to:

Michael L. Adams, LTC  
Carl R. Darnall Army Medical Center  
Department of Psychology  
6000 Darnall Loop  
Fort Hood, Texas 76544-4752

If you have not already received a copy of the brochure entitled "Military Health System Notice of Privacy Practices," you may request one. DD Form 2005, Privacy Act Statement - Military





**Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure 4**

Health Records (located on your medical records jacket), contains the Privacy Act Statement for the records. If you have any questions or concerns about your privacy rights, you should contact the Brooke Army Medical Center Privacy Officer at phone number (210) 916-9259 or Central Texas Veterans Health Care System Privacy Officer at 1-800-423-2111, ext 42003.

This Authorization does not have an expiration date.

You are the subject or are authorized to act on behalf of the subject. You have read this information, and you will receive a copy of this form after it is signed.

\_\_\_\_\_  
**Volunteer's Signature or  
Legal Representative**

\_\_\_\_\_  
**Volunteer's SSN**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Volunteer's Printed Name or  
Legal Representative**

\_\_\_\_\_  
**Sponsor's SSN**

\_\_\_\_\_  
**Relationship of Legal Representative to Volunteer**

\_\_\_\_\_  
**Signature of Witness**

\_\_\_\_\_  
**Date**



Appendix C:1

**Institutional Review Board (IRB)**  
**Temple VA Medical Center**  
 Temple, TX

**IRB APPROVAL - Continuing Review**

Date: March 23, 2009

From: Sandra Morissette, Ph.D., Interim Chairperson

Investigator: Paul B. Hicks, M.D., Ph.D.

Protocol: Predictors of Treatment Response to Fluoxetine in PTSD Following A Recent History of War Zone Stress Exposure

ID: 00308 Prom#: 0016 Protocol#: N/A

The following items were reviewed and approved at the 02/11/2009 meeting, contingent upon stipulations in each item marked with an asterisk (\*):

- Abstract (01/23/2009)
- \* Consent Form (01/23/2009)
- Consent Form - BAMC/Darnell Consent form
- Continuing Review - CTVHCS IRB Progress Report for continuing review (01/23/2009)
- Investigator Agreement (01/23/2009)
- Amended protocol (03/18/2009)
- \* Submission is needed of the missing attachments
- TO BE ANNOUNCE: Primary Reviewers Worksheet
- Project Data Sheet (01/23/2009)
- Request to Review Research Proposal/Project - Updated application for continuing review (01/23/2009)

Consent Form (01/23/2009) was returned to you with stipulations. The following revised items incorporate the stipulations and are now approved:

- Consent Form - Revised (03/18/2009)

Submission is needed of the missing attachments was returned to you with stipulations. The following revised items incorporate the stipulations and are now approved:

- Submission is needed of the missing attachments (03/23/2009; Scanned)

Approval is granted for a period of 12 months and will expire on 03/23/2010. Your Continuing Review is scheduled for 01/13/2010, and the requirements are attached.

The protocol was determined to have the following level of risk:  
 Minimal

The protocol was determined to have the following level of benefit to participants:  
 Prospect for direct benefit to participants

Page 1 of 3

The Central Texas Veterans Health Care System is not connected with, has no authority over, and is not responsible for human research conducted at any other institution, except where a Memorandum of Understanding specifies otherwise. Separate consent forms, initial reviews, continuing reviews, amendments, and reporting of serious adverse events are required if the same study is conducted at multiple institutions.

1. The IRB reviewed the above continued review documents at the February 11, 2009 meeting. The IRB members approved request for continued human use, for 12 months continuation, contingent upon the requested changes. The consent form must be amended as follows:

a. A statement must be added to the consent form regarding "the particular treatment or procedure may involve risks to the participant which are currently unforeseeable."

b. The approved data disposition statement must be added to the protocol under the section entitled "Data Confidentiality," i.e., "Any and all paper AND electronic documentation containing confidential personally identifiable information, protected health information, and any other sensitive information will be disposed/destroyed according to current VA regulations at the time of disposal/destruction of documentation." Need to also add to the protocol: use of data, disclosure of data, transfer/transmission of data, storage of data and return/destruction of data.

c. A Release of Information form is required in addition to the Health Insurance Portability and Accountability Act (HIPAA) form, which is an attachment to the informed consent form. The HIPAA form and protocol must be amended to state a Release of Information form will be signed if outside documents are requested.

d. DHL must be removed from the consent form as a means of mail delivery. FedEx is the only acceptable mail carrier for the documents.

e. The Human Firewall Subcommittee members will need to review the questionnaires to verify that they do not contain any data information.

2. The above revised documents were received with your memorandum dated March 18, 2009. These items were reviewed and approved by the IRB Chair as successfully addressing the stipulations required to approve the continuing review. The approval period is from March 24, 2009, to March 23, 2010.

3. The scanned questionnaires will be presented to the Human Firewall Subcommittee at the March 30, 2009, meeting.

4. You are complying with the institutional requirements for human subject protection and for documentation of the participation of human subjects in this study.

5. Your study will be subjected to further continuing review on March 23, 2010. Request the continuing review submission forms be submitted to this office on January 12, 2010, for review by the IRB. If the protocol or consent form is modified in any way or discontinued for any reason before the next continuing review, please notify the Subcommittee prior to placing any modifications into place. If modifications of any kind are put into place without IRB approval, this is a violation and non-compliance with federal and VHA regulations and policies.

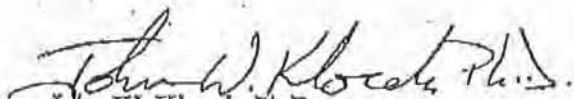
6. Unanticipated problems and serious adverse events of this study must be reported in writing by the investigator to this Subcommittee within 24 hours of the occurrence, whether or not these are attributed to the research project itself or to unrelated factors. In addition, adverse reactions to drugs must be reported to the

Page 2 of 3

The Central Texas Veterans Health Care System is not connected with, has no authority over, and is not responsible for human research conducted at any other institution, except where a Memorandum of Understanding specifies otherwise. Separate consent forms, initial reviews, continuing reviews, amendments, and reporting of serious adverse events are required if the same study is conducted at multiple institutions.

Committee on Pharmacy and Therapeutics.

7. The consent form with HIPAA language is approved (version dated 3/18/2009).
8. Thank you for your cooperation and for your support of our efforts to protect human subjects.
9. If you have any questions or concerns, please do not hesitate to contact Lorrie Thomas, Program Specialist/OA, at extension 41974.



John W. Klocek, Ph.D.  
CTVHCS IRB Chair

The following other committee reviews are scheduled:

- Subcommittee on Research Safety (SRS) [12/08/2009]
- Human Firewall Subcommittee (HFS) [01/04/2010]
- Research & Development (R&D) Committee [01/26/2010]

Approval by each of the following is required prior to study continuation (unless Exempt):

- Human Firewall Subcommittee (HFS) [Approval Granted 02/09/2009]
- Research & Development (R&D) Committee [Approval Granted 02/24/2009]

Approval for study continuation is contingent upon your compliance with the requirements of the Research Service for the conduct of studies involving human subjects.

The Central Texas Veterans Health Care System is not connected with, has no authority over, and is not responsible for human research conducted at any other institution, except where a Memorandum of Understanding specifies otherwise. Separate consent forms, initial reviews, continuing reviews, amendments, and reporting of serious adverse events are required if the same study is conducted at multiple institutions.

Institutional Review Board (IRB)  
Temple VA Medical Center  
Temple, TX

---

**IRB APPROVAL - Amendment**

Date: June 12, 2009

From: Marjory Williams, Ph.D., R.N., Chairperson

Investigator: Paul B. Hicks, M.D., Ph.D.

Protocol: Predictors of Treatment Response to Fluoxetine in PTSD Following A Recent History of War Zone Stress Exposure

ID: 00308 Prom#: 0016 Protocol#: N/A

The following items were reviewed and approved at the 06/10/2009 meeting:

- Memo fm PI re: review of study by OHRP guidelines (06/01/2009)

The following Institutional Review Board (IRB) members were not in attendance and did not vote: Paul B. Hicks, M.D., Ph.D.

1. The IRB members reviewed and approved the above protocol amendment, which consisted of a request for approval consideration by the IRB for the study being engaged in research with the main research site being listed as the Department of Defense (DoD), Carl R Darnall Army Medical Center, Resilience and Restoration Center, Fort Hood, Texas.
2. The above request was approved in accordance with the Office for Human Research Protections (OHRP) memorandum dated October 16, 2008, regarding Guidance on Engagement of Institutions in Human Subjects Research, Part IV, IRB Review Considerations for Cooperative Research. Under the OHRP guidelines the above study was previously reviewed by the full CTVHCS IRB and was presented at the June 10, 2009, meeting for determination of approval under the above guidelines.
3. The IRB determined that this is a multi-site study with the CTVHCS and the DoD. No portion of the study will be conducted at CTVHCS except for medication preparation and storage of de-identified data in an Excel spreadsheet on the VA server W-drive. Research subjects will be consented, monitored, and will receive follow-up at the research site, Carl R Darnall Army Medical Center, Resilience and Restoration Center, Fort Hood, Texas, in accordance with the approved protocol. Research subjects will only be active duty soldiers from Fort Hood and no veterans from CTVHCS will be participants. The CTVHCS IRB must review items for compliance only. The IRB of record will be the Brooke Army Medical Center (BAMC), which operates under FWA00004092.
4. As stated above, this study is approved with the BAMC as the IRB of record. The CTVHCS IRB must be informed of the following:

- a. The main site must currently have and continue to maintain an approved Federal Wide Assurance.
  - b. Any modification made to the protocol or informed consent must be presented to the IRB.
  - c. A mechanism must be in place to verify the BAMC continuing review process of the above study.
  - d. Any violations, deviations, adverse events, or serious adverse events must be submitted.
5. The above items will be submitted to the CTVHCS IRB as notification of actions taken by the BAMC IRB to ensure the study is being conducted in accordance with VA and Federal policies and procedure. CTVHCS is not the IRB of record.
6. If additional information is needed please contact Lorrie Thomas, Program Specialist, at extension 41974.



Marjory D. Williams, Ph.D., R.N.  
CTVHCS, IRB Chairperson

**Department of  
Veterans Affairs**

**Memorandum**

**Date:** June 1, 2009  
**From:** Paul B. Hicks, M.D., Ph.D., Principal Investigator (151)  
**Subj:** Institutional Review Board (IRB) Approval for Study 00308  
**To:** Chairperson IRB (151)

1. I request that the study entitled, "Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure (00308)" be approved by the IRB in accordance with the Office for Human Research Protections (OHRP) memorandum dated October 16, 2008, regarding Guidance on Engagement of Institutions in Human Subjects Research, Part IV, IRB Review Considerations for Cooperative Research.

2. Under the OHRP guidelines the above study can be reviewed and hopefully approved by the full CTVHCS IRB as being a multi-site study with the VA and the Department of Defense (DoD).


3. No portion of the study will be conducted at CTVHCS except for medication preparation and storage of de-identified data in an Excel spreadsheet on the VA server W-drive.

4. Research subjects will be consented, monitored, and receive follow-up at the research site, Carl R Darnall Army Medical Center, Resilience and Restoration Center, Ft Hood, Texas, in accordance with the approved protocol.

5. Research subjects will only be active duty soldiers from Fort Hood and no veterans from CTVHCS will be participants.

6. If approved using the above process, the CTVHCS IRB must review items for compliance only. The IRB of record will be Brooke Army Medical Center (BAMC), which operates under FWA00004092.

7. If additional information is needed, please contact me at 254-743-2643.

  
Paul B. Hicks, M.D., Ph.D.

Appendix D:

Research & Development (R&D) Committee  
Temple VA Medical Center  
Temple, TX

---

**APPROVAL - Continuing Review**

Date: February 25, 2009

From: Charles G. Burgar, M.D., Chairperson

Investigator: Paul B. Hicks, M.D., Ph.D.

Protocol: Predictors of Treatment Response to Fluoxetine in PTSD Following A Recent History of War Zone Stress Exposure

ID: 00308 Prom#: 0016 Protocol#: N/A

The following items were reviewed and approved at the 02/24/2009 meeting:

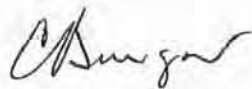
- Abstract (01/23/2009)
- Amendment - Update form and team member listing (01/23/2009)
- Conflict of Interest - Dr. Hicks (01/23/2009)
- Consent Form (01/23/2009)
- Consent Form - Revised consent form with data disposition info (01/07/2009)
- Continuing Review - SRS (02/11/2009)
- Continuing Review - CTVHCS IRB Progress Report for continuing review (01/23/2009)
- Project Data Sheet (01/23/2009)
- Safety Papers (01/23/2009)
- Request to Review Research Proposal/Project - Updated application for continuing review (01/23/2009)

The following Research & Development (R&D) Committee members recused themselves (or were otherwise excused) from deliberations and did not vote: Keith A. Young, Ph.D.

1. The R&D members approved your study. The approval period is for a 12-month continuation period from February 24, 2009 to February 23, 2010.
2. Your study will be subjected to further continuing review on February 23, 2010. Request the continuing review submission forms be submitted to this office on December 22, 2009, for review by the R&D. If the protocol is modified in any way or discontinued for any reason before the next continuing review, please notify the Subcommittee. If modifications of any kind are put into place without subcommittee approval, this is a violation and non-compliance with federal and VHA regulations and policies.



3. If you have any questions or concerns, please do not hesitate to contact Ruth Merton, Research Program Specialist, at extension 41787.



Charles G. Burgar, M.D.

The following other committee reviews are scheduled:

Subcommittee on Research Safety (SRS) [12/08/2009]

Human Firewall Subcommittee (HFS) [01/04/2010]

Institutional Review Board (IRB) [01/13/2010] ✓

Approval by each of the following is required prior to study continuation (unless Exempt):

Human Firewall Subcommittee (HFS) [Approval Granted 02/09/2009]

Research & Development (R&D) Committee

# Appendix G:

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT BETWEEN  
CLINICAL INVESTIGATION REGULATORY OFFICE  
U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND  
AND  
CENTRAL TEXAS VETERANS RESEARCH FOUNDATION

The Clinical Investigation Regulatory Office, U.S. Army Medical Research and Materiel Command (hereinafter "Federal Laboratory"), and Central Texas Veterans Research Foundation (hereinafter "Collaborating Party") enter into this Cooperative Research and Development Agreement (CRADA) for performing the medical Research, Development, Testing, and/or Evaluation (RDTE) work described in the Statement of Work (SOW) attached hereto as an Appendix, and agree as follows:

**Article 1**  
**General**

1.1. Authority. This CRADA is entered into pursuant to the Stevenson-Wydler Technology Innovation Act of 1980 as amended by the Federal Technology Transfer Act (Title 15, United States Code (U.S.C.) §§3701 et seq.), which permits directors of Federal laboratories to enter into cooperative research and development agreements and intellectual property licenses for intellectual property owned by or assigned to the United States Government. This is not a procurement contract, grant, or cooperative agreement as those terms are used in 31 U.S.C. §§6303, 6304, and 6305.

1.2. Entire Agreement. This CRADA includes the attached SOW (Appendix) and together they constitute a single, entire document hereinafter referred to as the "Agreement."

1.3. Purpose. The purpose of this Agreement is to expedite the transfer of federal technology from the Federal Laboratory to the private sector (represented by the Collaborating Party) through the sharing of resources and information towards the successful completion of the RDTE project (the "Study"). The medical objective of the Study is described in the SOW.

1.4. Statement of Work. The RDTE project, which is described in the SOW, will be conducted under a clinical research protocol which has been reviewed by the appropriate Institutional Review Board in accordance with Army Regulation 40-38, Clinical Investigation. The SOW incorporates all of the terms and provisions of these Articles by reference. In cases of apparent conflict between the terms and provisions of the SOW and these Articles, the terms and provisions of the Articles shall control.

1.5. Consideration. The Federal Laboratory and the Collaborating Party agree that they are entering into this Agreement for the mutual benefit of each Party. The Federal Laboratory and the Collaborating Party will cooperate in support of the clinical investigation protocol specified in the SOW. The RDTE project entered into under this Agreement will benefit the Federal Laboratory by providing valuable research experience for the Principal Investigator and medical residents involved and by providing valuable access to new drugs and medical devices for the medical treatment of Army patients. In addition, patients involved in the RDTE project may benefit directly from the medical treatment received and all medical patients will potentially benefit from the knowledge gained as a result of the RDTE project. The Collaborating Party will also benefit from the medical knowledge gained, through the evaluation of the clinical characteristics of emerging health technologies that will be applied for the public good.

1.6. Principal Investigator. The RDTE project conducted under the SOW will be supervised by a Principal Investigator named therein. The Principal Investigator may be changed for good cause by written notification to the other Party(ies).

1.7. Federal Laboratory Representative. The person signing this Agreement on behalf of the Federal Laboratory represents that he or she has the authority to enter into this Agreement. Notwithstanding this authority, the Secretary of the Army has reserved to the Assistant Secretary of the Army (Research, Development, and Acquisition) the authority provided by 15 U.S.C. §3710a(c)(5)(A) to disapprove or require modification of this Agreement within 30 days of the date it is presented to the Assistant Secretary. If the Assistant Secretary disapproves this Agreement, the Agreement is null and void. If the Assistant Secretary requires modification of this Agreement, the Collaborating Party shall have 30 days from notification of such

action to ratify the modification(s) or terminate this Agreement.

1.8. Collaborating Party Representative. The person signing this Agreement on behalf of the Collaborating Party represents that he or she has the authority to bind the Collaborating Party to the terms of this Agreement and the execution and delivery of this Agreement does not contravene any material provision of, or constitute a material default under, any material agreement binding on the Collaborating Party or any valid order of any court, any regulatory agency, or other body having authority to which the Collaborating Party is subject.

## Article 2 Definitions

2.1. "Agreement" refers to the entire CRADA including the SOW.

2.2. "Adverse Drug Experience" means an adverse event as defined under 21 C.F.R. §310.305, Records and Reports Concerning Adverse Drug Experience, and other applicable Federal Regulations.

2.3. "Background inventions" mean inventions other than subject inventions.

2.4. "Clinical Brochure" means a document containing all the relevant information about a drug, including animal screening, preclinical toxicology, and detailed pharmaceutical data. Also included, if available, is a summary of current knowledge about pharmacology, mechanism of action, and a full description of the clinical toxicities.

2.5. "Collaborating Party" means the person(s), intermediary(ies), or entity(ies), including medical and pharmaceutical companies, sponsoring a research project pursuant to this Agreement.

2.6. "Computer software" or "software" means computer programs, source code, source code listings, object code listings, designs, details, algorithms, processes, flow charts, formulae, and related material that would enable the software to be reproduced, recreated, or recompiled. Computer software does not include computer databases or computer software documentation.

2.7. "FDA" means the Food and Drug Administration, Department of Health and Human Services.

2.8. "Federal Laboratory" means the Clinical Investigation Regulatory Office, U.S. Army Medical Research and Materiel Command, Fort Sam Houston, which has been designated by the Secretary of Army as a Federal laboratory.

2.9. "Government" means the United States of America and the agencies thereof.

2.10. "Government purpose" means any activity in which the Government is a Party, including cooperative agreements with international or multinational defense organizations, or sales or transfers by the Government to foreign governments or international organizations, and competitive procurements. Government purpose does not include for commercial purposes.

2.11. "Invention" means any invention or discovery which is or may be patentable or otherwise protected under Title 35 of the United States Code or any novel variety of plant which is or may be protected under the Plant Variety Protection Act (7 U.S.C. §§2321 et seq.).

2.12. "Made" when used in conjunction with any invention means the conception or first actual reduction to practice of such invention.

2.13. "Party" or "Parties" refers to the Federal Laboratory, the Intermediary, or the Collaborating Party or all (in singular or plural usage as indicated by the context).

2.14. "Principal Investigator" means an individual who actually conducts a clinical investigation (i.e. under whose immediate direction a drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the Principal Investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team (21 C.F.R. §312.3).

2.15. "Proprietary information" means information which embodies trade secrets or which is confidential technical, business, or financial information provided that such information:

- a. is not generally known, or is not available from other sources without obligations concerning its confidentiality;
- b. has not been made available by the owners to others without obligation concerning its confidentiality;
- c. is not described in an issued patent or a published copyrighted work or is not otherwise available to the public without obligation concerning its confidentiality;
- d. can be withheld from disclosure under 15 U.S.C. §3710a(c) (7) (A)&(B) and the Freedom of Information Act, 5 U.S.C. §552 et seq; and
- e. is identified as such by labels or markings designating the information as proprietary.

2.16. "Raw Data" means the primary quantitative and empirical data first collected by the intramural and extramural investigators from experiments and clinical trials conducted under the scope of this Agreement.

2.17. "Subject data" means any technical data first produced in the performance of work under this Agreement.

2.18. "Subject invention" means any invention conceived or first actually reduced to practice in the performance of work under this Agreement.

2.19. "Technical data" means recorded information, regardless of the form or method of the recording, of a scientific or technical nature (including computer software documentation and databases). The term does not include computer software or data incidental to the administration of this Agreement, such as financial or management information.

### Article 3 Cooperative Research

3.1. Review of Work. Periodic conferences may be held between the Parties for the purpose of reviewing the progress of the cooperative effort. It is understood that the nature of this cooperative effort is such that completion within the period of performance specified or within the resources allotted cannot be

guaranteed. Accordingly, it is agreed that all cooperative research and development activities performed by either Party are to be performed on a best efforts basis.

3.2. Changes. If at any time the Principal Investigator, a Collaborating Party, or the Federal Laboratory determines that the research data dictates a substantial change in the direction of the work, he or she shall promptly notify the Parties, and the Parties shall make a good faith effort to agree to any necessary changes to the SOW consistent with the basic scope of research.

3.3. Assignment of Personnel. If the SOW contemplates the assignment of one Party's personnel to the other Party's facilities, then the employees shall remain employees of the assigning Party and will not be considered as employees of the other Party for any purpose, including but not limited to any requirements to provide workers' compensation, payment of salary or other benefits, or withholding of taxes. Assigned personnel will observe the other Party's security, safety, health, and environmental facility regulations. Assigned personnel can be denied access or removed by the other Party from its facilities at its discretion. Collaborating Party personnel assigned to a Federal Laboratory will work under the direction of the Principal Investigator only. That direction will be limited to matters within the scope of the actual research and will not extend to any matters that are normally encompassed by the employer-employee relationship. For example, the Collaborating Party is responsible for determining the working hours of its assigned personnel.

#### **Article 4** **Reports**

4.1. Progress Reports. As provided in the SOW, the Parties will prepare and exchange written reports, in a timely manner, on the progress of their work, results obtained, problems encountered, and recommendations for further research and development. To the extent reasonable, further detail concerning the contents of the reports shall be provided upon request, if necessary for the other Party to fully understand the results achieved. At a minimum, the Principal Investigator will submit annual progress reports to the Parties.

4.2. Final Report. As provided in the SOW, the Parties will prepare and exchange a final report at the completion of the

cooperative effort performed under this Agreement, on the progress of their work, results obtained, problems encountered, and recommendations for further research and development. To the extent reasonable, further detail concerning the contents of the report(s) shall be provided upon request if necessary for the other Party to fully understand the results achieved.

4.3. Adverse Drug Experiences, Annual Reports, Other Investigational New Drug Data. The Federal Laboratory will provide the Collaborating Party with copies of all adverse drug experience reports. The Federal Laboratory shall establish and maintain records and make reports to the FDA for the following Adverse Drug Experiences: (1) all serious, unexpected adverse drug experiences, (2) any significant increase in the frequency of serious unexpected adverse drug experiences, and (3) any significant increase in the frequency of therapeutic failure.

## **Article 5**

### **Transfer of Funds**

5.1. Payment Schedule. The payment schedule, described in the SOW, is subject to modification by mutual consent of all Parties in the event unforeseen circumstances arise which delay initiation of this project, including delays due to insufficient volunteer enrollment, actions from responsible review or regulatory authorities, lack of equipment, malfunctions, or insufficient support personnel. In the event of cancellation or termination of a research project, the Collaborating Party shall not be responsible for payments beyond such cancellation or termination date except for payments which have accrued prior to said date and as yet remain unpaid. The U.S. Government shall not reimburse the Collaborating Party for its expenditures prior to cancellation or termination of the research project.

5.2. Federal Laboratory. The Federal Laboratory shall not provide any Federal funds directly to the Collaborating Party. The Federal Laboratory shall contribute equipment, material and services toward the cooperative research and development effort as set forth in the SOW.

5.3. Collaborating Party. The Collaborating Party shall transfer funds and other resources to the Federal Laboratory for the performance of research and development as set forth in the SOW.



5.4. Salaries and Travel. Unless otherwise provided in the SOW, each Party shall provide financial support to its respective personnel in the performance of this Agreement, including salary, reimbursement for travel, and other expenses as appropriate.

5.5. Accounting Records. The Federal Laboratory and the Collaborating Party shall each maintain separate and distinct current accounts, records, and other evidence supporting all its expenditures under this Agreement. The accounts and records of the Federal Laboratory which are relevant to the conduct of this project shall be available for reasonable inspection and copying by the Collaborating Party or its authorized representative.

## Article 6 Personal and Real Property

6.1. Personal Property. Any tangible personal property provided by a Party during the performance of this Agreement shall remain the personal property of the Party providing it, unless otherwise agreed in the SOW. Property provided by a Party to another Party may only be used for the performance of the cooperative effort under this Agreement, unless otherwise agreed in the SOW. Government property may be repaired or modified by the Collaborating Party at its expense only after obtaining the written approval of the Federal Laboratory. Any repair or modification of the property shall not affect the title of the Government. The Federal Laboratory makes no warranty, express or implied, with respect to property contributed or loaned by it. Upon completion of the cooperative effort performed under this Agreement, each Party shall immediately account for the property in its possession and return, at its expense, all property belonging to the other Party in the condition in which it was received, normal wear and tear excepted. Any disposal of property shall be in accordance with applicable Federal, State, and local environmental laws and regulations.

6.2. Real Property. Any real property made available for use by a Party to another Party for the performance of this Agreement shall remain the property of the Party providing it. Any use of such property shall be in accordance with all applicable Federal, State, and local laws and regulations to include environmental laws and regulations.

**Article 7**  
**Patents**

7.1. Disclosure. Each Party shall promptly disclose in writing to the other Party subject inventions made by its employees or subcontractors in sufficient detail to enable someone with skill in the art to make and use the inventions.

7.2. Federal Laboratory Inventions. The Federal Laboratory, on behalf of the Government, shall retain title to each subject invention made solely by its employees. The Federal Laboratory may file patent applications on these subject inventions at its own expense. The Federal Laboratory grants to the Collaborating Party a royalty-free, nonexclusive, irrevocable license to practice or have practiced worldwide by or on behalf of the Collaborating Party subject inventions covered by any resultant patents. Such nonexclusive license(s) shall be evidenced by a confirmatory document prepared by the Federal Laboratory in a form satisfactory to the Collaborating Party.

7.3. Collaborating Party Inventions. The Collaborating Party shall retain title to each subject invention made solely by its employees. The Collaborating Party may file patent applications on these subject inventions at its own expense. The Collaborating Party grants to the Government a royalty-free, nonexclusive, irrevocable license to practice or have practiced worldwide by or on behalf of the Government for Government purposes subject inventions covered by any resultant patents. Such nonexclusive license(s) shall be evidenced by a confirmatory license agreement prepared by the Collaborating Party in a form satisfactory to the Federal Laboratory. If the Collaborating Party transfers or releases the rights to employee inventions provided for by this paragraph, such transfer or release shall be subject to the Government purpose license granted to the Government.

7.4. Joint Inventions. Title to subject inventions made jointly by employees of the Federal Laboratory and the Collaborating Party shall be held jointly by the Government and the Collaborating Party. The Collaborating Party shall have the initial option to file patent applications on joint subject inventions at its own expense.

7.5. Filing of Patent Applications. The Party having the right to retain title and/or file patent applications on a specific subject invention may elect to file patent applications thereon

provided it so advises the other Party within 120 days from the date of the report of the subject invention. In the event that the Party, having the right to file patent applications, fails to advise the other Party, within 120 days of the report of the subject invention, of its intent to file patent applications (and in which countries it intends to file), then the other Party may elect (but is not required) to file patent applications on such subject invention in those countries instead. If the other Party elects to file patent applications, the Party initially having the right to file patent applications on the subject invention agrees to assign to the other Party its rights, title, and interest in such subject invention in those countries in which the other Party elects to file, subject to the retention by the assigning Party of a royalty-free, nonexclusive, irrevocable license to practice or have practiced worldwide by or on behalf of that Party the subject invention covered by any resultant patents. The Party filing an application shall provide a copy thereof to the other Party.

NOTE: Any patent application filed on any invention made under this Agreement shall include in the patent specification thereof the statement: "This invention was made in the performance of a Cooperative Research and Development Agreement with the Department of the Army. The invention may be manufactured and used by or for the Government of the United States for all government purposes without the payment of any royalty."

7.6. Patent Expenses and Cooperation. The expenses attendant to the filing of patent applications as specified above shall be borne by the Party filing the patent application. Each Party shall provide the other Party with copies of patent applications it files in the U.S. Patent and Trademark Office or any foreign patent offices, along with the power to inspect and make copies of all documents retained in the official patent application file by the applicable patent office. The Party filing the patent application shall have the right to control the prosecution of the application. The Parties agree to cooperate with each other in the preparing and prosecution of patent applications.

7.7. Maintenance Fees. The fees payable to a patent office in order to maintain the patent's enforcement will be paid by the Party owning the patent. If that Party decides not to pay the maintenance fees, it shall promptly notify the other Party, who may pay the maintenance fees if it desires to maintain the enforcement of the patent.

7.8. Exclusive Licensing of Government Inventions. The Federal Laboratory, on behalf of the U.S. Government, agrees to grant, at the Collaborating Party's option, a limited-term, exclusive license in each Government invention (Federal Laboratory made and jointly made) subject to the reservation of a royalty-free, nonexclusive, paid-up license to practice and have practiced worldwide the subject invention by and on behalf of the U.S. Government for government purposes. The Federal Laboratory agrees to enter into negotiations with the Collaborating Party, as requested, for the exclusive licensing of Government inventions for any field of use at a fair and reasonable royalty rate to be negotiated in good faith. The Collaborating Party shall exercise the option to obtain an exclusive license by giving written notice thereof to the Federal Laboratory within three months after disclosure of the invention. The royalty rate and other terms and conditions of the license shall be set forth in a separate license agreement and shall be negotiated promptly after notice is given.

7.9. Assignment and Transfer. The Collaborating Party agrees that any nonexclusive license granted to the Collaborating Party by the Government pursuant to this Article may not be assigned, sublicensed, or otherwise disposed of except to a corporate affiliate of the Collaborating Party or to the successor of the Collaborating Party or its corporate affiliate. Exclusive licenses granted to the Collaborating Party pursuant to paragraph 7.8 may be sublicensed by the Collaborating Party.

7.10. Background Inventions. The Parties grant each other, to the extent that each has the authority to do so, expressed or implied, royalty-free, nonexclusive licenses to practice or have practiced on their behalf, background inventions necessary for the performance of work under this Agreement. However, this Agreement does not grant any implied licenses for practicing background inventions in the performance of work not being conducted under this Agreement.

7.11. Commercialization of Subject Inventions. The Collaborating Party agrees that with respect to any subject invention in which it has acquired title or an exclusive license under this Agreement, the Government has the right to require the Collaborating Party or an assignee or exclusive licensee of the subject invention to grant a nonexclusive license in any field of use to a responsible applicant or applicants upon terms that are reasonable under the circumstances, and if the Collaborating Party, assignee, or exclusive licensee refuses such request the

Government has the right to grant such a license itself, if the Government determines that one or more of the following conditions exist:

7.11.1. Practical Application. Such action is necessary because the Collaborating Party, assignee, or licensee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention. Practical application means to manufacture in the case of a composition or product; to practice in the case of a process or method; or to operate in the case of a machine or system; and, in each case, under conditions as to establish that the invention is being utilized and that its benefits are to the extent permitted by law or Government regulations available to the public on reasonable terms.

7.11.2. Health or Safety. Such action is necessary to alleviate health or safety needs which are not reasonably satisfied by the Collaborating Party, assignee, or licensee.

7.11.3. Public Use. Such action is necessary to meet requirements for public use specified by Federal regulation and such requirements are not reasonably satisfied by the Collaborating Party, assignee, or licensee.

7.12. Other Inventions. Inventions which are developed by either Party before or after the term of this Agreement remain the sole property of that Party.

## **Article 8 Copyrights**

8.1. Works Created by Collaborating Party. Ownership to copyrights for original works of authorship created solely by employees of the Collaborating Party or for hire by the Collaborating Party in the course of performance of work under this Agreement are retained by the Collaborating Party. The Collaborating Party shall mark any such works with a copyright notice showing the Collaborating Party as an owner and shall have the option to register the copyright at the Collaborating Party's expense. The Collaborating Party grants to the Government a royalty-free, nonexclusive, irrevocable license to use, modify, prepare derivative works, reproduce, distribute, perform, and display worldwide such copyrighted works by or on

behalf of the Government for Government purposes. The Collaborator will mark prominently each such copyrighted work with the words: "This work was created in the performance of a Cooperative Research and Development Agreement with the Department of the Army. The Government of the United States has a royalty-free government purpose license to use, duplicate or disclose the work, in whole or in part and in any manner, and to have or permit others to do so, for government purposes."

8.2. Joint Works. Ownership of copyrights for joint works prepared by employees of (or for hire by) the Federal Laboratory and the Collaborating Party in the course of performance of work under this Agreement are retained solely by the Collaborating Party. The Collaborating Party, however, grants to the Government a royalty-free, nonexclusive, irrevocable license to use, modify, prepare derivative works, reproduce, distribute, perform, and display worldwide such copyrighted works by or on behalf of the Government for Government purposes.

8.3. Software. The Party creating software in the course of the performance of work under this Agreement will provide the other Party with the source code, object code, and minimum support documentation needed by a competent user to use the software.

## **Article 9 Trademarks**

9.1. Trademark Use. The Parties recognize that the Collaborating Party may seek to obtain trademark protection for goods developed under this Agreement which it subsequently commercially markets. The Parties agree that the Government may indicate on any similar goods produced by or for the Government that the goods are a Government version of the goods protected by the trademark. The Government shall also have the right to use the trademark in print or communications media.

9.2. Qualifying Notice. Prior to the use of the trademark by the Government, the Parties will negotiate any reasonable qualifying language that must accompany the trademark.

## **Article 10 Proprietary and Protected Information**

10.1. Exchange of Data. The Parties agree to exchange all subject data produced in the course of the performance of this Agreement. All information or data exchanged between the Parties in the course of, or in contemplation of, this Agreement may be used and disseminated without restriction by the Parties for any purpose unless the data or information is proprietary or otherwise protected as provided in paragraph 10.2 or Article 8.

10.2. Proprietary and Protected Information.

10.2.1. Form. Proprietary or protected information may be disclosed to another Party orally, electronically, visually, in writing, or in any other tangible or intangible form. If it is initially disclosed in a nonfixed media, then the Party disclosing the data must furnish the other Party with the information in a fixed media with appropriate marking within ten days of its initial disclosure. Failure to furnish the fixed media within ten days or to prominently mark the information as proprietary or otherwise protected will not automatically result in the loss of the information's protected status, but will excuse any Party's unauthorized disclosure or use of the information caused by the failure to meet the ten-day suspense to properly mark the information.

10.2.2. Collaborating Party Background Information. The Collaborating Party shall place a proprietary legend on all proprietary information that it furnishes to the Federal Laboratory under this Agreement which was produced or obtained prior to this Agreement or during the term of this Agreement, but not in the course of the performance of this Agreement. The legend shall prominently and explicitly identify which material is proprietary and which material is not proprietary. Any such marked proprietary information furnished by the Collaborating Party to the Federal Laboratory under this Agreement, or in contemplation of this Agreement, shall be used by the Federal Laboratory only for the purpose of carrying out this Agreement and for Government administrative and oversight purposes. Such marked proprietary information, as long as it maintains its proprietary status, shall not be disclosed or otherwise made available outside the Government without the consent of the Collaborating Party.

10.2.3. Federal Laboratory Background Information. The Federal Laboratory shall place a nondisclosure legend on all protected

information it produced or obtained prior to this Agreement or during the term of this Agreement, but not in the course of the performance of this Agreement, that it furnishes to the Collaborating Party under this Agreement and that it asserts is protected. The legend shall prominently and explicitly identify which material is protected and which material is not protected. Any such marked protected information furnished by the Federal Laboratory to the Collaborating Party under this Agreement, or in contemplation of this Agreement, shall be used by the Collaborating Party only for the purpose of carrying out this Agreement. Such marked protected information, as long as it maintains its protected status, shall not be disclosed or otherwise made available to anyone other than the Collaborating Party without the consent of the Federal Laboratory.

10.2.4. Subject Data. Subject data produced by employees of either Party or jointly by employees of the Parties may be designated as protected material by either Party if such information would be proprietary information if obtained from a non-Federal Party. Unless a lesser period of time is set forth in the SOW, the Federal Laboratory will provide appropriate protection against dissemination of such information, including exemption from 5 U.S.C. Chapter 5, Subchapter II, for five years after the data is developed, unless the information loses its protected status earlier. The Federal Laboratory shall have the right to use subject data for government purposes. The Collaborating Party may use subject data for any purpose. Protected subject data must contain a prominent legend stating: (1) it is protected, (2) the rights to use of the Parties, and (3) the date the protected status is due to expire.

10.2.5. Other Proprietary or Protected Information. Proprietary or protected information other than subject data or background information that is furnished by the Collaborating Party to the Federal Laboratory under this Agreement and which is marked proprietary or protected shall be used by the Federal Laboratory only for the purpose of carrying out this Agreement and for Government administrative and oversight purposes. Such marked proprietary or protected information, as long as it maintains its proprietary or protected status, shall not be disclosed or otherwise made available outside the Government without the consent of the Collaborating Party. Proprietary or protected information other than subject data or background information that is furnished by the Federal Laboratory to the Collaborating Party under this Agreement and which is marked



proprietary or protected shall be used by the Collaborating Party only for the purpose of carrying out this Agreement. Such marked proprietary or protected information, as long as it maintains its proprietary or protected status, shall not be disclosed or otherwise made available to anyone other than the Collaborating Party without the consent of the Federal Laboratory.

10.2.6. FDA Documents. If this Agreement involves a product regulated by the FDA, then the Collaborating Party or the Federal Laboratory, as appropriate, may file any required documentation with the FDA. In addition, the Parties authorize and consent to allow each other or its contractor or agent access to, or to cross-reference, any documents filed with the FDA related to the product.

10.2.7. Standard of Care. Each Party is obligated to use reasonable care in the protection of proprietary and protected information.

## **Article 11**

### **Prepublication Review**

11.1. Publication. The Parties anticipate that their employees may wish to publish technical developments and/or research findings made under this Agreement. Each Party shall submit to the other Party prior to publication or other public disclosure, any proposed publication or disclosure pertaining to work under this Agreement. The other Party shall provide a written response within 30 days either objecting or not objecting to the proposed publication or public disclosure. The proposed publication or public disclosure shall not be deemed objectionable unless the proposed publication contains proprietary information, protected information, or material that would create potential statutory bars to the filing of U.S. or corresponding foreign patent applications, or for any other reasonable basis.

11.2. Protection of Proprietary Rights. If requested in writing by either Party, the Collaborating Party, the Principal Investigator, and/or the Federal Laboratory shall withhold such submission for publication an additional 60 days to allow for filing a patent application or taking such measures as the requester deems appropriate to establish and preserve its

proprietary rights in the information in the manuscript or disclosure.

## Article 12 Export Control

12.1. Compliance. The Parties understand that information and technology resulting from the performance of this Agreement may be subject to export control laws and regulations, and each Party is responsible for its own compliance with such laws and regulations. Nothing in this Agreement waives any such statutory or regulatory requirement.

## Article 13 U.S. Competitiveness

13.1. Manufacture. The Parties agree that a purpose of this Agreement is to provide substantial benefit to the U.S. economy. To the extent feasible, the Parties agree to exercise reasonable efforts to manufacture substantially in the United States, products embodying intellectual property developed under this Agreement.

## Article 14 Liability

14.1. NO WARRANTY. EXCEPT AS SPECIFICALLY STATED ELSEWHERE IN THIS AGREEMENT OR THE SOW, THE PARTIES MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO THE CONDITIONS OF THE RESEARCH, INVENTIONS, OR TECHNICAL DATA, OR PRODUCTS EXCHANGED, MADE, OR DEVELOPED UNDER THIS AGREEMENT, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE, TECHNICAL FEASIBILITY, OR FREEDOM FROM INFRINGEMENT OF INTELLECTUAL PROPERTY RIGHTS OF THE RESEARCH, INVENTIONS, TECHNICAL DATA, OR PRODUCTS. NEITHER PARTY SHALL BE LIABLE FOR LOST PROFITS, LOST SAVINGS, SPECIAL, CONSEQUENTIAL, INCIDENTAL, OR OTHER INDIRECT DAMAGES, EVEN IF SUCH PARTY IS MADE AWARE OF THE POSSIBILITY THEREOF.

14.2. Products Liability. To the extent not specifically prohibited by applicable State or local law, the Collaborating

Party agrees to indemnify and hold harmless the Government for any loss, claim, damage, expense, or liability of any kind occurring as a result of the making, using, or selling of a product, process, or service by or on behalf of the Collaborating Party, its assignees and licensees, which was derived from work performed under this Agreement. In respect to this provision, the Government shall not be considered an assignee or licensee of the Collaborating Party as a result of reserved Government rights under this Agreement. The Government's liability for losses, claims, damages, or expenses of the Collaborating Party occurring as a result of the making or using of a product, process, or service by or on behalf of the Government shall be governed by the provisions of the Federal Tort Claims Act.

14.3. Parties' Employees. To the extent not specifically prohibited by applicable State or local law, the Collaborating Party shall indemnify and hold harmless the Government for any loss, claim, damage, expense, or liability of any kind involving an employee or independent contractor of the Collaborating Party arising in connection with the performance of work under this Agreement, except to the extent that such loss, claim, damage, or liability arises from the negligence of the Federal Laboratory or its employees. The Government's liability for the loss of property, personal injury or death, or otherwise arising out of any negligent act or omission of its employees in connection with the performance of work under this Agreement shall be governed by the Federal Tort Claims Act.

14.4. Notice and Assistance. The indemnification provisions of this Article shall apply only if the Party upon which the claim or lawsuit is asserted gives the other Party prompt notice of the claim or lawsuit and allows that Party to participate in the defense/adjudication of the claim or lawsuit as is permitted by applicable laws and Government regulations.

## **Article 15**

### **Force Majeure**

15.1. Force Majeure Events. Neither Party shall be liable for any unforeseen event beyond its reasonable control not caused by the fault or negligence of such Party, which causes such Party to be unable to perform its obligations under this Agreement and which it has been unable to overcome by the exercise of due

diligence. Such unforeseen events include, but are not limited to, fire, storm, flood, earthquake or other natural catastrophes, accidents, acts of civil disturbance or disobedience, war, rebellion, insurrection, labor strikes or disputes, compliance with any laws, requirements, rules, regulations, or orders of any governmental authority or instrumentality thereof, sabotage, invasion, quarantine, and embargoes.

15.2. Best Efforts. The excused Party shall use its best efforts to resume performance as quickly as possible and shall suspend performance for only such period as is reasonably necessary as a result of the force majeure event.

#### **Article 16 Severability**

16.1. Contrary to Law. Any provision of this Agreement, to include the SOW, that is prohibited by applicable law is void, but the remaining provisions shall survive.

#### **Article 17 Termination**

17.1. Mutual Consent. The Parties may elect to terminate this Agreement, or portions thereof, at any time by mutual consent.

17.2. Unilateral Action. Either Party may unilaterally terminate this Agreement at any time by giving the other Party written notice, not less than 30 days prior to the desired termination date.

17.3. Termination Costs. Unless otherwise specifically provided in this Agreement, each Party shall be responsible for all of the costs for which it bears responsibility under this Agreement which have been incurred through the effective date of termination. Each Party shall be solely responsible for any costs it incurs after the effective date of termination.

17.4. Continuing Obligations. In the event of termination, the Parties shall specify the disposition of all property, patents, and other results of work accomplished or in progress under this Agreement, when such disposition is not otherwise specified in

this Agreement. All obligations under this Agreement to safeguard proprietary and other protected information and relating to rights in intellectual property or technical data shall survive any termination of this Agreement. The termination of this Agreement shall not affect the rights and obligations of the Parties accrued prior to the effective date of termination.

## **Article 18 Disputes**

18.1. Resolution Procedures. The Parties recognize that disputes arising under this Agreement are best resolved at the working level. Both Parties are encouraged to be imaginative in designing mechanisms and procedures to resolve disputes at the lowest level possible as soon as practicable. The Parties agree to use their best efforts to resolve any dispute amongst themselves. Any dispute arising under this Agreement which is not disposed of by agreement of the Parties at the working level shall be submitted jointly to the signatories of this Agreement or their successors or their designees for resolution. Although the Parties may agree to use alternate disputes resolution (ADR) techniques to resolve disputes, nothing in this Agreement precludes either Party from pursuing resolution of a dispute using other legal review available by law.

18.2. ADR Process and Costs. If the Parties decide by mutual consent on an appropriate ADR method (to include the choice of mediator, judge, or panel members), they shall bear the costs of the ADR process equally.

18.3. Obligations. Pending the resolution of a dispute pursuant to this Article, the Parties agree to diligently continue performing all obligations in accordance with the SOW.

## **Article 19 Modifications**

19.1. Modifications. If either Party desires to modify this Agreement, the Parties, upon reasonable notice of the proposed modification by the Party desiring the change, shall confer in good faith to determine the desirability of such modification. Any resulting modification shall not be effective until a

written amendment is signed by the duly authorized representatives of the Parties. Any material modification of this Agreement is subject to the authority of the Assistant Secretary of the Army (Research, Development, and Acquisition) as provided in paragraph 1.7 of this Agreement to disapprove or require modification within 30 days of the date it is presented to the Assistant Secretary.

#### **Article 20 Interpretation**

20.1. Entire Agreement. This Agreement includes Articles 1 - 27 and the SOW (Appendix). Together, they constitute the entire agreement between the Parties with respect to the subject matter hereof and all prior representations or agreements relating hereto have been merged into the documents and are superseded in totality by this Agreement.

20.2. Precedence. In the event of a conflict between the terms and provisions of the SOW and the terms and provisions in the Articles, the terms and provisions in the Articles shall control.

#### **Article 21 Notices**

21.1. Notices. All notices, pertaining to or required by this Agreement, shall be in writing and shall be delivered by hand or sent by certified mail, return receipt requested, express mail, or private delivery service addressed as specified below. Any Party may change such address by written notice given to the other Party in the manner set forth.

Mailing Address of Federal Laboratory:

Clinical Investigation Regulatory Office (ATTN: MCMR-RPC)  
U.S. Army Medical Research & Materiel Command  
1608 Stanley Road, Suite 2  
Fort Sam Houston, TX 78234-5055

Mailing Address of Collaborating Party:

Central Texas Veterans Research Foundation

Central Texas Veterans Health Care System (151)  
1901 S. Veterans Memorial Drive  
Temple, TX 76504

21.2 Waiver. None of the provisions of this Agreement shall be considered waived by any Party unless such waiver is given in writing to the other Party. The failure of a Party to insist upon strict performance of any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law, shall not be deemed a waiver of any right of any Party hereto.

#### **Article 22 Nonassignment**

22.1. Nonassignment. This Agreement may not be assigned or otherwise transferred by either Party without the prior written consent of the other Party.

#### **Article 23 Officials Not To Benefit**

23.1. Officials Not to Benefit. No member of Congress shall be admitted to any share or part of this Agreement, or to any benefit that may arise therefrom; but this provision shall not be construed to extend to this Agreement if made with a corporation for its general benefit.

#### **Article 24 Endorsements**

24.1. No Endorsements. By entering into this Agreement, the Federal Laboratory does not directly or indirectly endorse any product or service provided by the Collaborating Party, its successors, assignees, or licensees. The Collaborating Party shall not in any way imply this Agreement is an endorsement by the Government of any such product or service.

24.2. Use of Name. The Collaborating Party may use, refer to, and disseminate reprints of scientific, medical, and other published articles which disclose the name of the Federal Laboratory consistent with U.S. copyright laws, provided such

use does not constitute, or imply, an endorsement of any commercial product or service by the U.S. Government. The Collaborating Party shall take every step possible to ensure that references to the articles are accurate, and shall explicitly state that any such reference does not claim, infer, or imply an endorsement or recommendation of the product or service by Government investigators, the Federal Laboratory, or the U.S. Government. The Collaborating Party shall not use the name of the Principal Investigator or the Federal Laboratory in any advertising, packaging, or promotional material in connection with a product or service. The Principal Investigator and the Federal Laboratory shall not use the name of the Collaborating Party in any publication or presentation regarding the Study except with the written permission of the Collaborating Party or as may be required by law.

#### **Article 25 Governing Law**

25.1. The construction, validity, performance, and effect of this Agreement for all purposes shall be governed by the laws applicable to the Government of the United States.

#### **Article 26 Duration of Agreement**

26.1. Effective Date. This Agreement will be effective upon the date that the last Party signs this Agreement.

26.2. Duration. It is mutually recognized by the Parties that the objectives to be attained by this Agreement cannot be rigidly defined in advance and that projected milestones are subject to adjustment by mutual agreement of the Parties. Notwithstanding, this Agreement will not extend beyond the latest period of time stated in the SOW executed under this Agreement.

26.3. Continuing Obligations. All obligations under this Agreement to safeguard proprietary and other protected information and relating to publication, liability, rights in intellectual property or technical data existing at the termination or expiration of this Agreement shall survive the termination/expiration of this Agreement.



**Article 27**  
**HIPAA Compliance**  
**Privacy of Protected Health Information**

27.1. Definitions. As used in this clause:

*Individual* has the same meaning as the term "individual" in 45 CFR 164.501 and shall include a person who qualifies as a personal representative in accordance with 45 CFR 164.502(g).

*Privacy Rule* means the Standards for Privacy of Individually Identifiable Health Information at 45 CFR part 160 and part 164, subparts A and E.

*Protected Health Information* has the same meaning as the term "protected health information" in 45 CFR 164.501, limited to the information created or received by the Collaborating Party from or on behalf of the Government.

*Required by Law* has the same meaning as the term "required by law" in 45 CFR 164.501.

*Secretary* means the Secretary of the Department of Health and Human Services or his/her designee.

Terms used, but not otherwise defined, in this Agreement shall have the same meaning as those terms in 45 CFR 160.103 and 164.501.

27.1.1. The Collaborating Party agrees to not use or further disclose Protected Health Information other than as permitted or required by the Agreement or as Required by Law.

27.1.2. The Collaborating Party agrees to use appropriate safeguards to prevent use or disclosure of the Protected Health Information other than as provided for by this Agreement.

27.1.3. The Collaborating Party agrees to mitigate, to the extent practicable, any harmful effect that is known to the Collaborating Party of a use or disclosure of Protected Health Information by the Collaborating Party in violation of the requirements of this Agreement.

27.1.4. The Collaborating Party agrees to report to the Government any use or disclosure of the Protected Health Information not provided for by this Agreement.

27.1.5. The Collaborating Party agrees to ensure that any agent, including a subcontractor, to whom it provides Protected Health

Information received from, or created or received by the Collaborating Party on behalf of the Government agrees to the same restrictions and conditions that apply through this Agreement to the Collaborating Party with respect to such information.

27.1.6. The Collaborating Party agrees to provide access, at the request of the Government, and in the time and manner designated by the Government to Protected Health Information in a Designated Record Set, to the Government or, as directed by the Government, to an Individual in order to meet the requirements under 45 CFR 164.524.

27.1.7. The Collaborating Party agrees to make any amendment(s) to Protected Health Information in a Designated Record Set that the Government directs or agrees to pursuant to 45 CFR 164.526 at the request of the Government or an Individual, and in the time and manner designated by the Government.

27.1.8. The Collaborating Party agrees to make internal practices, books, and records relating to the use and disclosure of Protected Health Information received from, or created or received by the Collaborating Party on behalf of, the Government, available to the Government, or at the request of the Government to the Secretary, in a time and manner designated by the Government or the Secretary, for purposes of the Secretary determining the Government's compliance with the Privacy Rule.

27.1.9. The Collaborating Party agrees to document such disclosures of Protected Health Information and information related to such disclosures as would be required for the Government to respond to a request by an Individual for an accounting of disclosures of Protected Health Information in accordance with 45 CFR 164.528.

27.1.10. The Collaborating Party agrees to provide to the Government or an Individual, in time and manner designated by the Government, information collected in accordance with this Clause of the Agreement, to permit the Government to respond to a request by an Individual for an accounting of disclosures of Protected Health Information in accordance with 45 CFR 164.528.

## 27.2. General Use and Disclosure Provisions.

27.2.1. Except as otherwise limited in this Agreement, the Collaborating Party may use or disclose Protected Health Information on behalf of, or to provide services to, the Government for the following purposes, if such use or disclosure of Protected Health Information would not violate the Privacy Rule or the Department of Defense Health Information Privacy

Regulation if done by the Government to carryout the purposes of this Cooperative Research and Development Agreement as stated in the Statement of Work.

27.3. Specific Use and Disclosure Provisions.

27.3.1. Except as otherwise limited in this Agreement, the Collaborating Party may use Protected Health Information for the proper management and administration of the Collaborating Party or to carry out the legal responsibilities of the Collaborating Party.

27.3.2. Except as otherwise limited in this Agreement, the Collaborating Party may disclose Protected Health Information for the proper management and administration of the Collaborating Party, provided that disclosures are required by law, or the Collaborating Party obtains reasonable assurances from the person to whom the information is disclosed that it will remain confidential and used or further disclosed only as required by law or for the purpose for which it was disclosed to the person, and the person notifies the Collaborating Party of any instances of which it is aware in which the confidentiality of the information has been breached.

27.3.3. Except as otherwise limited in this Agreement, the Collaborating Party may use Protected Health Information to provide Data Aggregation services to the Government as permitted by 45 CFR 164.504 (e) (2) (i) (B).

27.3.4. Collaborating Party may use Protected Health Information to report violations of law to appropriate Federal and State authorities, consistent with 45 CFR 164.502(j)(1).

27.4. Obligations of the Government. Provisions for the Government to Inform the Collaborating Party of Privacy Practices and Restrictions.

27.4.1. Upon request, the Government shall provide the Collaborating Party with the notice of privacy practices that the Government produces in accordance with 45 CFR 164.520, as well as any changes to such notice.

27.4.2. The Government shall provide the Collaborating Party with any changes in, or revocation of, permission by Individual to use or disclose Protected Health Information, if such changes affect the Collaborating Party's permitted or required uses and disclosures.

27.4.3. The Government shall notify the Collaborating Party of any restriction to the use or disclosure of Protected Health

Information that the Government has agreed to in accordance with 45 CFR 164.522.

27.5. Permissible Requests by the Government.

27.5.1. The Government shall not request the Collaborating Party to use or disclose Protected Health Information in any manner that would not be permissible under the Privacy Rule if done by the Government, except for providing Data Aggregation services to the Government and for management and administrative activities of the Collaborating Party as otherwise permitted by this clause.

27.6. Termination.

27.6.1. A breach by the Collaborating Party of this clause, may subject the Collaborating Party to termination under any applicable default or termination provision of this Agreement.

27.7. Effect of Termination.

27.7.1. If this Agreement has records management requirements, the records subject to the Clause should be handled in accordance with the records management requirements. If this Agreement does not have records management requirements, the records should be handled in accordance with paragraphs (2) and (3) below.

27.7.2. If this Agreement does not have records management requirements, except as provided in paragraph (3) of this section, upon termination of this Agreement, for any reason, the Collaborating Party shall return or destroy all Protected Health Information received from the Government, or created or received by the Collaborating Party on behalf of the Government. This provision shall apply to Protected Health Information that is in the possession of subcontractors or agents of the Collaborating Party. The Collaborating Party shall retain no copies of the Protected Health Information.

27.7.3. If this Agreement does not have records management provisions and the Collaborating Party determines that returning or destroying the Protected Health Information is infeasible, the Collaborating Party shall provide to the Government notification of the conditions that make return or destruction infeasible. Upon mutual agreement of the Government and the Collaborating Party that return or destruction of Protected Health Information is infeasible, the Collaborating Party shall extend the protections of this Agreement to such Protected Health Information and limit further uses and disclosures of such Protected Health Information to those purposes that make the return or destruction infeasible, for so long as the Collaborating Party maintains such Protected Health Information.

27.8. Miscellaneous.

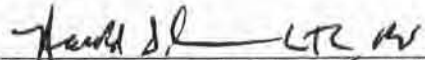
27.8.1. Regulatory References. A reference in this Clause to a section in the Privacy Rule means the section as in effect or as amended, and for which compliance is required.

27.8.2. Survival. The respective rights and obligations of Business Associate under the "Effect of Termination" provision of this Clause shall survive the termination of this Agreement.

27.8.3. Interpretation. Any ambiguity in this Clause shall be resolved in favor of a meaning that permits the Government to comply with the Privacy Rule.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives as follows:

For the U.S. Government (Federal Laboratory):

BY:  LTC MC DATE: 8 Oct 08  
Colonel Donald A. Gagliano, MC  
Director, Clinical Investigation Regulatory Office  
U.S. Army Medical Research & Materiel Command  
Phone Number: (210) 221-2511/9322

For Central Texas Veterans Research Foundation (Collaborating Party):

BY:  DATE: 10/27/08  
Debbie Boyd  
Executive Director  
1901 S. Veterans Memorial Drive  
Temple, TX 76504  
Phone Number: (254) 743-2295

**APPENDIX  
STATEMENT OF WORK**

A. IDENTIFICATION.

A.1. Subject Category: Medicine & Biology (Clinical Medicine), Code 57E, Title: "Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure." Short Title: "Fluoxetine in the Treatment of PTSD."

A.2. The Clinical Investigation Regulatory Office (Federal Laboratory) and Central Texas Veterans Research Foundation (Collaborating Party) desire to collaborate in research and development and will cooperate in support of the clinical investigation protocol at the Carl R. Darnall Army Medical Center (CRDAMC) entitled, "Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure," (the "Study") by Michael Adams, PhD (Principal Investigator), serving at the Carl R. Darnall Army Medical Center, 36000 Darnall Loop, Fort Hood, Texas 76544-4752, acting under the guidance of the Federal Laboratory.

A.3. This Statement of Work (SOW) is executed under authority of the Stevenson-Wydler Technology Innovation Act of 1980 as amended by the Federal Technology Transfer Act (15 U.S.C. §§3701 et seq.) and hereby incorporates all of the terms and provisions of the CRADA. Together, the CRADA and this SOW constitute the entire Agreement of the Parties. In the case of a conflict between the provisions of this SOW and the CRADA, the terms and provisions of the latter shall control.

B. PURPOSE.

B.1. Whereas, the Federal Laboratory and the Collaborating Party are entering into this Agreement for the mutual benefit of each Party. This joint research project will benefit the Collaborating Party by providing preliminary treatments for PTSD in future veterans. The project will benefit the Federal Laboratory by providing valuable research experience for the medical residents of the teaching program involved. In addition, patients at Carl R. Darnall Army Medical Center (CRDAMC) with Posttraumatic Stress Disorder will benefit through

---

facilitating studies of the use of fluoxetine to treat PTSD in active duty soldiers.

C. MEDICAL OBJECTIVE.

C.1. This project will attempt to demonstrate the efficacy of fluoxetine for the treatment of Posttraumatic Stress Disorder in soldiers with a recent history of war zone stress exposure.

D. DESCRIPTION OF WORK.

D.1. "Predictors of Treatment Response to Fluoxetine in PTSD Following a Recent History of War Zone Stress Exposure." 300 male/female outpatients, over 18 years of age, from the Carl R. Darnall Army Medical Center, will be enrolled in this study to determine whether fluoxetine can be used as a treatment for Posttraumatic Stress Disorder in soldiers recently returning from combat exposure.

D.2. There will be two phases to the study. In Phase I, fluoxetine + usual psychological care will be compared with placebo + usual psychological care over a 12-week period. Subsequently, in Phase II, all subjects will be offered the opportunity to enroll in a 20-week open-label trial on fluoxetine. If response is inadequate, adjunctive treatment with either buspirone or bupropion will be offered.

D.3. All performance under this SOW will cease at either the completion of the study, exhaustion of funds, unilateral or mutual termination, or 31 August 2013, whichever occurs first.

E. RESOURCES PROVIDED BY COLLABORATING PARTY.

E.1. The Collaborating Party will furnish the following research resources:

E.2. Investigational Drugs: Up to \$487,200.00 for 20mg capsules of Fluoxetine.  
To be provided at no cost by the Collaborating Party.

E.3. Approved Drugs Up to \$306.08 for 150mg tablets of

Bupropion SR.  
To be provided at no cost  
by the Collaborating Party.

Up to \$205.31 for 5mg tablets of  
Buspirone.  
To be provided at no cost  
by the Collaborating Party.

E.4. Consumable Supplies: Up to \$200.00 for 600 vaccutainer tubes for blood draws.

E.5. Loan of Equipment: The Collaborating Party will loan three desktop computers for the duration of the study. These computers are valued at \$1,500 each for a total of \$4,500.

E.6. Funds: The Collaborating Party shall pay Brooke Army Medical Center (BAMC) and Carl R. Darnall Army Medical Center (CRDAMC) \$2,200.00 as outlined in E.4. and E.7.

E.7. Other: The Collaborating Party will provide \$2,000.00 as reimbursement of IRB- and CRADA-related expenses to the Department of Clinical Investigation, Brooke Army Medical Center upon execution of this Agreement.

E.8. The above are hereinafter referred to as "Resources." Information relating to them, including data generated under this Agreement, is hereinafter referred to as "Information." CRDAMC agrees that the Resources and Information will be used for research and clinical purposes only as provided in this Agreement. The Resources shall not be sold, offered for sale, used for commercial purposes, or furnished to any other Party without advance written approval from the Collaborating Party.

E.9. Financial Obligation. The continued performance of research by Carl R. Darnall Army Medical Center (CRDAMC) under this Agreement is conditioned on the payment of funds to CRDAMC and BAMC by the Collaborating Party as specified below. CRDAMC and BAMC will use the accounting procedures as required by applicable Army and Defense Finance and Accounting Service regulations for the handling of funds during the performance of the research. Carl R. Darnall Army Medical Center shall not be obligated to perform any of the research specified herein or to take any other action required by this Agreement if the agreed-to funds are not transferred as required. The



expiration/termination of this Agreement does not extinguish the obligation to pay any funds which have been earned by, or are due and owed at, the date of expiration/termination.

E.10. Payment Schedule. The Collaborating Party is offering goods and services with an estimated value of up to \$494,411.30. Payment of funds will be made by the Collaborating Party when approval is granted for this Agreement.

E.11. Reimbursements. The Collaborating Party shall deposit funds in a distinct Department of the Army account under control of the Directorate of Resource Management, and managed by the Department of Clinical Investigation, Brooke Army Medical Center. The deposit shall be made in the form of a check made payable to the "Treasurer of the United States" and mailed to the following address:

Department of Clinical Investigation  
ATTN: Mr. Jeff Quillin (MCHE-CI)  
3400 Rawley E. Chambers Avenue, Suite A  
Fort Sam Houston, TX 78234-6315

E.12. Accounting Records. When funds are provided to Brooke Army Medical Center, it shall maintain distinct accounts, records, and other evidence supporting expenditures under this Agreement. Brooke Army Medical Center shall provide the Collaborating Party an annual report accounting for the use of funds and a final fiscal report within four months after completing this Agreement or ending its research activities under this Agreement, if requested by the Collaborating Party. The financial accounts and records pertaining to this Agreement shall be available for reasonable inspection and copying by the Collaborating Party or its authorized representative(s).

E.13. The Payment Schedule is subject to modification by mutual consent of all Parties in the event unforeseen circumstances delay initiation of this project, including delays due to: insufficient volunteer enrollment, actions from responsible review or regulatory authorities, lack of equipment or malfunctions, or insufficient support personnel.

F. RESOURCES PROVIDED BY FEDERAL LABORATORY. Support will be provided by the Carl R. Darnall Army Medical Center as outlined in the associated protocol.

G. REPORTS. Carl R. Darnall Army Medical Center agrees to report in a timely manner the results of any research conducted with the Resources to the Collaborating Party. Carl R. Darnall Army Medical Center agrees to provide all data supporting research results to the Collaborating Party.

H. PRINCIPAL INVESTIGATOR.

All notices required by this Agreement to be sent to the Principal Investigator will be sent to the following address:

Michael L. Adams, PhD  
Chief, Triage (R&R Center)  
Carl R. Darnall Army Medical Center  
36000 Darnall Loop  
Fort Hood, TX 76544-4752  
Phone Number: (254) 553-0921