TASK PLAN PP-3664-9

under the

MEMORANDUM OF UNDERSTANDING
CONCERNING COMBATING TERRORISM RESEARCH AND DEVELOPMENT
which entered into effect on MAY 17, 2006

Concerning

Biomarkers for Mild Traumatic Brain Injury, Blast Injury and Post Traumatic Stress Disorder
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INTRODUCTION

This Task Plan PP-3664-9 is made pursuant to Memorandum of Understanding between the Department of Defense of the United States of America and the Department of the Prime Minister and Cabinet of Australia (now Department of Defence of Australia) for Combating Terrorism Research and Development (CTRD MOU), the terms of which are hereby incorporated by reference. This Task Plan records the understandings of the Department of Defense of the United States of America (USDOD) and the Defence Science and Technology Organisation of Australia (DSTO) (the ‘Participants’) on Biomarkers for Mild Traumatic Brain Injury, Blast Injury and Post Traumatic Stress Disorder. For background information please refer to Annex A.

DEFINITION OF TERMS AND ABBREVIATIONS

<table>
<thead>
<tr>
<th>TERM</th>
<th>DEFINITION / ABBREVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHREC</td>
<td>Australian Defence Human Research Ethics Committee</td>
</tr>
<tr>
<td>BI</td>
<td>Blast injury</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRS</td>
<td>Magnetic resonance spectroscopy</td>
</tr>
<tr>
<td>mTBI</td>
<td>Mild traumatic brain injury</td>
</tr>
<tr>
<td>NRC</td>
<td>National Research Council of Canada</td>
</tr>
<tr>
<td>PTSD</td>
<td>Post traumatic stress disorder</td>
</tr>
<tr>
<td>2D COSY</td>
<td>Two Dimensional Correlated Spectroscopy</td>
</tr>
</tbody>
</table>

OBJECTIVES

The objectives of this Task Plan are to use MRI and MRS (specifically 2D COSY) to monitor neurochemical biomarkers. This will include the following activities:

1. Monitor soldiers before deployment and upon return
2. Use neurological and cognitive tests to identify PTSD, BI or mTBI in the returned soldiers.
3. Correlate the conventional clinical results with the MR results.
4. Follow those affected soldiers (identified by either or both MR and clinical results).
5. Develop classifiers to analyze the conditions of PTSD, BI and mTBI.

STATEMENT OF WORK

The following work will be conducted by the Participants under this Task Plan:

Over a two-year period MR scans of approximately 100 Australian soldiers based in Australia will be performed prior to deployment and upon their return. This may include Australian Federal Police, States Police and others. The MR scans will be conducted by DSTO. The data will then be processed by DSTO. The MR data will be correlated with neurological and cognitive testing undertaken by DSTO. The conditions of BI, mTBI, PTSD and chronic pain will be documented.
The allocation of the work will be as follows:

**DSTO will:**

1. Develop a research agreement to undertake the schedule of work as outlined in this Task Plan
2. Manage the conduct of the study in accordance with the objectives of this Task Plan
3. Deliver a final report

**USDOD will:**

1. Participate in progress and program management reviews and attend program meetings in Australia and the United States.
2. Provide technical feedback on the status of the program as necessary.
3. Review test plans and other project documentation and provide comments and feedback as necessary

### BREAKDOWN AND SCHEDULE OF WORK

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Due Date from Start in months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obtain ethics approval for the study of Australian soldiers in Australia</td>
<td>+3</td>
</tr>
<tr>
<td>Collect data from approximately 100 soldiers prior to deployment from Australia</td>
<td>+3-12</td>
</tr>
<tr>
<td>Collect data from the same 100 soldiers upon return</td>
<td>+13-23</td>
</tr>
<tr>
<td>Review and validate data correlation between scans and assessments</td>
<td>+13</td>
</tr>
<tr>
<td>Interpret the data using resonance ratios</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Monitor those affected every three months</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Review data for significance of correlation</td>
<td>+20</td>
</tr>
<tr>
<td>Develop classifiers for BI</td>
<td>+20-23</td>
</tr>
<tr>
<td>Report findings</td>
<td>24</td>
</tr>
</tbody>
</table>

The Task Managers will transmit quarterly status reports in an electronic format to the Program Managers.
FINANCIAL PROVISIONS

The participants estimate the cost to perform the STATEMENT OF WORK under this Task Plan to be US$2.10M. The following estimates apply:

<table>
<thead>
<tr>
<th></th>
<th>FY12</th>
<th>FY13</th>
<th>FY14</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Contributions</td>
<td>$185,000</td>
<td>$340,000</td>
<td>$525,000</td>
<td>$1.05M</td>
</tr>
<tr>
<td>Australian Contributions</td>
<td>$185,000</td>
<td>$340,000</td>
<td>$525,000</td>
<td>$1.05M</td>
</tr>
<tr>
<td>Total Contributions:</td>
<td>$370,000</td>
<td>$680,000</td>
<td>$1,050,000</td>
<td>$2.10M</td>
</tr>
</tbody>
</table>

Any cooperative efforts of the Participants over and above the jointly determined work set forth in the Statement of Work and Sharing of Work sections, or which exceed the participants’ total contribution established in this Task Plan, will be subject to amendment of this Task Plan or require approval of a new Task Plan.

MANAGEMENT

In accordance with paragraph 4.6 of the CTRD MOU, the task managers are:

Australia:

Dr Sarah Benson
Program Manager
F2 Fairbairn Business Park
Phone: 61-2-61286443
Sarah.Benson@dsto.defence.gov.au

United States:

Amanda Toman
Program Manager
4800 Mark Center Drive
Alexandria, VA 22350-2600
Phone: 1-571-372-7277
Email: amanda.toman@cttso.gov
PRINCIPAL ORGANIZATIONS INVOLVED

Australia:
- Defence Science and Technology Organisation
- Department of Defence and Veteran Affairs
- Australian Federal Police
- Australian States Police

United States:
- Department of Defense

DISPOSITION OF DELIVERABLES

Australia receives:
1. Clinical and MR data from soldiers before and after deployment,
2. Distinction between or common markers of PTSD, BI, PTSD compared to unaffected controls,

United States receives:
1. Clinical and MR data from soldiers before and after deployment,
2. Distinction between or common markers of PTSD, BI, PTSD compared to unaffected controls,

CLASSIFICATION

The highest level of Classified Information that may be exchanged under this Task Plan is: Restricted. This existence of this Task Plan is For Official Use Only and its contents are For Official Use Only.

COMMERCIALIZATION AND TECHNOLOGY TRANSFER

An International Technical Transition Plan will be required for the development effort, with a draft due for review within six months of the start of the effort, and a final draft no later than two months prior to completion of the effort. Plans will be sent to the TSWG Technology Transition Manager at TechTrans@TSWG.gov for review. The follow items are possibilities to consider in addressing a technical transition plan:

1. Description of the technology and its application(s).
2. Description of intellectual property to include ownership and license(s).
4. Description of principal and subcontractors and their responsibilities.
5. Discussion of applicable U.S., European, and International Standards.
6. Discussion of Test Plans.
7. Intended Market for the technology when commercialized.
8. Security considerations
9. Concept for Commercialization
10. Training and Operational Support

A format and detailed instructions for the International Technology Transition Plan, as well as assistance in developing the plan, can be obtained from the TSWG Technology Transition Manager.
ENTRY INTO EFFECT, DURATION AND TERMINATION

This Task Plan PP-3664-9 will enter into effect upon signature by the participants and will remain in effect for two years unless terminated under the conditions specified in the CTRD MOU. This Task Plan may be extended by written concurrence of the participants.

The respective benefits and responsibilities of the participants regarding 'Financial Provisions' and 'Entry into Effect, Duration and Termination' will continue to apply, notwithstanding termination or expiration of this Task Plan.

Task Manager for the United States

[Signature]

Task Manager for Australia

[Signature]

Date: 30 August 2012

Date: 21 September 2012

FOR OFFICIAL USE ONLY
Annex A:

PROBLEM STATEMENT/CURRENT STATUS

Head Injury: There is increasing recognition of immediate and long-term neurological problems from head injuries either by impact or blast. The current working hypothesis is these cause neurodegenerative changes resulting over time in a progressive decline of memory and executive functioning, depression, apathy, impulsivity, anger, irritability, suicidal behavior, and aggressiveness. These symptoms are considered precursors to dementia.

Autopsy studies on elite athletes with repetitive head injury reveal a distinct pattern of neuropathological changes, now known as chronic traumatic encephalopathy where tau-immunoreactive proteins in the cerebral cortex with a relative absence of beta-amyloid deposits. However, this protein can only be identified post-mortem, which cannot be used to identify brain injury in living subjects.

PTSD: The current conflicts in Iraq and Afghanistan, and the increasing burden of terrorism across the world, have resulted in a steady increase in the number of patients seen with military and military-type injuries. It is now realized that long and short term effects of PTSD can cause severe disfunctionality including behavioral instability that can result in disturbing outcomes such as unprovoked manslaughter. There is currently no established objective test for PTSD.

An increasing number of men and women serving in Australian forces are being diagnosed with PTSD after deployment with statistics indicating that 2% of the 3,000 deployed per annum are diagnosed with PTSD. This indicates that 60 soldiers per annum have symptoms consistent with the current subjective neurological testing. This figure is likely to be much higher. The outcome of PTSD can be a problem for security and/or terrorism. The cause is a chemical dysfunction in the brain caused by persistent unrelenting stress or impact.

Magnetic Resonance Spectroscopy: The new Two Dimensional MR Correlated Spectroscopy method provides an in life test to diagnose and monitor the effect of BI, mTBI and PTSD using MR on a clinical scanner.

The Goal: To generate data that will lead to the development of tools to diagnose and monitor the effect of BI, mTBI and PTSD, and make this available for use worldwide.
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D The University, in consideration of the Contract Sum has agreed to carry out such research, being the research project more particularly described in Schedule 1 to this Agreement.

E The Commonwealth has approved the making of the Contract Sum available to the University on the conditions set out in this Agreement.
<table>
<thead>
<tr>
<th>Contract Sum</th>
<th>means the financial assistance specified in Item J of Schedule 1 to be provided by the Commonwealth under the Agreement for expenditure on the Research Project</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specified Personnel</td>
<td>means the personnel specified in Schedule 1 as personnel required to undertake the Research Project or part of the work constituting the Research Project</td>
</tr>
</tbody>
</table>
3. THE CONTRACT SUM

3.1 The Commonwealth shall, subject to the observance by the University of the provisions of this Agreement, pay the Contract Sum to the University in the amount, at the time or times and in instalments (if any) as specified in Item N of Schedule 1, upon receiving the invoices therefore and provide to the University such other assistance as is specified in Schedule 1.

3.2 Without limiting the rights of the Commonwealth, the Commonwealth may at its absolute discretion withhold, suspend or reduce the Contract Sum due under this Agreement in whole or in part until the University has performed, to the Commonwealth’s satisfaction, its obligations under this Agreement.
3.3 The University shall use the Contract Sum only for the Research Project and not for any other purpose.

3.4 The University shall provide from its own resources the facilities and services necessary for the efficient conduct of the Research Project other than those approved facilities and services to be acquired from the Contract Sum as specified in Schedule 1.

4. PAYMENT

4.1 Where Schedule 1 provides that the University is to be paid by progressive instalments, linked to the achievement of milestones in the Research Project, the Commonwealth shall be entitled, without derogating from any other right it may have, to defer payment or reduce the amount of any instalment if and so long as the University has not completed to the satisfaction of the Commonwealth that part of the Research Project to which that instalment relates.

4.2 Where a claim for payment is approved, the Commonwealth shall make payment within 30 days of the approval of the claim unless agreed otherwise.

5. TAXES AND DUTIES

5.1 Except as provided by this clause 5, all taxes, duties and government charges imposed or levied in Australia or overseas in connection with the performance of this Agreement shall be borne by the University.

5.2 The amounts payable under this Agreement include an amount to cover any liability of the University for Goods and Services Tax (GST) on any supplies made by the University under this Agreement which are taxable supplies within the meaning of the A New Tax System (Goods and Services Tax) Act 1999 (the GST Act).

5.3 In relation to taxable supplies made under this Agreement, the University agrees that it will issue the Commonwealth a tax invoice in accordance with the GST Act prior to payment by the Commonwealth of the Contract Sum.
8. SPECIFIED PERSONNEL

8.1 the Research Project in accordance with the terms of this Agreement.

8.2 The University must ensure that the Specified Personnel have or are eligible to obtain security clearance to the required level of the national security sensitivity and classification of the Research Project.

8.3 Where Specified Personnel are unable to undertake work in respect of the Research Project, the University must notify the Commonwealth immediately and will, if so requested by the Commonwealth and after consultation with the Commonwealth, provide replacement personnel acceptable to the Commonwealth at no additional charge and at the earliest opportunity.

8.4 The Commonwealth may, at its absolute discretion, give notice requiring the University to remove personnel (including Specified Personnel) from work in respect of the Research Project. The University will promptly arrange for the removal of such personnel from work in respect of the Research Project and their replacement with personnel acceptable to the Commonwealth.

8.5 If the University is unable to provide a replacement with suitable skills or in a sufficient time to enable the University to complete the Research Project, the Commonwealth may terminate the Agreement in accordance with clause 17.
8.6 Any requirement to replace any of the University's personnel during the course of the Research Project (whether at the request of the Commonwealth or not) will not constitute an act or event that is beyond the reasonable control of the University in meeting the requirements of the Agreement.

9. STUDENT PARTICIPATION

9.1 Subject to clause 9.2, the Commonwealth agrees that a person who is studying a course related to the Research Project who is not appointed as an employee of the University, but is a student of the University (the 'Student'), may work on the Research Project as part of his or her studies, provided that:

(a) the Student is not the recipient of an Australian Postgraduate Award (unless the University can provide evidentiary material to the satisfaction of the Commonwealth, that the payment to the Student out of the Contract Sum is an over award payment to the Student reflecting the value of the Student to the Research Project and is not payment to the Student for research in the field/s already covered by an Australian Postgraduate Award).

9.2 In addition to the requirements set out in clause 9.1, the Student can only work on the Research Project provided that the University obtains prior to the Student commencing work on the Research Project:

(a). the Commonwealth's written approval prior to any participation of the Student in the Research Project; and

(b). a deed poll from the Student in a form acceptable to the Commonwealth under which the Student:

i. assigns to the University any Intellectual Property in any Developed Material he or she creates under or otherwise in connection with the Research Project;

ii. agrees to maintain confidentiality and not disclose to any third party any Developed Material, Commonwealth Material and information arising from, or related to the Research Project; and

iii. agrees, subject to the prior written approval of the Commonwealth, to only make use of the Intellectual Property referred to in clause 9.2(b)i for the purpose of producing an academic thesis or other academic papers as part of the Student's undergraduate or postgraduate studies (“the Examinable Material”).

9.3 The Commonwealth may impose any terms and conditions it considers appropriate when giving its approval under clause 9.2(b)iii.
9.4 The Parties agree that any Examinable Material is to be treated as Confidential Information unless otherwise indicated by the Commonwealth.

9.5 Where the Commonwealth provides its approval in accordance with clause 9.2 (b)iii, the University agrees to obtain from the Student the relevant Examinable Material prior to any examination of the same by the University for assessment for academic grading purposes and provide it to the Commonwealth.

9.6 The Commonwealth will consider the Examinable Material provided by the University in accordance with clause 9.5 and determine at its sole discretion whether its disclosure or examination should in any way be restricted. The Commonwealth will consider the Examinable Material within 30 days of receipt.

9.7 For the avoidance of doubt nothing in this Agreement shall prevent the Student from producing Examinable Material as part of their PhD studies.

9.8 Where the Commonwealth determines that the disclosure or examination should be restricted, the Student will still be able to have their Examinable Material assessed and graded provided that the University:

(a) notifies the Commonwealth of the details of the proposed examiners prior to any such examination; and

(b) obtains written consent from the Commonwealth, which consent will not be unreasonably withheld, to the engagement of the examiners to assess the Examinable Material.

9.9 The Commonwealth may require the University to obtain from the examiners referred to in clause 9.8 a form of non-disclosure agreement as directed by the Commonwealth prior to any such examination.

9.10 The University agrees to provide the executed deed poll required under clause 9.2(b) to the Commonwealth prior to the Student commencing any work on the Research Project.
18. FINANCIAL PROVISIONS

18.1 The liability of the Commonwealth to support the Research Project is limited to the Contract Sum stipulated in Schedule 1.

18.2 The University must ensure that

(a) any moneys forming part of the Contract Sum are, upon receipt, deposited in an appropriate bank account;

(b) the account referred to in clause 18.2 will be in the form of a general ledger item identified by a unique project number which is established for the sole
purpose of accounting for, and administering, any moneys forming part of the
Contract Sum provided by the Commonwealth under this Agreement and
separate from the University's operational accounts; and
(c) income and expenditure in relation to the Contract Sum are recorded separately
from other transactions of the University.

18.3 Contract Sum moneys that have not been spent or committed for expenditure in the
Contract Period must be repaid by the University to the Commonwealth within 3
months of the end of the Contract Period or such other period as may be agreed in
writing by the parties.

18.4 A commitment for expenditure of Contract Sum moneys must not be made where the
resultant expenditure is likely to occur more than 3 months after the end of the
Contract Period.

18.5 Except with the prior written approval of the Commonwealth, the University must
not use any of the following as any form of security for the purpose of obtaining or
complying with any form of loan, credit, payment or other interest:

a. the Contract Sum;

b. this Agreement or any of the Commonwealth's obligations under this
   Agreement; or

c. any Capital Items.
27. OTHER FINANCIAL ASSISTANCE

27.1 The University agrees to inform the Commonwealth in writing should it receive financial assistance from a third party for the Research Project during the Contract Period.
Item E. Specified Personnel

Professor Carolyn Mountford
Director, Centre for MR in Health
University of Newcastle
Aus cell: +61 419 255 866
e-mail: Carolyn.mountford@newcastle.edu.au

- Program director

Program Manager
Item J. **Contract Sum**

The Contract Sum is **$77G** (plus GST). The Contract Sum will be paid in instalments as specified in the payment schedule at Item N below.

The Research Project will be funded through the following means:

<table>
<thead>
<tr>
<th>Source</th>
<th>Cash</th>
<th>In-kind</th>
<th>Total (AUD, excluding GST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSTO / Defence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uni of Newcastle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Item K.
Item L  Assistance

Not Applicable