1. **NUMBER – TITLE OF TASK AUTHORIZATION**


2. **VALIDATION OF SCOPE OF CONTRACT**

2.1 The following task(s), as written in the SOW of the main contract (W7714-145967/001/SV) apply to this Task Authorization (TA):

   a. **Field Studies and Trials** - Design and conduct studies and trials, including clinical trials.

   b. **Data Analysis** - Perform state of the art analysis of data from experimental studies, clinical trials, field studies or trials, and existing databases.

   c. **Presentations to Government and Health Care System Stakeholders** - Prepare and deliver presentations to Government and Healthcare system stakeholders.

3. **ACRONYMS**

   - CAF: Canadian Armed Forces
   - CAPS: Clinician Administered PTSD Scale
   - DSM: Diagnostic and Statistical Manual
   - fMRI: Functional Magnetic Resonance Imaging
   - PTSD: Post-Traumatic Stress Disorder
   - SA: Scientific Authority
   - SGHRP: Surgeon General Health Research Program
   - TA: Task Authorization

4. **REQUIREMENT**

4.1 Moral injury is an emerging construct to more fully capture the many possible psychological, ethical, and spiritual/existential challenges among soldiers who served in modern wars. To conduct a prospective cohort study in Canadian Armed Forces (CAF) personnel and veterans experiencing Post-Traumatic Stress Disorder (PTSD) to identify specific neural activation patterns and blood-based biomolecular signatures associated with the processing of traumatic memories, which may stem in part from situations they experienced during deployment(s) that conflicted with their beliefs about what is and is not morally/ethically appropriate.

5. **BACKGROUND**

5.1 CAF personnel serving in combat zones are confronted with ethical and moral challenges, most of which are navigated successfully because of effective rules of engagement, training, leadership, and the purposefulness and coherence that arise in cohesive units during and after various challenges. However, even in optimal operational contexts, some combat and operational experiences can inevitably transgress deeply held beliefs that undergird a military member’s humanity. Transgressions can arise from individual acts of commission or omission, the behaviour of others, or by bearing witness to intense human suffering or the grotesque aftermath of battle. An act of serious transgression that leads to serious inner conflict because the experience is at odds with core ethical and moral beliefs is termed **moral injury** (Thompson, 2015).

5.2 On a conceptual level, moral injury is different from long-established post-deployment mental health problems. Until recently, it had been assumed that the chief cause of post-combat mental health problems was life-threat trauma and to a lesser degree war-zone traumatic loss(es). It is increasingly evident that the psychological effects of warzone exposure can go beyond just fear-related conditioning and anxiety caused by being put into
potentially life-threatening positions during deployment. Members of the military also encounter situations that may come into conflict with their own deeply held beliefs around what is and is not morally/ethically correct behaviour, which in turn can also affect their psychological and social functioning post-deployment. Moral injury is believed to be caused by events in which the individual perpetrated, witnessed, failed to prevent, or learned about later that occurred while on operations that violated deeply held moral beliefs or ethical standards and caused the individual significant inner conflict (Litz et al., 2009). Although recognized extensively in historical literature and descriptive accounts, there is renewed interest in the emotional, spiritual, and psychological wounds that stem from the ethical and moral challenges that warriors face in combat, especially nontraditional forms of combat, such as guerilla war in urban environments (Drescher et al., 2011).

5.3 Research suggests that morally injurious acts such as killing and atrocities are associated not only with PTSD (particularly re-experiencing and avoidance, rather than hyperarousal), but also with a host of other mental health problems and debilitating outcomes. The link between guilt and suicide, a putative outcome stemming from moral injury, is also an important area of inquiry. Being the target of killing or injuring in war is associated with PTSD and being the agent of killing or failing to prevent death or injury is associated with general psychological distress and suicide attempts. Indeed, combat guilt was found to be the most significant predictor of both suicide attempts and preoccupation with suicide and self-harm behaviours, suggesting that guilt may be an important mediator (Brian et al., 2014).

5.4 Although the idea that war can be morally compromising is not new, empirical research about moral injury is in its infancy, and there are more unanswered questions than definitive answers at this point. A recent systematic review (Nazarov et al., 2015) confirmed that, based on published studies, strong evidence exists that links direct and indirect exposure to such situations and feelings of guilt and shame, feelings that have in turn, been linked with a variety of averse mental health outcomes including PTSD. Neuroimaging studies have been done with individuals who have been diagnosed with PTSD resulting from long-term, repeated interpersonal traumas such as childhood sexual abuse (Lanius et al., 2002, 2011; Bluhm et al., 2011) and suggests specific neural targets for treatment of PTSD and its dissociative subtype (Daniels et al., 2016); however, similar studies have not been conducted with individuals whose incident trauma was acute and occurred later in life as would be the case with veterans. As well, the existence of specific central neurological and peripheral biological underpinnings of how morally injurious events are processed, and more specifically, how repeatedly recalling these events (a common component of many psychotherapeutic approaches to treating PTSD) might be processed has not been determined. The research study proposed herein aims to fill this knowledge gap.

6. OBJECTIVES

6.1 The primary aim of the proposed study is to determine the neural activation patterns of CAF members and veterans when exposed to 1) reminders of morally injurious traumatic events, 2) reminders of traumatic but not morally injurious events, and 3) reminders of neutral, non traumatic events.

6.2 A second aim is to determine what affect the virtual presence of another individual has on neural activation patterns while the participant is in the heightened emotional state brought about by the aforementioned traumatic memory presentation.

6.3 A third aim is to evaluate a panel of promising blood-based biomarkers that may be associated with the risk/resilience for PTSD and suicidality in association with moral injury.

7. SCOPE

7.1 The Contractor must conduct a prospective observational cohort study to investigate the to identify neural activation patterns associated with the processing of traumatic memories in CAF members and veterans experiencing
PTSD which may stem in part from situations they experiences during deployment(s) that conflicted with their beliefs about what is and is not morally/ethically appropriate; that is to say, they have experienced a “moral injury.”

7.2 To achieve these aims, three (3) groups of men: two (2) groups will be composed of CAF members/veterans who have experienced a traumatic event during a deployment (30 individuals diagnosed with PTSD according to the Clinician Administered PTSD Scale [CAPS] for the DSM-5; and 30 CAF members/veterans who do not have a lifetime history of PTSD), and one (1) group of Healthy Control participants (30 males with no military history) who have experienced a traumatic event at some point in their lives. All participants who meet inclusion criteria and agree to participate will be administered a series of standard psychological measures to assess the individual for the presence of psychiatric disorders, trauma history, symptoms of anxiety and depression, and other relevant symptoms, as well as be asked to undergo an fMRI.

7.3 The scope of work will include the following:
   a. The contactor must conduct all planning, coordination, training, execution, and implementation necessary to conduct the longitudinal observational cohort study, including participant recruitment¹, clinical assessments, neuroimaging, and biological sample collection; and
   b. The Contractor must ensure they have adequate resources for designing, testing, and implementing the trial and are staffed for the data collection, statistical analysis and publication of the resulting research findings.

8. APPLICABLE DOCUMENTS & REFERENCES

¹ CAF subjects will be recruited under separate CFHS Joining Instructions with the assistance of the SA.
9. TASKS TO BE PERFORMED

Phase 1 - Study Planning and Scoping

9.1 Prepare Human Subjects Research Ethics Protocols for submission to each of the participating institutional Research Ethics Boards for approval;

9.2 Develop a Research Protocol for a longitudinal observational cohort study to investigate the natural course of disease/recovery from PTSD in CAF members and veterans (including, but is not limited to: subject recruitment plan with benchmarks; data management plan; blood collection plan; statistical analysis plan);

9.3 Recruit and train all required staff – including, but not limited to, clinicians, therapists, graduate students/postdoctoral fellows, and technicians in accordance with the approved Research Protocol; and

9.4 Purchase all necessary equipment and clinical/laboratory supplies.

Phase 2 – Subject Testing and Data Collection

9.5 Initiate enrolment of eligible volunteers in accordance with institutional and regulatory guidelines to complete fMRI neuroimaging in CAF members/veterans. CAF subjects will be recruited under separate CFHS Joining Instructions with the assistance of the SA;

9.6 Monitor participant enrolment and data quality metrics;

9.7 Coordinate participant data collection (i.e., clinical evaluation, neuropsychological testing, fMRI analyses, blood sample collection) and establish a database; and

9.8 Coordinate biological specimens storage at Contractor’s site during course of study and shipment of remaining samples to DRDC Toronto for subsequent analysis of selected genomic and proteomic biomarkers.

Phase 3 – Data Analysis and Reporting

9.9 Complete all data analysis, statistical analyses, and tabulation/presentation of results in accordance with standard scientific publishing guidelines;

9.10 Prepare and submit Quarterly Progress Reports summarizing study progress to date. The March progress report each year will summarize all results/findings to date, and provide conclusions and recommendations with respect to the requirement to pursue the study;

9.11 Prepare and submit a Draft Study Report and a Final Study Report detailing all evidence-based data captured during the conduct of the entire study; including executive summary, background, objectives, methods, results, conclusions, and recommendations for future research directions in this domain;

9.12 Prepare and submit a PowerPoint presentation to present research findings at scientific meetings; and

9.13 Prepare draft scientific manuscripts, in association with the SA and DRDC co-investigators, suitable for publication in the open peer-reviewed literature.

10. DELIVERABLES (DESCRIPTION AND SCHEDULES)

All deliverables must be submitted and completed by March 2019. The Contractor must prepare and submit the following deliverables to the SA:
ANNEX A

- STATEMENT OF WORK -
Task Authorization (TA) – 27

FOR SUB CONTRACT WITH CIMVHR

<table>
<thead>
<tr>
<th>Deliverable Number</th>
<th>Task reference</th>
<th>Description (Quantity and Format) and Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1</td>
<td>9.1</td>
<td>Human Subjects Research Ethics Protocols for submission to each of the participating institutional Research Ethics Boards no later than 1 month after the authorization to begin work.</td>
</tr>
<tr>
<td>10.2</td>
<td>9.2</td>
<td>Research Protocol to be delivered no later than 2 months after the authorization to begin work.</td>
</tr>
<tr>
<td>10.3</td>
<td>9.10</td>
<td>Quarterly Progress Reports to be submitted every 3 months.</td>
</tr>
<tr>
<td>10.4</td>
<td>9.11</td>
<td>Draft Study Report no later than 30 days prior to the end of the research project. The SA will require no more than 5 business days to provide feedback to the Contractor.</td>
</tr>
<tr>
<td>10.5</td>
<td>9.11</td>
<td>A Final Study Report addressing issues and concerns identified by the SA on the Draft Study Report to be submitted within 15 days of receipt of feedback from the SA.</td>
</tr>
<tr>
<td>10.6</td>
<td>9.12</td>
<td>PowerPoint presentation no later than 1 month prior to scientific meeting</td>
</tr>
<tr>
<td>10.7</td>
<td>9.13</td>
<td>Draft scientific manuscript(s) suitable for publication in open literature no later than 30 days prior to the end of the TA.</td>
</tr>
</tbody>
</table>

11. MANDATORY SELECTION CRITERIA

11.1 This prospective observational cohort study must be completed by a world-leading Canadian fMRI and PTSD clinical and academic investigator group.

12. LANGUAGE OF WORK

12.1 Documentation and deliverables must be submitted in the English language.

13. LOCATION OF WORK

13.1 The bulk of the work (i.e., patient enrolment, neuroimaging, blood sampling, clinical assessments) must be performed on the Contractor’s site. Contract staff (i.e., a postdoctoral fellow) will require access to DRDC Toronto to assist with the specialized biomolecular analyses using DRDC’s flow cytometric and imaging cytometry laboratories.

14. TRAVEL

14.1 The Contractor may be required to travel to present research findings at scientific meetings. Contractor travel must have the prior written authorization of the Scientific Authority and the Technical Authority, and must be undertaken in accordance with the National Joint Council Travel Directive and with the other provisions of the directive referring to "travellers", rather than those referring to "employees".

14.2 Travel expenses incurred by DND/CAF personnel participating in this study are not chargeable under this TA.

14.3 Actual travel costs incurred by Canadian citizens (civilians) who volunteered to participate in this study will be reimbursed where applicable.

15. MEETINGS

None
FOR SUB CONTRACT WITH CIMVHR

16. GOVERNMENT SUPPLIED MATERIAL (GSM)

None

17. GOVERNMENT FURNISHED EQUIPMENT (GFE)

None

18. SPECIAL CONSIDERATIONS OR CONSTRAINTS

18.1 See Section 11.

19. SECURITY

19.1 The Contractor will not require access to PROTECTED and/or CLASSIFIED information or assets. The security classification for the work is “UNCLASSIFIED”. The Contractor will be escorted at all times while at DRDC Toronto.

☐ RELIABILITY STATUS ☐ PROTECTED A ☐ PROTECTED B

20. INTELLECTUAL PROPERTY (IP) OWNERSHIP

20.1 The Contractor will own any Foreground IP created by virtue of the main contract (W7714-145967/001/SV).

21. CONTROLLED GOODS

X Not applicable
☐ Applicable

22. BUDGET

The Sub Contractor will be paid by CIMVHR as per the terms of Contract # W7714-145967 between Defence Research and Development Canada and CIMVHR. The amount of funding available is allocated by fiscal year (April 1 - March 31st) and is approximately $450,000 over 3 years ($180,000 for 2016-17, $150,000 for 2017-18 and $120,000 for 2018-19. Details TBD upon award.

A draft budget must be submitted with the proposal along with a budget justification. A detailed budget will be developed post award in consultation with CIMVHR. Interested parties should request budget documents and information on creating their budget from Jocelyne Halladay.