National Defence Défense nationale

- STATEMENT OF WORK -
Task Authorization (TA) – 62

1. NUMBER– TITLE OF TASK AUTHORIZATION

TA 62 – Investigating Intra-articular Treatment Strategies for Early-Stage Joint Tissue Damage In the Canadian Armed Forces

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. **Experimental and Clinical Studies** - Design and conduct of experiments involving both human and animal studies.

b. **Tools and Treatments -** Develop software or hardware tools and pharmacological products related to the diagnosis and treatment of healthcare issues in the target population.

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

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

e. **Advice -** Provide recommendations on peer review research proposals, publications, experimental studies, surveys, and scientific evidence.

3. ACRONYMS

CAF	Canadian Armed Forces
CFHS	Canadian Forces Health Services
DRDC	Defence Research and Development Canada
OA	Osteoarthritis
PRP	Platelet-Rich Plasma
SA	Scientific Authority
SGHRP	Surgeon General Health Research Program
TA	Task Authorization

4. REQUIREMENT

4.1 The following services of the Sub Contractor are required: investigate the etiology of post-traumatic knee osteoarthritis (OA) through advanced molecular medicine and engineering techniques, perform *in vitro* and/or *in vivo* investigations of post-traumatic osteoarthritis disease progression, investigate Health Canada Approved pharmacological and regenerative medicine attenuation strategies, document all procedures and generate output data tables for generation of academic publications/manuscripts by DRDC and/or other labs.

5. BACKGROUND

5.1 The objective of the research contract is to study Osteoarthritis disease progression and develop an intra-articular treatment protocol that can be used by the Canadian Armed Forces for members suffering from mild to moderate Osteoarthritis. It is expected that the treatment protocol will include a well-studied regenerative medicine technique, Platelet-Rich Plasma (PRP) therapy.

5.2 Despite the number of previous trials that have been conducted, there is a specific need to evaluate PRP preparation protocols and identify characteristics of a standard treatment schedule (i.e., total number of injections and frequency of treatment). Furthermore, a more robust understanding of the mechanism of therapeutic action is required and the characteristics of the PRP preparation that would qualify as a suitable dose for maximal therapeutic benefit. The indications and contraindications of a suitable patient is also an area requiring further research.

5.3 Due to the physical demands of certain military occupations, past studies have shown a disproportionate number of Osteoarthritis cases at each age range of a military population, compared to the general public (see Talbot, 2020). The goal of the work is to be able to treat/rehabilitate mild to moderate cases of post-traumatic Osteoarthritis with an intra-articular injection and regular physical therapy.

6. OBJECTIVES

6.1 Investigate post-traumatic osteoarthritis disease progression from initial injury onwards to better understand the role of intra-articular treatments.

6.2 Evaluate all available PRP preparation protocols to determine the characteristics of a dose that will have the maximum therapeutic benefit.

6.3 Identify characteristics of a standard treatment schedule and any indications/contra-indications for PRP therapy.

6.4 Identify the indications, and contraindications, for a patient that is likely to respond well to treatment.

7. SCOPE

7.1. The Sub Contractor will provide research study documentation, in the form of a contract report and draft scientific manuscripts (see 10.5 and 10.7, below) outlining a suitable protocol for Platelet-Rich Plasma therapy, and acceptablebiochemistry characteristics of a prepared dose.

7.2. To achieve this aim, the Sub Contractor will perform the following:

a. Thoroughly test different platelet-rich plasma therapy preparation protocols to identify one that consistently results in doses of maximal therapeutic benefit.
b. Utilize leading *in vitro* and/or *in vivo* techniques to evaluate differences in protocols.
c. Document all procedures, protocols, trial notes, and final data for internal and external reporting and publication.

7.3 The Sub Contractor must ensure they have adequate resources for developing study design, writing proceduresand protocols, experimentation, and statistical analysis.

8. APPLICABLE DOCUMENTS & REFERENCES

FORCE Evaluation Operations Manual, 3rd Edition (2021). Retrieved from www.cafconnection.ca/force_evaluation.

Talbot, M. Joint replacements in the Canadian Armed Forces. Canadian Journal of Surgery. 2020; 63(5): E409-E411. Doi:10.1503/CJS.016419

9. TASKS TO BE PERFORMED

9.1 Prepare and submit Progress Reports every 2 months summarizing all results/findings to date, and provide conclusions and recommendations with respect to the requirements. Current versions of all data tables, notes, and laboratory protocols to be included with the Bimonthly Progress Reports. Regularly updating a shared virtual folder with all such documentation for review by DRDC and CFHS co-investigators will be acceptable in lieu of the Bimonthly Progress Reports.

9.2 Write and submit protocols for research ethics approval of all studies.

9.3 Purchase all necessary equipment and laboratory reagents/supplies.

9.4 Recruit all participants for Tissue Collection (Blood Draw) and for human *in vivo* studies.

9.5 Perform a full, thorough biochemical investigation of PRP therapy preparation protocols for identification of procedures that consistently result in doses that are expected to have maximal therapeutic benefit. It is expected that the Sub Contractor will test platelet-rich vs. platelet-poor plasma, leukocyte-rich vs. leukocyte-poor preparations, platelet activation/degranulation, plasma vs. serum, etc.

9.6 Investigate the PRP preparation protocols from Task 9.5 with *in vitro* OA models to evaluate the cellular responses to the different preparations.

9.7 Clinically investigate the different PRP preparation protocols from Tasks 9.5 and 9.6 to determine which protocol offers the most therapeutic benefit, which is to be defined by improved function on physical tasks, improved range of motion, and patient reported outcomes. The trial must have a proper control group and blinding (single-blind). Utilization of leading clinical disability and pain scales is expected (e.g., WOMAC). The patient population must be representative of the CAF. Specifically, patients must be 16 to 60 years of age, with a minimum physical activity level of 3hrs per week, and be able to meet the standard of each element of the CAF annual FORCE test. The FORCE test consists of the following:

a. Sandbag lift – Thirty (30) consecutive lifts of a 20kg sandbag from the floor to above a height of 1.0m within 3.5mins, alternating between left and right sandbags that are laterally separated by 1.25m.
b. Intermittent Loaded Shuttles – Ten (10) consecutive shuttles (1 shuttle = 20m there, 20m back), alternating between loaded shuttles with a 20kg sandbag and unloaded shuttles, totaling 400m, in a maximum time of 5:21 (min:sec).
c. Sandbag Drag – Carry one 20kg sandbag and pull a minimum of 4x20kg sandbag over 20m without stopping.
d. 20m Rushes – starting from a prone position, complete two shuttle sprints (1 shuttle = 20m there, 20m back dropping to the prone position every 10 m for a total of 80 m, in maximum time of 51 seconds.

Exclusion criteria will include the following: inflammatory arthritis, moderate to advanced OA (Kellgren & Lawrence grade III or above), previous injection to the joint. A minimum of 40 participants in total across all trial groups will be included in the study.

9.8 Complete all data analyses, statistical analyses, and tabulation/presentation of results in accordance with standard scientific publishing guidelines.

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

9.10 Prepare and submit a Draft Contract Report and a Final Contract Report detailing all evidence-based data captured over the course of the TA; including executive summary, background, objectives, methods, results, conclusions, and recommendations for future research directions in this domain. The Sub Contractor Report will be published for public viewing on a Government of Canada website. The SA will provide a report template to the research team.

10. DELIVERABLES

All deliverables must be submitted and completed by 16 March 2022. The Sub Contractor must prepare and submit thefollowing deliverables:

Deliverable Number	Task reference	Description (Quantity and Format) and Schedule	Quantity and Format	Delivery Date
10.1	9.1	Bimonthly Progress Reports. The SA will approve the Progress Reports and/or provide feedback within one business day. SA approval is required for work to continue.	Electronic format, Microsoft Word.	Every 2 months after issuance of Task Authorization.
10.2	9.2	Submit Research Ethics Protocol for collection of human biological fluids.	REB Clearance to be forwarded to SA upon receipt. Electronic format, Microsoft Word.	10 weeks after issuance of Task Authorization.
10.3	9.2, 9.7	Submit Research Ethics Protocol for final data collection with human participants.	REB Clearance to be forwarded to SA upon receipt. Electronic format, Microsoft Word.	10 weeks after issuance of Task Authorization.
10.4	9.5	Submit written, detailed procedures for generation of each autologous intra-articular therapy that was tested.	Electronic format, Microsoft Word.	16 weeks after issuance of Task Authorization.
10.5	9.9	Submit Draft Scientific Manuscripts suitable for publication in open literature.	Electronic format, Microsoft Word.	By 11 March 2022.
10.6	9.10	Submit a Draft Contract Report. The SA will require no more than 3 business days to provide feedback.	Electronic format, Microsoft Word.	By 04 March 2022.
10.7	9.10	Submit a Final Contract Report addressing feedback by the SA on the Draft Contract Report.	Electronic format, Microsoft Word.	By 16 March 2022.

11. MANDATORY SELECTION CRITERIA

11.1 The successful team will collectively have the following minimum qualifications:

a) A strong record of publications and research grants for knee Osteoarthritis research.

b) Previously performed intra-articular injections in the knee with successful patient outcomes

c) Have access to medical imaging to properly diagnose knee Osteoarthritis.

d) Be composed of a research team with access to a variety of instruments to conduct *in vitro* and human studies and analyze biomarkers in blood and tissue

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12. LANGUAGE OF WORK

Documentation and deliverables must be submitted in the English language.

13. LOCATION OF WORK

The work must be performed on the Sub Contractor's site.

14. TRAVEL

All 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".

15. MEETINGS

15.1 An initial virtual project meeting will take place within 5 business days of issuance of the Task Authorization.

15.2 Additional project meetings can be requested by either the Research Team or the SA, and must take place within five (5) business days of the request.

16. GOVERNMENT SUPPLIED MATERIAL (GSM)

None

17. GOVERNMENT FURNISHED EQUIPMENT (GFE)

None

18. SPECIAL CONSIDERATIONS OR CONSTRAINTS

None

19. SECURITY

The Sub Contractor will not require access to PROTECTED and/or CLASSIFIED information or asset, nor to restrictedaccess areas.

X Not applicable

20. INTELLECTUAL PROPERTY (IP) OWNERSHIP

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

21. 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 $87,000.00 for FY 2021-22. Full budget 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.

22. CONTROLLED GOODS

X Not applicable

23. BASIS OF PAYMENT REQUESTED

X Limitation of expenditure

24. METHOD OF PAYMENT REQUESTED

X Progress payments