National Defence Défense nationale

- STATEMENT OF WORK -
Task Authorization (TA) – 53

FOR SUB CONTRACT WITH CIMVHR

1. NUMBER – TITLE OF TASK AUTHORIZATION

TA 53 – First-Generation Smallpox Vaccine Potency Testing

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 Studies** – Design, develop and qualify an *in-vitro* cell based plaque assay to assess the potency of the first-generation smallpox vaccine.

b. **Data Analysis -** Perform analysis of data from experimental studies.

c. **Report -** Prepare and deliver report(s) to the Department of National Defence (DND).

3. ACRONYMS

CAF	Canadian Armed Forces
CAM	Chorioallantoic Membranes
DND	Department of National Defence
cGMP	Current Good Manufacturing Practices
GoC	Government of Canada
ICH	International Conference on Harmonization
mL	Millilitre
PFU/mL	Plaque Forming Units per millilitre
PHAC	Public Health Agency of Canada
SA	Scientific Authority
SOP	Standard Operating Procedure
SOW	Statement of Work
TA	Technical Authority

4. REQUIREMENT

4.1 The following services of the Sub Contractor are required: to design, develop and qualify an *in-vitro* cell based plaque assay to assess the potency of the first-generation smallpox vaccine expressed in terms of plaque forming units per millilitre (PFU/mL).

5. BACKGROUND

5.1 The Department of National Defence (DND) and the Public Health Agency of Canada (PHAC) maintain stockpiles of first-generation freeze-dried and frozen-liquid smallpox vaccine manufactured by Sanofi Pasteur. Smallpox vaccine is indicated for active immunization against smallpox disease. It may be used for primary vaccination and revaccination. The stockpile of smallpox vaccine and diluent is currently maintained and stored under current Good Manufacturing Practices (cGMP) conditions at Sanofi Pasteur facilities under long-term storage conditions. Under these storage conditions smallpox vaccine does not have a labelled expiry date. If smallpox vaccine were to be requested by DND, it would be packaged and formally released from the Sanofi Pasteur facilities with an assigned expiry date.

5.2 Historically, Sanofi Pasteur has provided potency testing services for the smallpox vaccine as per contracts with the Government of Canada (GoC). Sanofi Pasteur will no longer be conducting the annual potency testing. As prescribed by the Canadian Food and Drug Regulations, the potency of the smallpox vaccine has historically been tested by titration on chorioallantoic membranes of chicken embryos (CAM assay). Multiple lots of the smallpox vaccine have been tested annually for potency on a rotational basis to support the extension of the product shelf-life. To date there has been no drop in vaccine potency.

5.3 Second and third-generation smallpox vaccines use plaque or flow-cytometry based assays to assess potency due to their superior reliability, accuracy, simplicity and speed.

6. APPLICABLE DOCUMENTS & REFERENCES

6.1 International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use Guidance Document: Validation of Analytical Procedures: Text and Methodology Q2(R1).

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7. TASKS TO BE PERFORMED

The Sub Contractor must perform the following tasks:

Phase 1 – Assay Design and Development

7.1 Assay Design, Development & Optimization: Plan and execute pilot cell-based plaque assay(s) to optimize assay methods and testing parameters including but not limited to assay controls, type of cell line(s), plating conditions, and growth times.

7.2 Protocol(s)/Method(s)/SOP(s): Prepare detailed protocol(s), method(s) and/or Standard Operating Procedure(s) (SOP) to describe the testing procedures to execute the cell-based plaque assay with the optimized methods and testing parameters assessed in Task 7.1. The required material, equipment, facilities, personnel, and time required to execute the assay must be described in these documents. Methods for capturing, recording and storing data must also be described. The protocol(s)/SOP(s) should be amenable to cGMP.

Phase 2 – Potency Testing

7.3 As directed by the SA and up to a maximum of 40 assay runs, test the potency of the smallpox vaccine lot(s) designated and provided by DND and/or PHAC in accordance with the protocol(s)/method(s)/SOP(s) developed in Task 7.2.

Phase 3 – Data Analysis and Reporting

7.4 Document, analyze and report all results from each individual assay run from Task 7.3 and report a vaccine potency result expressed in PFU/mL. The report(s) must include any errors or deviations experienced during Task 7.3.

Phase 4 – Assay Qualification & Validation

7.5 Qualification/Validation Plan: Prepare a plan to assess, characterize, qualify and then validate the assay to demonstrate the suitability of the assay for its intended purpose in accordance with the principles described in ICH Q2(R1) and cGMP. Assay characteristics that must be considered include but are not limited to: accuracy, precision (repeatability and intermediate precision), limit of detection, limit of quantification, linearity and range. The plan must outline the required material, equipment, facilities, personnel, budget and time required to execute the plan.

7.6 Assay Validation: Execute assay validation plan from Task 7.5.

8. DELIVERABLES (DESCRIPTION AND SCHEDULES)

All tasks and deliverables must be completed and submitted to CIMVHR by 16 March 2020.

Deliverable Number	Task reference	Description of Deliverables	Quantity and Format	Delivery Date
8.1	7.1	Experimental study plan to test different parameters for smallpox vaccine plaque assay.	Electronic format, Microsoft Word.	Within four (4) weeks after issuance of Task Authorization.
8.2	7.1	Report describing optimized assay methods and testing parameters.	Electronic format, Microsoft Word.	Within twenty (20) calendar days of completing Deliverable 8.1
8.3	7.2	Finalized assay protocol(s), method(s) and/or SOP(s).	Electronic format, Microsoft Word.	Within fifteen (15) calendar days of completing Deliverable 8.2.
8.4	7.3	Test results from the potency assay(s) authorized to be run on lots of smallpox vaccine designated by the SA expressed in PFU/mL.	Electronic format, Microsoft Word or Excel	Within fifteen (15) calendar days of written authorization from the SA.
8.5	7.4	Full report documenting all assay results and errors or deviations.	Electronic format, Microsoft Word.	Before 16 March 2020.
8.6	7.5	Assay Qualification/Validation Plan.	Electronic format, Microsoft Word.	Before 16 March 2020.
8.7	7.6	Complete method validation report.	Electronic format, Microsoft Word.	Before 16 March 2020.

9. MANDATORY SELECTION CRITERIA

9.1 The successful team will collectively have the following mandatory criteria:

(1) be a Canadian academic microbiology and immunology investigator group with dedicated access to adequate and appropriate laboratory personnel, equipment and facilities;

(2) the lead investigator must be an expert and leader in vaccinia, variola or orthopox virus research;

(3) the investigator group must have demonstrated experience running cell based plaque assays;

(4) The academic institution must have demonstrated experience with current Good Manufacturing Practices (cGMP).

10. LANGUAGE OF WORK

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

11. LOCATION OF WORK

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

12. TRAVEL

12.1 The Sub Contractor is not required to travel.

13. MEETINGS

13.1 The Sub Contractor must participate in bi-weekly teleconferences as requested by the SA. If requested, the Sub Contractor must facilitate no more than three (3) in-person meetings at the Sub Contractor facility.

14. GOVERNMENT SUPPLIED MATERIAL (GSM)

14.1 No less than one (1) but no more than twenty (20) vials of freeze-dried smallpox vaccine and diluent for reconstitution.

14.2 No less than one (1) but no more than twenty (20) vials of frozen-liquid smallpox vaccine and diluent for reconstitution.

14.3 No less than ten (10) L but no more than five hundred (500) aliquots of reconstituted freeze-dried smallpox vaccine from lot 3017-11.

14.4 Historical potency data and results from the CAM assay.

15. GOVERNMENT FURNISHED EQUIPMENT (GFE)

15.1 None

16. SPECIAL CONSIDERATIONS OR CONSTRAINTS

16.1 The freeze-dried and frozen-liquid vaccine will be shipped to the Sub Contractor under appropriate storage conditions with temperature monitoring equipment.

16.2 The vaccine diluent(s) will be shipped to the Sub Contractor at 2˚ to 8˚C with temperature monitoring equipment.

16.3 The aliquots of reconstituted freeze-dried vaccine will be shipped to the Sub Contractor at 2˚ to 8˚C no more than five (5) calendar days from the date of reconstitution with temperature monitoring equipment.

16.4 Shipping costs for items listed in paragraphs 16.1 – 16.3 will be paid by DND and are not to be included in the budget for this SOW.

17. SECURITY

17.1 All work is unclassified and the Sub Contractor will not have access to any classified information.

X Not applicable ☐ RELIABILITY STATUS ☐ PROTECTED A ☐ PROTECTED B

18. INTELLECTUAL PROPERTY (IP) OWNERSHIP

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

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19. CONTROLLED GOODS

X Not applicable
☐ Applicable

20. BASIS OF PAYMENT REQUESTED

☐ Firm price
☐ Ceiling price
X Limitation of expenditure

21. METHOD OF PAYMENT REQUESTED

☐ Single payment
☐ Milestone payments
X Progress payments (Quarterly)

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. Funding is allocated by fiscal year (April 1 - March 31st) and is approximately $113,000.00 for FY 2019/20 including applicable overhead. Final 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 (Jocelyne.Halladay@queensu.ca).