Validation Services for a new Clinical Trial Manufacturing Facility

Background

The National Research Council of Canada is building a new Clinical Trial Manufacturing Facility (CTMF) that will house the process and equipment for the production and the quality control of protein, viral vector or virus-like particle vaccines or biologics.

The products are mainly intended for the Canadian market, regulated by Health Canada under the authority of the Food and Drugs Act. The facility will require being compliant with Canadian Good Manufacturing Practices (GMP) as well as FDA current GMP (cGMP) and Eudralex requirements.

The new manufacturing rooms and airlocks (personnel and material) will be built in an extension to the existing NRC's premises located in Montreal, Quebec and will consist of classified grade C and D areas.

The facility will include equipment and infrastructures necessary for viral seed stock preparation, subculture, cell culture and viral production, purification and warehousing.

Detailed Statement of Work

Equipment and systems related to manufacturing a product for human use for clinical trial must be qualified. Validation is the process of qualifying and commissioning by establishing documented evidence that provides a high degree of assurance that a specific piece of equipment, utility or system will consistently operate as designed, meeting a predetermined set of specifications.

The qualifications must be carried out in accordance with Canadian GMP standards as well as FDA current GMP (cGMP) and Eudralex requirements

As part of this mandate, the professionals must:

1. Provide commissioning and validation (C&Q) services for utilities and production equipment. This includes:
    1.1. Planning protocol preparation and/or report, review and approval
    1.2. Prepare protocols
    1.3. Coordinate review and approval
    1.4. Execution of approved protocols, resolve deficiencies, prepare results and closure reports
    1.5. Review of executed results and closure of data packages
    1.6. Ensuring all deficiencies are closed.
2. Compilation, review and approval of Vendor Turnover Package (VTP).
3. Pre- and post- review and approve all commissioning related testing documentation of non-GMP systems.
4. Provide bilingual SOPs (standard operating procedure) for operation and maintenance for each of the utilities and equipment as well as training for each of those SOPs.
5. Work in collaboration with all teams and report regularly to NRC Clinical Trial Manufacturing Facility (CTMF) senior project manager as well as the Section Head, GMP Biologics of HHT, NRC.
6. Expect a monthly sponsor meeting with NRC management.
7. Coordinate with the construction manager and NCR representatives to facilitate the executions of protocols.
8. Ensure testing strictly follows established quality procedures/practices and approved protocols.
9. Ensure that all members of the qualification team understand the mandate.
10. Ensure compliance with objectives, established deadlines and approved budgets as well as the quality of deliverables.

11. Ensure compliance with applicable laws and regulations, in particular the Law on Contracting by Public Bodies, the resulting regulations as well as the CNR's contract management and procurement policy as well as any decree or any rule applicable, where applicable, to the implementation of the project.
12. Ensure the fluidity of carrying out tasks related to the project.
13. Make sure to participate in the constant improvement of the processes and tools used for the realization of the project.
14. Ensure compliance with health and safety standards.
15. Ensure compliance with Good Manufacturing Practices (GMP) (Health Canada, FDA and Eudralex).

Documentation Leveraging

The project strategy for systems and equipment is to leverage testing and documentation created in earlier phases of the project into later phases of the project. Certain activities performed during the construction may be used to support commissioning. Certain activities performed in commissioning protocols may be used to support qualification. The activities that can be leveraged from commissioning to qualification must be approved by quality assurance department. Some testing to be leveraged should be witnessed by validation team to assure the validity of the data recorded.

Industry Specifications and Standards

This validation strategy will comply with current regulatory recommendations based on Health Canada, FDA, Eudralex, International Conference on Harmonization (ICH) and other relevant industry practices and guidelines (ISPE).

Deliverables

In consultation with NRC representatives, the consultant will be responsible to performed, but not limited to, the following:

Key Responsibility	Activity	Deliverables
Project Strategy and Schedule	• Develop methodology to complete project within specified timelines • Establish project timelines • Provide project management for completion of validation work	1. Draft documented methodology and Work Plan to be reviewed by NRC and opportunity for revisions if required 2. Final documented methodology and Work Plan.
Budget Tracking	• Provide budget tracking for validation work	3. Final documented methodology and Work Plan.
Commissioning and Validation (C&Q)	In consultation with NRC representatives, the consultant will: • Develop equipment commissioning and validation protocols • Develop traceability matrix (TM) for critical systems to ensure requirement from URS, FRS, DDS are properly captured in IOQ and PQ • Write installation, operation and performance qualifications (IQ / OQ / PQ), according to the VMP-01 • Execute protocols including closure reports, documentation and resolving of deficiencies	4. Commissioning and validation protocols. 5. Traceability Matrix 6. Executed commissioning and validation protocols. 7. Closure reports including recommendations to address any deficiencies.

	• Review of executed results and closure of data packages	
SOPs	• Develop equipment operational and maintenance SOPs for each clean utilities and production equipment	8. Standard Operational Procedures 9. Formal training sessions
Turnover Packages	• Lead the timely compilation, review and approval of engineering Turnover Documentation Packages	10. Completed Turnover Documentation Packages
Commissioning of non-GMP systems	• Pre-and post-review and approve all commissioning related testing documentation of non-GXP systems	11. Completed non-GMP commissioning

Refer to Appendix F for a detailed list of deliverables.

Items outside of the scope of this engagement

1. Validation Master Plans (VMP)
2. User Requirement Specification (URS) of equipment
3. Technical specifications (drawings, technical sheets, shop drawings)
4. Process Validation
5. Cleaning Validation
6. Analytical Methods Validation
7. Laboratory equipment Validation

Primary Work Location

1. Protocols must be written remotely.
2. SOPs can be written on site.
3. All tests must be carried out on site located at the following address: 6100 Royalmount, Montréal, QC. Civic address number may change.

Information to be provided by NRC

- Validation Master Plan (VMP)
- URS of equipment
- Technical specifications

Schedule

The consultant will achieve this mandate, submitting interim and final deliverables as follows:

	Deliverable	*Starting Date*
1	Kick off meeting	July 11, 2022
2	Schedule planning	Aug 10, 2022
3	Writing of protocols – last protocol	Feb 02, 2023
4	Writing of SOPs – Last SOP	June 30, 2023
5	Execution of protocols – Last protocol	Sept 29, 2023
6	Project completion & closeout meeting	Oct 27, 2023

Resources Skills

In view of the tasks and responsibilities entrusted to the consultant, they must demonstrate, throughout the term of the mandate, the following skills:

1. Possess skills, deep knowledge and experience in GMP and pharmaceutical environment (experience in biomanufacturing mABs and viral vector will be an advantage):
    i. The project manager must have at least fifteen (15) years in GMP & pharmaceutical environment.
    ii. 50 % of the team members must have at least seven (7) years in GMP & pharmaceutical environment.
    iii. 50 % of the team members must have at least two (2) years in GMP & pharmaceutical environment.
2. Knowing how to manage priorities and exercise good judgment.
3. Have good teamwork skills and show leadership.
4. Ability to work in a dynamic and rapidly developing environment.
5. Demonstrate autonomy and initiative.
6. Good ability to plan, organize, direct and control execution schedules.
7. Technological knowledge, including office software.

A consulting team with GMP and vaccine manufacturing expertise plus support staff with specific expertise would be required to complete the tasks in the timeframe set out below.

**The consulting shall provide resume and hourly rate for each member of the qualification team.

** Consultants meeting all criteria maybe called for Teams presentation & interviews.

Project Management

It is anticipated that this mandate would be managed by a project director.

NRC will appoint a project manager, to liaise with designated project director from the consultant.

**Execution by lots and Subcontracting

This mandate is divided into many lots of equipment. The consultant(s) will be selected according to Appendix – B - Evaluation Criteria and Basis of Selection. The consultant may be selected to carry out all the lots, a portion of the lots or single lot. For this purpose, the consultant can exclude certain lot(s) or can add a subcontractor who has more specialized expertise in a specific type of equipment to execute specific lot(s). In such cases, the consultant must indicate in his bid the subcontractor(s) who will be engaged for this purpose. NRC reserves the rights to accept or refuse any subcontracting at its sole discretion.

**Instruments

The selected consultant must provide all the necessary measuring instruments for the qualifications. He must indicate in his bid the instruments (type, manufacturer & model) that will be used.

**Turnaround time for requested services

Given the current pandemic situation, consultant must be readily available for on-site work under a 4 hour notice period. On-site presence is required to allow daily access to the site during the execution of the protocols.

**Work Language

The SOPs will be in French and English. All other documents will be written in English. Communications with all the teams and operators on site will be in French. The validation team members should be able to write and speak French and English (intermediate level). The consultant project manager should have advanced level of French to participate in construction coordination meetings which are conducted only in French. The proper translation of the work is under the full responsibility of the successful consultant (s) and subject to final review and approval by NRC.

https://www.tpsgc-pwgsc.gc.ca/app-acq/sat-ths/clients/competences-proficiency-eng.html
https://www.tpsgc-pwgsc.gc.ca/app-acq/sat-ths/clients/competences-proficiency-fra.html

**Financial Proposal

The consultant must submit a detailed price for his service offer by completing Appendix C- Pricing Form and as per section 7 of RFP document. The consultant must break down his price by lots, including the number of hours required for each professional for writing documents and performing tests.

Timelines

The consultant must present his strategy how he intends to carry out the mandate within the time frame indicated in the section ''Schedule''.