

Request for Proposal (RFP)

Assessment of Manufacturers including Contract Development and Manufacturing Organizations (CDMOs) for Feasibility of Clinical Lot Manufacturing of HIV Vaccine Immunogens in India

Contracting Agency

IAVI

Unit No. 810, 8th Floor, Emaar Capital Tower – 1,
Mehrauli Gurugram Road, Sikandarpur, Sector 26,
Gurugram, Haryana-122002 India



Translating **science**
into **global** health impact

Contents

| | |
|---|---|
| 1. Objective | 3 |
| 2. Background | 3 |
| 3. Project Overview and Expected Deliverables | 4 |
| 4. Key areas to be assessed for the Manufacturers and CDMOs | 4 |
| 4.1. Manufacturing capacities for recombinant proteins | 4 |
| 4.2. Manufacturing capacities for Messenger RNA (mRNA) | 5 |
| 4.3. Additional assessment parameters | 5 |
| 5. Proposal Structure | 5 |
| 6. Selection Process | 6 |
| 7. Evaluation Criteria for the applying consulting firm | 7 |
| 8. Submission Details | 8 |
| 8.1. Submission process | 8 |
| 8.2. Duration of the Project, Budget, and Payment Terms | 8 |
| 8.3. Timelines | 8 |
| 9. Confidentiality | 8 |
| 10. Contact Information | 8 |

1. Objective

Conducting a comprehensive landscape analysis of manufacturers and contract development and manufacturing organizations (CDMOs) in India to assess the feasibility of clinical lot manufacturing of HIV immunogens for potential early phase vaccine trials in India and/or other regions.

2. Background

IAVI is a nonprofit scientific research organization dedicated to addressing urgent, unmet global health challenges including HIV, tuberculosis, and emerging infectious diseases. Our mission is to translate scientific discoveries into affordable, globally accessible public health solutions. Through scientific and clinical research in Africa, India, Europe, and the U.S., IAVI is pioneering the development of biomedical innovations designed for broad global access. We develop vaccines and antibodies in and for the developing world and seek to accelerate scientific discovery and development by fostering unique collaborations among academia, industry, local communities, governments, and funders to explore new and better ways to address public health threats that disproportionately affect people living in poverty. Our global reach, including a clinical research network in five countries including sub-Saharan Africa and in India, has allowed us to make fundamental contributions to understanding the epidemiology, transmission, virology, and immunology of HIV. This work played a key role in facilitating the design of promising HIV vaccine immunogens, as well as the discovery of broadly neutralizing antibodies (bnAbs) that are now being advanced as potential HIV prevention products.

With this backdrop, one of the key efforts that IAVI is leading, is toward the germline targeting (GT) approach for developing an effective HIV vaccine. Reverse vaccinology and rational design form the basis of this approach. Envelope trimeric glycoprotein (Env) on the surface of HIV-1 is the target of neutralizing antibodies (nAbs) and is critical in vaccine design strategies. In rare (<10%) HIV infected individuals, referred to as elite neutralizers, bnAbs have been found to develop in natural course of infection that typically exhibit broad and potent neutralization of heterologous HIV-1 variants. These bnAbs are directed against relatively conserved epitopes in the Env. Several classes of bnAbs having distinct epitope specificities on HIV-1 Env have been discovered. Elicitation of bnAbs, capable of preventing entry into the target cells by diverse HIV-1 variants, has been a major focus of HIV vaccine development in the recent decades.

The novel germline targeting vaccine design approach utilizes GT immunogens to selectively activate rare precursors of bnAbs followed by a series of intermediate booster immunogens to drive precursor evolution towards mature bnAbs. The IAVI G001 trial reported the unprecedented elicitation of HIV broadly neutralizing precursors in a first in human (FIH) Phase I clinical trial. These pivotal findings provide hope that an HIV vaccine remains viable and have ushered in a renewed focus on designing and evaluating immunogens that are tailored to elicit specific humoral responses. IAVI, in partnership with several partners, have designed and characterized multiple Env trimers that can elicit nAb responses and are also in the process of trying out booster immunogens to progress the B-cell maturation process. Thus, in a relatively short period of time, several immunogens are likely to go into early phase clinical trials, either as recombinant trimeric proteins or as mRNA. Hence, there is a need for manufacturers and CDMOs who are able to cater to the above needs.

While IAVI currently works with CDMOs globally, given that India has world class manufacturing facilities, it is imperative to understand the existing capacities and capabilities of Indian manufacturers and CDMOs and assess if they can contribute to the needs of the field at this juncture.

3. Project Overview and Expected Deliverables

Through this call, IAVI invites qualified, experienced and interested consulting firms to submit proposals toward conducting the landscaping of manufacturers and CDMOs in India for assessing the feasibility of small-scale clinical lot manufacturing of HIV immunogens.

The selected consulting firm will conduct an in-depth assessment of the Indian manufacturers and CDMOs with specific focus on the technical capacities and capabilities and commercial interests with regard to clinical lot manufacturing of HIV immunogens either as recombinant proteins or through mRNA platform.

At the end of the assessment, the consulting firm will be required to submit a detailed report and a pitch deck (PowerPoint slide deck) highlighting the key findings, and a list of potential manufacturers and CDMOs with the required capacities, capabilities and interests who may be considered for the small-scale clinical lot manufacturing of HIV immunogens for early phase trials in India and/or other regions.

4. Key areas to be assessed for the Manufacturers and CDMOs

The feasibility assessment of the manufacturers and CDMOs should entail but not be limited to following parameters:

4.1. Manufacturing capacities for recombinant proteins

- i. *Cell line development*- The manufacturer/CDMO must have the capacity to create cell line for clinical production as per regulatory standards by both FDA and EMA. Capacities regarding several avenues such as, generation of monoclonal cell lines, creation of stable cell pools, or the use of a transient expression system can be assessed.
- ii. *Master Cell bank (MCB) creation*- The manufacturer/CDMO must have the capacity to create, test and characterize a MCB from the selected and tested research cell bank (RCB) as per appropriate regulatory standards such as ICH Q5B, ICH Q5D. The MCB should be generated in compliance with Current Good Manufacturing Practice (cGMP) regulations and with fully traceable, animal-component free materials. Capacities for storage and maintenance of the MCB should also be assessed.
- iii. *Upstream process development*- IAVI estimates upstream titers ≥ 0.3 g/L in a bioreactor working volume of ≤ 50 L will be sufficient for cGMP manufacturing. Thus, capacities in this regard should also be assessed.
- iv. *Downstream process development*- The major focus of process development activities will be on downstream process development that will generate a process suitable for cGMP production. Capacities related to purification, adequate yield and impurity monitoring should be in place.
- v. *Analytical Method Development and Qualification*- Manufacturers/CDMOs need to be assessed for their analytical expertise appropriate for viral envelop proteins, clinical assays and release testing methods.
- vi. *Formulation development*- Capacities of manufacturers/CDMOs for liquid formulation development, adequate stability of drug substance and drug product, stress degradation studies and stability indicating assays should also be assessed.
- vii. *Drug substance manufacturing*- The Manufacturer/CDMO should be able to do cGMP manufacturing of drug substance with a targeted yield of >2 g ensuring the highest global standards of safety and quality.
- viii. *Drug product manufacturing, and fill finish*- The manufacturer/CDMO should have the expertise and experience in drug product development, including drug formulation development, manufacturing process development & optimization, scale-up, process validation, and quality control in adherence to stringent regulatory compliances to ensure product safety and efficacy.

4.2. Manufacturing capacities for Messenger RNA (mRNA)

- i. *mRNA platform and Lipid Nanoparticle (LNP) formulation development*- The manufacturer/ CDMO must be equipped with the capacity for mRNA development given the gene/nucleotide sequence and must possess specialized knowledge and expertise in generating stable LNP formulation of mRNA as an effective delivery system. The manufacturer/CDMO must have expertise in analytical method development for mRNA/LNPs and GMP capability for scaled up mRNA synthesis and LNP formulation.
- ii. *mRNA technology transfer*- Additionally, the manufacturer/ CDMO must be able to tech transfer the mRNA and LNP formulation design and development process as and if required.

4.3. Additional assessment parameters

- i. *Technical Capacity – Does the manufacturer/CDMO have suitable infrastructure, required Equipments, compatible technology platforms and adequate manufacturing facilities for clinical lot manufacturing?*
- ii. *Skilled Workforce and previous experience – Do they have the technical expertise and experience in optimization of vaccine manufacturing processes? Have they been engaged in process optimization and small-scale clinical lot manufacturing of any other vaccines?*
- iii. *Quality Control and Assurance*- How well do they implement the quality control measures and how compliant are they with GMP standards? Do they have the technical capacity for batch testing, release, and stability studies in place for ensuring consistency and purity?
- iv. *Regulatory Compliance*- Are the manufacturers/CDMOs compliant with the regulatory guidelines for vaccine manufacturing? Are they equipped to mitigate challenges that may arise in meeting regulatory requirements?
- v. *Raw Material*- Do they have a robust raw material sourcing and supply chain mechanism to ensure uninterrupted and timely production?
- vi. *Risk Assessment and Mitigation Strategies*- How strong are their risk assessment and mitigation strategies?
- vii. *Costs and Timelines – What are the anticipated costs associated with clinical lot manufacturing processes and what is the tentative timeline for end-to-end manufacturing including optimization, formulation and scaling for clinical lot delivery?*
- viii. Any other additional details if applicable.

5. Proposal Structure

Please go through the following sub-sections carefully and ensure that applications align with the following criteria.

The applicants will be evaluated in 2 stages. To qualify for consideration for a contract award within the framework of this request for proposals as a part of Stage 1 (details mentioned below in section 6), kindly submit a written proposal (not exceeding 5 pages) in English. The proposal should encompass the following details:

- i. Cover Letter - A formal letter introducing the proposal, signed by an authorized representative of the applying organization.
- ii. Provide a concise background, including particulars of qualifications and relevant expertise of the team.
- iii. Describe approach and methodology for conducting the landscape analysis and feasibility assessment, including detailed milestone and timeline gantt.
- iv. Outline the expected outcomes, anticipated challenges and mitigation strategies.

- v. Demonstrate documented ability and capacity (technical knowledge, regulatory awareness, commercial knowledge) to execute the work to high standards, within stipulated timelines, and adhering to budget constraints.
- vi. Present an estimate of the expected cost/rate for completing the work, along with fee rates for additional services. This should include a budget break-up per sub-head and a detailed narrative/justification per sub-head.
- vii. Include two instances of comparable work undertaken with similar clients (contact details may be requested if we decide to seek references) highlighting relevant experience. Also mention if the applicant has an existing database of manufacturers and CDMOs.
- viii. Please submit the following additional annexures to strengthen your application:
 - o Organization Profile - Detailed information about the applying consulting firm, including its history, mission, structure, and relevant experience.
 - o Team Composition and Resumes - Resumes of key team members who will be involved in the landscaping analysis, showcasing their qualifications and expertise.

Applying consulting firms are encouraged to furnish comprehensive details in their application to enable an informed and equitable evaluation. Any requests for modifications to the proposal post-submission will not be considered. Proposals that do not meet the eligibility criteria and/or fail to directly address the specified call area will not undergo the evaluation process, irrespective of their quality.

6. Selection Process

Applications will be evaluated in the following 2 stages:

Stage 1:

- Applications (as per section 5 mentioned above) will undergo an administrative check and will be screened for completeness, and all the necessary documentation.
- The applications will then be evaluated and scored based on the evaluation criteria mentioned below in section 7.
- The top shortlisted applicants will then be invited for a virtual presentation.

Stage 2:

- Each shortlisted applicant will be required to make a 10-15 min presentation highlighting the details of their approach, implementation methodology, expected outcomes and budget.
- The final applicant will then be selected based on the technical appropriateness, financial suitability and timeliness of the proposals.

Only those applicants who will be proceeding to Stage 2 will be informed by the tentative date mentioned below in the timelines section.

7. Evaluation Criteria for the applying consulting firm

Prospective consulting firms will be evaluated based on the following key criteria to ensure a comprehensive selection process:

| Criteria | Sub-Criteria | Score out of 10 (1 lowest, 10 highest) | | |
|---|---|---|------------------------|-----------------------|
| Technical appropriateness | Does the applicant have a profound understanding of vaccine manufacturing processes/technologies, showcasing a depth of knowledge that aligns with the intricacies of early developmental optimization, formulation and clinical lot manufacturing? | 1-10 | | |
| | Does the applicant have comprehensive familiarity with regulatory requirements in the pharmaceutical and vaccine manufacturing industry to ensure adherence to established standards and compliance? | 1-10 | | |
| | Remarks: | Total Score | Weightage (0.3) | Weighted Score |
| Proven Experience | Does the applicant have a demonstrated track record of successfully conducting landscape analysis and feasibility assessment specifically in the field of product/vaccine manufacturing preferably in India and also other LMICs for similar context? | 1-10 | | |
| | Does the applicant have a known network of manufacturers and CDMOs in India? | 1-10 | | |
| | Remarks: | Total Score | Weightage (0.3) | Weighted Score |
| Implementation Plan | Does the proposal entail clearly defined and justified approach and methodology (including field visits for technical data collection, validation, and stakeholder consultations) for conducting the landscape analysis and feasibility assessment? | 1-10 | | |
| | Are there enough number of team members with relevant experience who have been considered for this project to ensure timely completion? | 1-10 | | |
| | Remarks: | Total Score | Weightage (0.2) | Weighted Score |
| Cost-Effectiveness & Risk Mitigation | Are the budgets reasonable and justified for the objective at hand? | 1-10 | | |
| | Does the firm have effective mitigation plan outlined if there are any challenges in meeting the outcomes in timely manner? | 1-10 | | |
| | Remarks: | Total Score | Weightage (0.2) | Weighted Score |
| | | Total Weighted Score (A) | | |
| | | Grand Total out of 100 (A x 2.5) | | |

8. Submission Details

8.1. Submission process

The proposal can be submitted online in the form of single PDF document to ctmfeasibility.iavi@gmail.com with a copy to jmukherjee@iavi.org and msharma@iavi.org till the mentioned submission deadline. Any proposal received beyond the deadline will not be considered for further evaluation.

8.2. Duration of the Project, Budget, and Payment Terms

The budget for the entire activity should be within a maximum cap of INR 30,00,000. Payment terms will be negotiated upon selection of the consulting firm. The project is scheduled to span a period of 6-8 months, commencing from the contract award date.

8.3. Timelines

The anticipated timeline for the procurement process is outlined in the table below. Nevertheless, IAVI retains the right to modify the schedule at its discretion.

| Activity | End Date |
|--|--------------------------------------|
| Release of RFP | 9 th February 2024 |
| Proposal Submission Deadline | 1 st March 2024, 5 pm IST |
| Notification to shortlisted applicants | 2 nd week of March |
| Final Selection | Last week of March |

9. Confidentiality

By accepting to take part in this RFP process, your firm agrees to keep in confidence all information imparted to you by IAVI during the period of consultancy, not to disclose it to third parties, and not to use it for any other purpose than for participation in the RFP process.

10. Contact Information

For inquiries and clarifications, please contact following personnel:

Dr. Joyeeta Mukherjee

Associate Director, R&D and Access, IAVI

jmukherjee@iavi.org

Dr. Monika Sharma

Senior Specialist, Product Development

MSharma@iavi.org