

Request for Proposals (RFPs)

**Industry-Academia Collaborative Mission for Accelerating
Early Development for Biopharmaceuticals – “Innovate in India (i3)
Empowering Biotech Entrepreneurs & Accelerating Inclusive
Innovation”**

Funded by

**Department of Biotechnology
Ministry of Science & Technology
Government of India**

**Co-funded through World Bank Loan Assistance
(Innovate in India for Inclusiveness Project)**

Implementing Agency

**Biotechnology Industry Research Assistance Council (BIRAC)
(*A Government of India Enterprises*)**

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Section I - Program Overview

Program Name

Industry-Academia Collaborative Mission For Accelerating Discovery Research To Early Development For Biopharmaceuticals - “Innovate in India (i3) Empowering biotech entrepreneurs & accelerating inclusive innovation.”

Funding agency

Department of Biotechnology (DBT) (Program co-funded by World Bank loan)

Implementing agency

Biotechnology Industry Research Assistance Council (BIRAC)

Program Overview ¹

Background

Global efforts to develop next generation technologies and tools have given us many novel and effective products that have enormously improved human health, for instance, vaccines for communicable diseases, biotherapeutics for non-communicable diseases and medical devices (including diagnostics) impacting across the healthcare continuum. However, there are multiple challenges and concerns being faced in development and availability of products such as exorbitant costs, unavailability of novel products and emerging scientific & clinical challenges.

India has the resources and an environment ripe for developing knowledge and innovation based bio-economy. Factors such as availability of technical manpower, substantial spending on university level research in basic sciences, a mature generics pharmaceutical industry, global standard Contract Research Organizations (CRO) and vaccine development hub have a potential to catapult India in the global biotechnological arena.

There are also lucrative market opportunities and huge scope of growth for India to capture global market, considering that India accounts only **~3% of the \$156B** global biopharmaceutical market that is by far the fastest growing segment of the pharmaceutical industry.

¹ Further details of the Program see National Biopharma Mission Document

Yet India lags 10-15 years behind their counterparts in the developed countries and face stiff competition from emerging economies like China, Korea. This could be attributed to multiple challenges and gaps in the biotherapeutics sector of the country, including isolated centres of excellence and infrastructure gaps in industry and academia, lack of product-oriented discovery and translational research, limited focus on early product validation resulting in enhanced time and reducing success rate and lack of talent trained in next-generation skills. Therefore, it becomes essential to address these challenges by strengthening internal resources (human, financial and infrastructure) across the biopharmaceutical development value chain and simultaneously streamlining and building stronger partnerships with national and global experts.

About the “Innovate in India (i3)” Program

Towards strengthening the emerging biotechnology enterprise in India, Department of Biotechnology (DBT) Ministry of Science & Technology has initiated the Mission Program entitled “*Industry-Academia Collaborative Mission for Accelerating Discovery Research to Early Development for Biopharmaceuticals - Innovate in India (i3) Empowering biotech entrepreneurs & accelerating inclusive innovation*” (“Program”). Biotechnology Industry Research Assistance Council (BIRAC) setup by DBT is the Implementing Agency of i3 Program (Program co-funded by World Bank loan).

The vision of the Program is to enable and nurture an ecosystem for preparing India’s technological and product development capabilities in biopharmaceuticals (including vaccines, biologics, medical devices and diagnostics) to a level that will be globally competitive over the next decade.

This scientifically driven enterprise, aims to sustain the manufacturing edge, advance the innovative environment and tap into the growing biopharmaceutical market by - generation of affordable biotechnology products; bridging critical gaps in skill and infrastructure; establishing technology platforms; enhancing clinical capacity and building a functional institutional framework that fosters inter-disciplinary and collaborative efforts.

This Request for Proposal (RFP) is to seek applications for either of the following:

1. GCLP Lab for Vaccine Clinical Immunogenicity Evaluation:

Applications are invited from institutes/companies/organizations to address the demands of vaccine developers in assessing the clinical immunogenicity of vaccine candidates in clinical trials so as to submit data to regulatory agencies

2. Translational Research Consortia (TRC):

Applications are hence solicited from academic institutions/research labs/industry to apply as a consortium (multi-disciplinary partnerships) for establishment of a Partnership Platform that would ensure a translational ecosystem to improve, standardize and provide support for advancing development and evaluation of vaccines and monoclonal antibodies for any of the diseases -Dengue, Influenza, Chikungunya and Respiratory Syncytial Virus (RSV).

Section II – Application, Evaluation and Monitoring Process

1. Application Timelines

Key Dates

Posted Date	30 June 2018
Application Due Date(s)	
GCLP Lab for Vaccine Clinical Immunogenicity Evaluation	15 August 2018
Translational Research Consortia (TRC)	31 August 2018

2. Application Guidelines and Process

The Proposal can be submitted online as per the required format. The call for the Proposal will be open for 06 weeks for GCLP labs and 08 weeks for TRC. The website will provide detailed user guide to facilitate the online proposal submission.

Process for submitting the proposals online is detailed below:

- Go to BIRAC's website or Go the URL:
<http://birac.nic.in/nationalbiopharmamission.php>
- Click on the RFP on NBM link under Programs and the active call would be highlighted.
- Click on the active call against which you wish to submit the proposal.
- Further details on 'How to Submit a Proposal' would be available in the User Guide available on the website.
- Log on to BIRAC website (<http://www.birac.nic.in>).
- If you are a registered user, log-in using the credentials, else you need to register your company/organization by clicking on New User Registration.
- In case of new user registration, a computer generated link will be sent to the email-id provided at the time of registration to generate a password.
- Once you login, you will be navigated to the proposal submission page under NBM link.

Recommendations:

- Applicants are advised to fill-up and submit their applications early without waiting for the last date in order to avoid any last minute contingencies. The system stops accepting applications automatically at midnight of the last date of receipt of application.
- Applicants are advised to provide sufficient details in their applications to allow for an informed and fair evaluation/review. Applicants are advised to provide self-contained proposals with essential supporting materials provided as uploads.
- Requests for changes in the proposal once submitted will not be encouraged.
- Providing incorrect information intentionally is viewed adversely.
- Please read through this RFP in its entirety and ensure that your application, budget and organization are in compliance with the eligibility criteria provided. Proposals for projects that do not meet the eligibility criteria and/or do not directly respond to the call area will not be reviewed, regardless of their quality. You are strongly encouraged to contact BIRAC if you are unsure about the eligibility or responsiveness of your project.

3. Evaluation Methodology

- PMU-NBM, BIRAC will screen the proposals for responsiveness to all the specified administrative and procedural provisions required in the RFP. If the application is found to be incomplete or unresponsive to the provisions described in the RFP, the application will be considered ineligible.
- Proposals that meet the eligibility criteria will be submitted for peer-review by national and international reviewers to assess the scientific merit (and other review criteria as specified above). Reviewers will be checked for conflicts of interest and will sign confidentiality agreements. Information may also be shared with selected third parties for the purposes of independent audit, evaluation and assessment of activities.
- The Scientific Advisory Group will collate the results of the reviews, make their own assessments and recommend shortlisted applications for further screening to the Technical Advisory Group.
- Grantees may also be invited for interviews or sought written clarifications when it is felt beneficial to ensure that any outstanding questions are resolved prior to concluding the full review.

- Due diligence process would be carried out by PMU-NBM, BIRAC.
- A final decision on applications to be funded will be made by the Technical Advisory Group.

All personal data will be stored and used by or on behalf of DBT/BIRAC in accordance with the Acts and confidentiality norms.

DBT/BIRAC reserves the right not to process your proposal should you be ineligible to be a proponent or should the subject of your proposal not fall within the RFPs' remit. Mere consideration of the Proposal in no way implies that section of Grant-in Aid will be forthcoming.

The applicant shall:

- Commit to obtain all applicable environmental authorizations, prior to the commencement of product development activities.
- Include qualified environmental / EHS engineer in the team for implementation of EHRMP.
- Comply with EMF requirements during all stages.

Requirements on Environmental aspects may be found at - www.birac.nic.in/webcontent/emf.pdf

4. Funding and Program Monitoring Mechanism

a. Funding: Grant-in-aid assistance for 4 years

b. Project Monitoring Committee (PMC)

The projects shall be monitored/and mentored regularly by an Expert Committee constituted by PMU-NBM, BIRAC for each project. Site visits shall be conducted by specially constituted Expert Committees comprising two to three Technical experts and one financial expert. The Project Monitoring Committee (PMC) is responsible for the following:

- Monitor the progress of the Project in conformity with the outputs, milestones, targets and objectives as contained in the Agreement.

Based on the foregoing, to assess and recommend:

- i. Release of next instalment or part release thereof by the BIRAC;
- ii. Revision of project duration;
- iii. Closing or dropping or modifying any of the components of the Project within the overall approved objectives, budget and time-frame;
- iv. Inclusion of additional industrial/institutional partner(s), if the applicant requests involvement of such partner(s), in the overall interest of the Project;

- v. Mentor(s) to overcome any technological problem faced in the Project implementation;
- vi. Revision of the financial assistance;
- vii. To advise on issues related to securing of IPR; and
- viii. To advise on any other matter as referred to it by BIRAC and/or otherwise reasonably necessary for effective discharge of its duties and/or achievement of aims and objectives of proposed Scheme.

c. Reporting of Progress

- i. On Successful completion of each Milestone, the applicant will be required to submit a detailed Milestone Completion Report (MCR) as per the prescribed format.
- ii. The MCR will be assessed by the PMC for its completion. On recommendation of the PMC, the next Milestone budget will be released.
- iii. The Applicant will have to submit a duly certified Statement of Expenditure for every 30th September and 31st March.
- iv. Format for Milestone Completion Report (MCR), Utilization Certificate and Statement of Expenditure will be made available as per requirement.

d. Other Requisites for Funds Disbursements to Company

In addition to signing of agreement between all the concerned parties, following requirements need to be completed before the first instalment can be released:

- A letter of authorization by the Head of the Academia and A Board Resolution form the Company Partner for acceptance of the Grant-in-Aid under NBM.
- **Opening up a No-Lien Account with a scheduled/nationalized Bank.**
- Commitment to comply with Clinical Research Validation and Management Framework (CRVMF)

All the above tools and instruments will be made available as per requirement.

Contact Information

Further information can be obtained at BIRAC website.

BIRAC Website: www.birac.nic.in

Contact Person:

Dr. Kavita Singh, Mission Director, PMU- National Biopharma Mission

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Section III - Details of the RFP for GCLP Lab. for Vaccine Clinical Immunogenicity Evaluation

1. Background

Over the last decade, India is being recognised as the epicentre for vaccine manufacturing in the world. Vaccine development requires extensive pre-clinical and clinical evaluation to prove their safety and efficacy. With a robust R&D pipeline of vaccines with the Indian companies it is critical that adequate infrastructure and resources are made available to the vaccine developers.

During clinical evaluation of vaccines, it is critical to estimate the elicited immune response through testing of serum or plasma, although other matrices may also be tested (e.g., urine, saliva, stools, etc.). Serological methods are most often ligand-based assays (e.g., ELISA) or functional assays (e.g., bacterial or virus killing assays). Cell mediated immunological (CMI) assays are also in the armament of vaccine immune response evaluations. Additionally, new vaccines usually demonstrate efficacy for their intended use by exhibiting impact on incidence of infection or disease. Currently, for evaluating the human immune response against some important vaccines the Indian vaccine manufacturers need to outsource these assays to globally recognized KoLs or WHO reference labs. Outsourcing outside India brings in additional cost implications and delays in availability of immunogenicity results and thereby delaying the regulatory approval for commercialization. It is therefore critical to establish these assays in laboratories which can function as national service facilities which are available to vaccine developers.

It has been internationally recognized that clinical laboratories processing specimens from clinical trials require an appropriate set of standards to guide good practices. These good practices ensure the reliability, quality, consistency and integrity of data generated by these laboratories. Good Clinical Laboratory Practices (GCLP) is established international quality system standards governing clinical laboratory and defines laboratory practices which support human sample analysis and result reporting to medical professionals (e.g., physicians) for the purpose of diagnosis and/or treatment of patients or clinical research subjects. The ICMR Guidelines for GCLP (2008) identifies the National Accreditation Board for Testing and Calibration Laboratories (NABL) which has been providing

accreditation services to medical laboratories since 1998 and the guidelines identify ISO 15189: 2007 standards.

Availability of validated serological assays for bacterial and viral vaccines in GCLP compliant laboratories can thus fill in a critical gap in vaccine development. The availability of well characterized and reproducible assays would permit rapid assessment of immunogenicity of products and the use of qualified methods following GCLP practices would assure that all data generated is useful to support product licensure.

Hence, by aiding in effective resource utilization, decrease in outsourcing costs, hastening clinical evaluation and ensuring quality data, the facility would enable lowering the cost of development and accelerating development of vaccines in the pipeline.

2. Objective of the call

The National Biopharmaceutical Mission Program aims to establish national service facility(s) that will provide services to vaccine developers in evaluating the immune responses in biological fluids samples collected from subjects enrolled in a clinical trial. The focus of National Biopharmaceutical Mission is on Pneumococcal, Dengue, Chikungunya and Influenza vaccines.

While these facilities will offer equal-opportunity nationwide access to services through an open application process, they will be a "preferred provider" facility for the products in pipeline being supported through this Program.

Applications are invited from institutes/companies/organizations to address the demands of vaccine developers in assessing the clinical immunogenicity of vaccine candidates in clinical trials so as to submit data to regulatory agencies.

3. Scope of the facility

The scope of the activities to be done at the laboratory are:

i. Technology transfer and technical support capabilities:

Lab. will be expected to assess platform technologies, adsorb assay technology transfer from collaborators (National and Global KoLs/WHO reference labs, research institutes etc.), Translation Research Consortia and other labs developing the immunoassays for

Pneumococcal, Dengue, Chikungunya and Influenza vaccines. The lab. will also be expected to adsorb new high-throughput immunological assessment assays.

ii. Assay validation:

Establishment, evaluation and documentation of the validation of assays as per ICH Guideline on Validation of Analytical Procedures Q2 (R1). The validation will include, evaluation of sensitivity, specificity, accuracy, precision, detection limit, range and limits for assays to be validated. The lab will be expected to get these immunoassays under the scope of National Accreditation Board for Testing and Calibration Laboratories (NABL, Medical/Biological).

iii. Support immunogenicity assessment for Phase I- Phase III vaccine clinical trials of: Pneumococcal, Dengue, Chikungunya and Influenza vaccines in compliance with regulatory requirements and/or WHO recommendations. For example:

- Assays to assess humoral responses e.g. serum binding titers, serum serotyping, virus neutralization assays, antibody effector function (like PRNT₅₀ assays for Dengue and Chikungunya, OPA for Pneumococcus).
- Assays to assess cell mediated immunity (CMI) responses e.g. antigen specific memory T cell differentiation and long term protective response by immuno-phenotyping and immunogenicity assays, measuring T-cell proliferation, identification of specific cytokines/chemokines in response to infection/vaccination as a measure of T cell response, inhibition of viral replication.

4. Expectations from the facility

- a. The facility should function as a fee-for-service model and maintain a minimum of ISO 15189:2012 and/or ISO 17025: 2005/ ISO 17025: 2017 accreditation and GCLP compliance through the complete term of 4 years.
- b. The facility should be able to build national and international linkages for access to international reference standards and should participate in international collaborative studies in establishment and calibration of such reference standards.
- c. The facility would agree to be linked or be mentored by globally recognized KoL or WHO reference labs based on the type of vaccine for transfer of disease specific technology/assays.
- d. The facility should be able to collaborate with “Translational Research Consortia (TRC) for vaccines” so as to adsorb the new high throughput assays that are developed through the TRC for validation.

- e. The lab. should participate in international external quality assurance testing panels and will be subjected to audit by vaccine manufacturers and other external bodies.
- f. Quality systems should be in place for all staff, equipment, facilities, assay conduct and reporting including qualified data systems for samples, assays and data RQC systems and independent QA processes.
- g. The lab. must have calibrated cold storage facilities including deep freezers with data loggers and be able to demonstrate temperature maintenance to ensure cold storage needs of reagents and samples.
- h. The laboratory should adhere to the processing timelines as per the clinical development program to get the results within accepted timeframes. Project Management support to vaccine developers should be available.
- i. The laboratory should have proactive involvement and compliance in terms of budgets and legal agreements discussions, as well as policies on publication of data.
- j. Logistically the lab. should be well connected (preferably by air).
- k. The dedicated lab. should be secure and well monitored.
- l. The lab is expected to provide service to multiple vaccine developers. Each year the lab. is expected to provide services to 3-4 vaccine developers for evaluating the immune response in serum samples collected from 1-2 clinical trials. The lab. should demonstrate capabilities to expand further if there is need.

5. Eligibility Criteria

Legal eligible Proponents:

- The proposals can be submitted:
 - Solely by an Indian Company or
 - Jointly by an Indian Company and Institutes/ Government entities/ R&D Organizations/ Non-profit organizations or
 - By a Consortium of Indian Companies along with Institutes/ Government entities/ R&D Organizations/ Non-profit organizations or
 - Solely by an Academia or research institution or in collaboration with other Academia or research institutions.

- **Criteria Particulars for the Proponent entities**

- *Indian companies*

An Indian Company is defined as one which is registered under the Indian Companies Act, 2013 and minimum 51% of the shares of the Company should be held by Indian Citizens holding Indian passport (Indian Citizens do not include Person of Indian Origin (PIO) and Overseas Citizenship of India (OCI) holders.

- *Institutes/ Government entities/ R&D Organizations/ Non-profit organizations*

This will include Academic Research Institutes, Universities, Research Foundation, Medical Colleges and Institutes – both public and private who are valid legal entities such as Trust, Society or established under central or state statute.

➤ Applicant organizations should demonstrate:

- Prior experience of performing humoral as well as CMI based immunity based assays to study immune response of vaccines in samples collected during human clinical trials, for submission of data to regulatory agencies.
- Prior experience of building national and international collaborations for technology transfer of immunoassays.
- A feasible road map to identify and build partnerships for transfer/collaboration of immunoassays for the above mentioned vaccines and describe potential partnership models to ensure providing services from this national facility to measuring immune response through validated assays.
- Receipt of prior funding from Government of India and demonstrated capabilities for work related to development of vaccines and assays for vaccines and developed linkages with industry.
- NABL accreditation via existing ISO 15189:2012 certification or has applied for NABL accreditation with evidence.
- Existing state-of-the-art facilities and the requisite space and high-end instrumentations like:
 - Instruments for ELISA based assays
 - BSLII and/or BSLIII facilities
 - Flow Cytometer (preferred)
- Capabilities of data management and maintaining data confidentiality.

- Robust quality management system with respect to sample receipt, handling outliers, handling assay repeats and reference standard management system.
- A track record of participation in prior clinical trials where assay data has been submitted to regulatory agencies and accepted, leading to licensure of the product (preferred).
- Ability to perform assays based on advanced technology platforms such as luminex, MSD, which allows minimum sample and maximum data (preferred).
- Prior experience of providing a fee-for-service model and ability to establish a financially sustainable model within 4 years of funding support.
- Adequate space in the existing facility for expansion of the laboratory.

6. Funding mechanism

Projects must be budgeted on a milestone basis. Funding will be awarded for 4 years, subject to the applicant complying with agreed milestones.

Allowable costs include

- *Personnel*: Only personnel performing assays transfer and validation experiments are allowed to claim costs. Researchers and PIs who receive a salary from the host institution as permanent or fixed term staff members may NOT claim salary reimbursement from BIRAC grants.
- *Consultants*: These may include both national and/or foreign consultants who provide a service and capability that is not available among the project partners. Preference should be given to national service providers.
- *Equipment*: Limited support for the cost of equipment may be requested.
- *Supplies and consumables*
- *Travel & accommodation*: Must be directly related to the execution of the project or travel related to seeking technology transfer.
- *Other research costs*
- *Institutional overhead*
- *Infrastructure*: Partial Maintenance of Infrastructure of the facilities pertaining to varied services including analytical work area, specimen collection room, waste disposal facility, fire safety equipment.

Non-allowable costs:

- Purchase or construction of a building/ space
- Rental costs for space
- Recruitment costs for staff
- Attendance at conferences
- Purchase of office furniture

7. Evaluation and Decision Making Criteria

a) Proposal merit

- Is the proposal's approach and background aligned with the RFP's objective?
- Has the applicant provided adequate description of the existing facility to understand the present capabilities?

- Does the proposal demonstrate adequate prior activities of the identified scope which will be useful for the proposed scope of work?
- What is the state of readiness of the applicant's laboratory for the proposed work?
- Has the proposal outlined a process of identifying relevant partners and building collaborations through sustainable models?
- Does the proposal lists the various vaccine companies to whom they have provided services?
- Does the proposal describes any immunoassay validated in the applicant's laboratory?

b) Team/Applicant:

- Is the applicant competent to ensure effective conduct of the proposed work? Does the team have relevant capabilities and appropriate experience for the same?
- Are the team roles and responsibilities, governance and organizational structure clearly defined?

c) Implementation and Infrastructure:

- Has the implementation methodology and work plan adequately detailed and realistic?
- Has the applicant provided sufficient evidence of maintaining robust quality systems and ensuring confidentiality of data generated in their laboratory?
- Has the applicant provided clear metrics for monitoring project progress including milestones, and outputs expected timelines, budget and benchmarks?
- Are the milestones and timelines proposed to achieve the goals of the project appropriate and feasible?
- Have the resources (technical and management people, equipment, collaboration, outsourcing needs etc.) required over the time frame been comprehensively mapped?
- Has the applicant identified potential collaborations to seek technology transfer from established laboratories?
- Has the applicant anticipated difficulties/risks that may be encountered? Have alternative tactics and mitigation plans been considered in case of failure?

d) Partnerships and Stakeholder Engagement:

- Has the applicant submitted supporting evidence of collaborations with other reference labs/ KOLs/ research institutes in the past?
- Have the prior collaboration's outcome clearly defined?
- Are the plans for training, knowledge and tech transfer well-articulated?
- Has a clear road map been provided by the applicant to building sustainable partnerships?

e) Operational Feasibility and Market Acceptability:

- Have the applicants successfully demonstrated capabilities of being a service provider?
- Are the future plans for ensuring sustainability post grant period well-thought-out?
- Is the proposed service model well- structured and appropriate? Are aspects like fees, accessibility mechanisms, ownership and management plans clearly defined?
- Does the Applicant have a unique value proposition (cost competitiveness, partner network, novel technologies) in comparison to competitors?

f) Cost Estimates:

- Is the proposed budget reasonable in light of the defined scope of work in terms of milestones and activities? Have reliable references been provided for justification?
- Is the resource allocation across various stages sufficient and appropriate?

Section IV - Details of the RFP for Translational Research Consortia (TRC)

1. Background

Despite decades of economic growth and development, infectious diseases remain the leading cause of mortality and morbidity in India and globally. Additionally, there are re-emerging infectious diseases which are potent threat to public health security and intriguingly most of these are viral in origin.

Global efforts to develop next generation technologies and tools have given us many novel and effective products that have enormously improved human health. However, there are multiple scientific and clinical challenges that obstruct the development of novel preventive and therapeutic solutions (vaccines and monoclonal antibodies).

Recently, vaccine candidates targeting various pathogens have yielded less than optimal results and efficacy in Phase II/III clinical trials despite promising preclinical efficacy data. These results highlight the limitations of current preclinical animal models and immunological assays as predictors of vaccine efficacy in humans. To optimally evaluate and compare vaccine immunogens, there is also need for novel and high-throughput assays that allow accurate, quick and reproducible measurements of immune responses. Capturing pathogenic diversity across geographies and time points would also aid in breadth and potency assessment of vaccines and antibodies and make the reagents and circulating strains available to researchers and industry for product development. In addition capabilities to advance therapeutic monoclonal antibodies need to be strengthened.

A strategic response to this would be to establish capabilities to address major problems in translation of vaccine and monoclonal antibody candidates through leveraging current capabilities of various institutes in the country through a consortium modality.

2. Objective of the call

The Program aims to establish Translational Research consortia/multi-disciplinary partnerships that would be focused on developing a translational ecosystem for supporting the ongoing vaccine development efforts and advancing existing discovery to late-stage preclinical and early clinical development of new or improved vaccines and monoclonal antibodies for diseases being supported through the Program i.e. Dengue, Influenza, Chikungunya and RSV.

Emphasis will be on developmental activities for generating better understanding of virus and circulating viral diversity; developing novel and high-throughput assays for transfer to GCLP labs; and setting an ecosystem to enable better evaluation of vaccines and monoclonal antibodies as biologics for infectious diseases.

Additionally, this work will be supported by a translational ecosystem that includes capabilities for small animal studies and development of animal models for the identified diseases; support and advice for - early clinical development, quality assurance and project management and tech transfer capabilities to support transfer of assays to, GCLP labs, industry, other research labs and facilities.

It would consolidate isolated centres of excellence and stimulate translational capabilities by leveraging the currently existing isolate centres to access and share cutting-edge technology, equipment, research methods, expertise and training through partnerships

Applications are hence solicited from academic institutions/research labs/industry to apply as a consortium (multi-disciplinary partnerships) for establishment of a Partnership Platform that would ensure a translational ecosystem to improve, standardize and provide support for advancing development and evaluation of vaccines and monoclonal antibodies for any of the diseases -Dengue, Influenza, Chikungunya and RSV.

3. Specific Objectives and Requirements of the Translational Research Consortia:

a. Access to Clinical Samples:

The consortium should have access to diverse sub-population groups from whom biological samples can be collected. These population groups can be longitudinal or cross-sectional cohorts from a well-defined geography and mapped demography.

b. Virology platform:

The consortium member should be having capabilities for:

- Establishment of viral isolates repository including the circulating and reference strains;
- Viral characterization including viral genome sequencing studies using next generation sequencing;
- Stock production of viruses (by making pseudo viruses / VLPs) for assessing the breadth of neutralization of the potential biologics;
- Creating inventory of primary virus panels (up to BSL3 containment);

- Development of novel neutralization assays and/or high throughput assays;
- Maintaining reference viral strains from WHO and NIH reference laboratories.

c. Antibody evaluation platform:

The consortium member should be having capabilities for:

- **Accelerating novel monoclonal antibody platforms in support of biologics development for Dengue, Chikungunya, RSV, and Influenza.**
- **Production of monoclonal antibodies with immuno-therapeutic / prophylactic potential for Dengue, Chikungunya, RSV & Influenza :** Using high-throughput and cutting edge antibody generation techniques for e.g. those utilize *ex vivo* identification of antibody producing cells such as memory or plasma cells derived from human patients / subjects
- **Systematic and In depth functional evaluation of mAb's:**
 - By their ability to bind and curtail the specific antigen/pathogen in question at a macromolecular level, and identification of precise epitopes;
 - Their ability to mediate effector functions via Fc associated functions - using cell based assays such as antibody dependent cell mediated cytotoxicity, complement dependent cytotoxicity; antibody-dependent cellular phagocytosis; antibody dependent enhancement of infection etc;
 - Explore the Fab associated functions such as their ability to be pan/broadly neutralizing at high potency for these anti-viral antibodies; receptor activation/blockade etc. so that their prophylactic / therapeutic potential can be explored;
 - Understand mechanism of action via holistic molecular characterization of the candidate monoclonal antibody binding to its target with respect to their primary, secondary & higher order structures;
 - Pharmacokinetic characteristics of the candidate monoclonal.
- **Proof of concept testing and evaluation of the candidate monoclonal antibody to be used as biologic.**
 - Able to perform small animal model based testing and evaluation for proof of concept studies to establish the prophylactic/therapeutic potential - pre-clinical safety, immunogenicity, tolerance, routes of administration, risk assessment and efficacy of candidate monoclonal antibodies.
 - Transfer the technology to interested Industry partner.

d. Vaccine evaluation platform:

The consortium member should be having capabilities for:

- Development of assays for evaluation of immune response to Dengue, Influenza, Chikungunya and RSV vaccines by optimization of functional and high throughput immunoassays even using advance cutting edge technologies and subsequent technology transfer to GCLP labs or vaccine developers.
- Evaluation and establishing the predictive capacity of the developed assays using existing, well-characterized human clinical and correlate assay results to known diseases.

e. Animal Facility:

A consortium member should have capabilities for:

- Conducting Immunization studies for establishing proof of concept or understanding the immunological characteristics of the product by assessing the relevant immune response, e.g. humoral and/or cell-mediated immune response.
- Design, Manage and/or conduct Challenge or Protection studies in Transgenic/Humanized Mice or other small animals as applicable;
- Develop new EPF free Transgenic/Humanized Mice models utilizing knock in and knock out (KO) methodologies through different technologies for gene editing.

f. Product Development Advisory Services:

Provide support and advice to facilitate translation of a candidate molecule from late-stage preclinical to early clinical development by:

- 4Providing manufacturing support through identification and management of manufacturing partners for production of clinical materials;
- Guiding and supporting clinical trial plans/designs, developing strategies for engagement of a epidemiology and demography mapped study population towards intended product outcomes, and identify and manage partners engaged in clinical development;
- Assisting in development of a regulatory strategy and support preparation of related filings, e.g. pre-IND, IND (India, USA and International).
- Aid in Product development planning, including supporting development of Product Development Plan and Target Product Profile and provision of tools for

monitoring of objectives vs. deliverables; Quality assurance support across entire process.

- Provide Project Management support along with advice and linkages with partners to support activities through different stages of product development.

4. Operational Structure of the Translational Research Consortium:

i. Individual TRCs would be built for a specific disease i.e. Dengue, Influenza, Chikungunya and RSV.

ii. Each TRC will be composed of the following UNITS:

- Access to Clinical Samples (mandatory)
- Access to Animal facility (mandatory)
 - Core research unit consisting of 2-3 identified platforms
 - Virology platform
 - Antibody evaluation platform
 - Vaccine evaluation platform
- Each TRC should demonstrate access to the Product Development Advisory Services either through an existing partner or a roadmap for identifying partnerships to be provided as part of the proposal.

iii. Each TRC should consist of multi-disciplinary teams composed of the relevant infectious disease expert, platform expert, clinical experts with access to appropriate clinical samples, and experts in assay development and establishment.

iv. Role of the Lead Principal Investigator (PI) and collaborating Investigators:

- The lead PI will be responsible for planning, development, implementation and management of the particular translational research consortium. Lead PI will coordinate with all the other units ensuring effective implementation and management of the overall consortium's scientific activities.
- Each unit will be represented by an Investigator who will be responsible for managing his/her respective operation unit.

v. Additional responsibilities of the Primary applicant:

- Responsible for submission of the complete proposal including letter of partnerships;
- Responsible for developing work-packages that would illustrate specific roles and responsibilities of each unit, cross-linkages and resources required;
- Responsible for the overall Project Implementation

- Should have a management and operations unit for overall management, coordination and supervision of the Consortium activities
- The Primary applicant must ensure that the expenses presented by unit partners correspond with the activities agreed by the unit partners
- To submit regular reports and other documentation on behalf of the Consortium

vi. Joint responsibilities of all the units:

- Develop a Strategic plan with common vision, mission, objective, goals, approach, activities, resource sharing plans, anticipated risks and alternative strategies to overcome them.
- Achieving the desired outcome by the end of the 4 year grant period

5. Expectations from the Consortium

- a) The consortium should be linked with GCLP labs for Vaccines for tech transfer and validation of the immunological assays being developed;
- b) The consortium should make available hyper-immune serum, naive serum, circulating viral strain for all the above mentioned diseases to GCLP labs for clinical immunogenicity evaluation and other vaccine developers supported under this program or other GoI programs or other initiatives of the Program if required;
- c) The consortia would have the ability to conduct activities so as to act as a bridge between academia and industry;
- d) The consortia will not conduct or be supported for discovery/blue-sky research activities.

6. Eligibility Criteria

Legal eligible Proponents:

- The proposals can be submitted:
 - Solely by an Indian Company or
 - Jointly by an Indian Company and Institutes/ Government entities/ R&D Organizations/ Non-profit organizations or
 - By a Consortium of Indian Companies along with Institutes/ Government entities/ R&D Organizations/ Non-profit organizations or
 - Solely by an Academia or research institution or in collaboration with other Academia or research institutions.

- **Criteria Particulars for the Proponent entities**

- *Indian companies*

An Indian Company is defined as one which is registered under the Indian Companies Act, 2013 and minimum 51% of the shares of the Company should be held by Indian Citizens holding Indian passport (Indian Citizens do not include Person of Indian Origin (PIO) and Overseas Citizenship of India (OCI) holders.

- *Institutes/ Government entities/ R&D Organizations/ Non-profit organizations*

This will include Academic Research Institutes, Universities, Research Foundation, Medical Colleges and Institutes – both public and private who are valid legal entities such as Trust, Society or established under central or state statute.

➤ The Primary Applicant (Lead PI) and each Investigator of other units should:

- Demonstrate prior respective experience in the relevant disease, platform technology or other respective area through prior publications and data published from their respective labs/ institutes;
- Have access to or a plan to build linkages to obtain the international reference standards;
- Experience in handling virus and development of assays for the specific diseases - Dengue, RSV, Chikungunya and Influenza;
- Have current linkages or proven capacity in building multi-institutional partnership programs (vaccine/mAbs) - national and globally.
- Have demonstrated capabilities in the following areas:
 - Viral characterization studies;
 - Development of virus panels for Viral neutralization and Mab isolation;
 - Breed and develop EPF free Transgenic/Humanized mice models.
- Have the following capabilities for platforms such as (but not limited to)
 - Next generation sequencing platform
 - Flow Cytometer
 - Mass Spectrometer

- High throughput ELISA based assays and Data analytics
 - BSLII and/or BSLIII facilities depending the disease focus
 - Have know-how and ability for guiding regulatory compliances and product licensure;
 - Together have capabilities for establishing, engaging and managing partnerships including industrial, IP valorization, contract negotiation, project management and monitoring;
 - Have forward thinking, interdisciplinary service culture and has capabilities for technology transfer, commercialization and building academic and industrial collaborations.
- It would be preferable if the Principal Investigator of respective units has:
- Received prior funding from the Government of India and demonstrated capabilities for work related to Viral vaccine development activities and/or Mab isolation & development;
 - Demonstrated capabilities of being a service provider and developed linkages with industry;
 - Applicant institutions that have been prior recipients of Government of India funding for creation of a high throughput technology platform support initiative to promote interdisciplinary research shall be preferred;
 - Demonstrated capability for setting up a vaccine evaluation laboratory.
- The Primary applicant shall need to provide:
- Established links with partners (Letters of support) that it shall bring together for the purposes of this RFP;
 - Anticipated deliverables for the TRC over the grant period.

7. Funding Criteria

Project must be budgeted on a milestone basis. Funding will be awarded for 4 years, subject to the project team meeting agreed milestones. The primary applicant and the proposed partner can specify their quantum percentage and their corresponding milestones. The funds will be disbursed to them separately subject to the achievement of milestone and reporting of progress.

Allowable costs include:

- *Personnel:* Only personnel carrying out product based research and development are allowed to claim costs. Researchers and PIs who receive a salary from the host institution as permanent or fixed term staff members may NOT claim salary reimbursement from BIRAC grants;
- *Consultants:* These may include both local and/or foreign consultants who provide a service and capability that is not available among the project partners. A motivation is required. Preference should be given to local service providers;
- *Equipment:* Minimal support for the cost of equipment including the analytical and non-analytical equipment may be requested;
- *Supplies and consumables*
- *Sub-contracts:* These may be to any national or international organization that provides a service or capability that is not available among the project partners but is essential to the project;
- *Travel & accommodation:* Must be directly related to the execution of the project;
- *Other research costs*
- *Institutional overhead:* An indirect costs rate of 5%;
- *Infrastructure:* Infrastructure of the facilities pertaining to varied services including analytical work area, specimen collection room, waste disposal facility, fire safety equipment.

Non-allowable costs:

- Purchase or construction of a building
- Rental costs for space that is owned by the institutions participating in the project
- Recruitment costs for staff
- Attendance at conferences
- Institutional overheads on funds that are being “on-granted” to consortium partners
- Purchase of office furniture.

8. Evaluation and Decision Making Criteria

a) Scientific Merit:

- What is the state of readiness for the proposed work based on background information and scientific work conducted?
- Does the proposal's approach align with the RFP's objectives?
- Has the Primary applicant provided a comprehensive description of the approach being planned?
- Is the planned approach compelling, comprehensive and feasible from scientific and timeline perspectives?
- Has the best strategy been chosen and alternative approaches considered?

b) Team/Applicant:

- Is the Primary applicant competent to ensure effective conduct of the proposed work? Does the primary have substantial background published research to demonstrate adequate experience for the disease area/platform?
- Does each unit Investigator have relevant capabilities and appropriate experience to the same?
- Are the team roles and responsibilities, governance and organizational structure clearly defined?

c) Implementation:

- Has the implementation methodology and work plan adequately detailed and realistic?
- Has the applicant provided clear metrics for monitoring project progress including milestones, and outputs expected timelines, budget and benchmarks? Do they seem feasible in the given time frame of 4 years?
- Have the resources (technical and management people, equipment, collaboration, outsourcing needs etc.) required over the time frame been comprehensively mapped?
- Has the applicant anticipated difficulties/risks that may be encountered? Have alternative tactics and mitigation plans been considered in case of failure?

d) Partnerships and Stakeholder Engagement:

- Are the needs and roles for engaging with partners and other stakeholders clearly defined?
- Are the proposed partners competent to carry out the projected work? Do they have relevant qualifications, experience and demonstrated potential?
- Do the proposed partners bring complementary expertise to the proposal?
- Have the modalities of collaboration and integration between partners outlined?
- How well defined and appropriate are the activities and methods proposed for engagement, learning and planning?
- Are the plans for training, knowledge and tech transfer well-articulated?

e) Operational Feasibility and Market Acceptability:

- Are the future plans for ensuring sustainability post grant period well-thought-out?
- Does the Applicant have a unique value proposition (cost competitiveness, innovation, partner network, novel technologies) in comparison to competitors?
- Would the proposed work have a constructive impact on future pipeline?

f) Cost Estimates:

- Is the proposed budget reasonable in light of the defined scope of work? Have reliable references been provided for justification?
- Is the resource allocation across various stages sufficient and appropriate?

End of document
