Request for Proposals (RFP) for Establishing Clinical Trial Networks (CTNs) And Strengthening Clinical Trial capacity

RFP 1: To establish Clinical Trial Networks (CTNs) for hospital-based trial in specialties of Diabetology, Ophthalmology, Rheumatology and Oncology.

RFP 2: To study epidemiology of Dengue & Chikungunya in different age-groups at existing DSS/DHS/DDESS* site(s) and to further prepare the sites for conduct of GCP compliant field-based clinical trials.

RFP 3: Establish new DSS/DHS/DDESS* sites within the country to have complete geographical representation of potential trial sites and to study epidemiology of Dengue & Chikungunya in different age-groups at these sites.

RFP 4: To Establish data management platform: An IT platform for community-based data collection, analysis and reporting.

Under

National Biopharma Mission

Implementing Agency

Biotechnology Industry Research Assistance Council (BIRAC)

(A Government of India Enterprise)

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)

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**Demographic Surveillance System / Demographic and Health Surveillance / Demographic, Development and Environmental Surveillance System*

Section I - Program Overview – National Biopharma Mission (NBM)

National Biopharma Mission is an Academia-Industry Collaborative Mission For Accelerating Discovery Research to Early Development For Biopharmaceuticals. The objective is to - "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)

Background[1]

Towards strengthening the emerging biotechnology enterprise in India, Department of Biotechnology (DBT), Ministry of Science & Technology, has initiated the National Mission Program entitled - An Industry-Academia Collaborative Mission for Accelerating Discovery Research to Early Development for Biopharmaceuticals – *"**Innovate in India (i3) Empowering biotech entrepreneurs & accelerating inclusive innovation**" ("Program").* Through a dedicated Program Management Unit (PMU), Biotechnology Industry Research Assistance Council (BIRAC) the Public Sector Undertaking (PSU) of DBT is the Implementing Agency of the *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. Through this RFP, NBM proposes to establish Clinical Trial Networks (CTNs) and Strengthen Clinical trial capacity.

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

RFP Area: Establishing Clinical Trial Network for Hospital based Trials for trials in patients for testing Biologicals

RFP 1: To establish Clinical Trial Networks (CTNs) for hospital-based trial in specialties of Diabetology, Ophthalmology, Rheumatology and Oncology.

RFP Area: Strengthening Clinical Trial Capabilities for vaccine efficacy trials in healthy population cohort

RFP 2: To study epidemiology of Dengue & Chikungunya in different age-groups at existing DSS/DHS/DDESS* site(s) and to further prepare the sites for conduct of GCP compliant field-based clinical trials.

RFP 3: Establish new DSS/DHS/DDESS* sites within the country to have complete geographical representation of potential trial sites and to study epidemiology of Dengue & Chikungunya in different age-groups at these sites.

RFP 4: To Establish data management platform: An IT platform for community-based data collection, analysis and reporting.

The applications are sought in two stages:

- **Stage I (Screening):** Request for Letter of Intent (LoI)
- **Stage II (Evaluation):** Request for Full Proposal

1 For further details of the Program, see the National Biopharma Mission Document.

Section II – Application process, Instructions, Applicant eligibility criteria and other processes for the RFPs.

1. Application Timelines

Key Dates

Call Opens	15th Aug 2019
Last Date of Submission of Letter of Intent (LoI)	10th Oct 2019; 1400 hrs
Last Date of Submission of Full Proposal	Will be communicated through email to shortlisted applicants after screening of LoI

2. Application Guidelines and Process

The LoI can be submitted online as per the format on BIRAC Website under National Biopharma Mission link. The call for the LoI will be open for 08 weeks. The website will provide detailed user guide to facilitate the online LoI submission.

Process for submitting the LoI online is detailed below:

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

Instructions:

a. Applicants are advised to fill-up and submit their LoI(s) early without waiting for the last date in order to avoid any last-minute contingencies. The system stops accepting applications automatically after **1400 hrs** of the last date of online submission.
b. 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 LoI with essential supporting materials provided as uploads as asked.
c. Requests for changes in the LoI once submitted will not be encouraged.
d. Providing incorrect information intentionally is viewed adversely.
e. Please read through this RFP in its entirety and ensure that the application, budget and organization are in compliance with the eligibility criteria provided. LoI 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.

f. Proposed budget shall be made inclusive of all applicable taxes and shall be considered accordingly.
g. Information on all relevant pre-existing agreements/ MoUs should be provided at the time of proposal submission if considered relevant to the proposal
h. Risk management proposal for the project should be submitted if project awarded.

3. Screening and Evaluation Methodology

Proposals will be evaluated in two stages:

- Stage I: Screening of Letter of Intent (s)
- Stage II: Evaluation of Full Proposal (only for shortlisted applicants)

Stage I: Screening of Letter of Intent(s)

a. PMU-NBM, BIRAC will screen the Letter of Intent (LoI) for compliance with all the specified administrative and procedural provisions required in the RFP. If the LoI is found to be incomplete or non-compliant to the provisions described in the RFP, the LoI will be considered ineligible.
b. LoI(s) that meet the eligibility criteria will be reviewed and assessed by the duly constituted panel. Information may also be shared with selected third parties for the purposes of independent audit, evaluation and assessment of activities.
c. The panel will recommend shortlisted applications for further submission of full proposals. The request for submission of full proposal will be sent only to the shortlisted applicants.

Stage II: Evaluation of Full Proposal

a. Full proposals along with the relevant supporting documents may be submitted online within the stipulated time as communicated to the shortlisted applicants. The system stops accepting applications automatically after **1400 hrs** of the last date of online submission. The proposals not received on or before **1400 hrs** of the last date would be considered withdrawn by the applicant.
b. Technical (TDD) and Financial Due Diligence (FDD) process (site visits) of the shortlisted LoI(s) (if required) would be carried out by PMU-NBM, BIRAC as part of the review process and as per the recommendations of the panel/Scientific Advisory Group (SAG). FDD will not be done for Govt. academic institutes, Govt. organizations and other institutions established under statutes.
c. The SAG will complete the review of full proposals and recommend shortlisted proposals for further discussions with the Technical Advisory Group.
d. Applicants may also be invited for interaction or sought written clarifications when it is felt beneficial to ensure that outstanding questions (if any) are resolved prior to concluding the full review.

e. Recommendation on proposals to be funded will be made by the Technical Advisory Group.
f. A final approval on proposals to be funded will be made by the Competent Authority of BIRAC.

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

DBT/BIRAC reserves the right not to process your proposal if you will be ineligible to be a proponent or if the *subject* of your proposal do not fall within the RFPs' remit. Mere consideration of the Proposal in no way implies that sanction of Grant-in Aid will be forthcoming unless other Technical, legal and financial requirements are fulfilled.

4. Eligibility Criteria

Who may apply?

The proposals can be submitted:

- Solely by Non-profit organizations / Societies / Trusts/ Foundation/ Associations/ Government entities/ Institutes/ Institutes established under Acts/statute OR
- Jointly by Non-profit organizations / Societies / Trusts/ Foundation/ Associations/ Government entities/ R&D Organizations / Institutes established under Acts

Criteria Particulars for the Proponent entities

Non-profit organizations/ Government entities/ Institutes/ R&D 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.

Relevant documents to be submitted at the time of LoI submission:

Applicant being an Indian academic scientist and researcher:

a. Copy of passport (from academic scientists & researchers) or self-declaration of Citizenship attested by a gazetted officer.
b. A declaration/authorization in favour of applicant, issued by Host Organization (which states that the host organization is willing to give facilities to applicant for the project applied for).

Indian institution/ universities/ public research organization:

a. Affiliation/registration certificate or statute reference for establishment.
b. Details regarding in-house R&D facility, if any.
c. If the institution/public research organization are registered under/as Society or Trust, then they have to submit the documents as mentioned in the case of

Society/Trust.

Society/ Trust/ NGO/ Foundation/ Association:

Society

a. Society registration certificate and Byelaws
b. Details regarding in-house R&D facility, if any.
c. CA certificate (supporting the fact that half of the members of the society are Indian citizens)

Trust

a. Trust deed and Registration Certificate
b. Details regarding in-house R&D facility, if any
c. CA certificate (supporting the fact that half of the members of the trustees are Indian citizens)

NGO/ Foundation/ Association

a. Registration details/ certificate.
b. Details regarding in-house R&D facility, if any.
c. If the NGO/ Foundation/ Association are registered under/as Society or Trust, then they have to submit the documents as mentioned in the case of Society/ Trust.

5. Requisites for Funding

Decision to fund will be as per sanction of the competent authority. Successful proponents shall enter into necessary funding agreements. The fund disbursement will be subject to completion of required formalities. The disbursement will be by way of Grant-in-aid assistance. The fund recipient shall be accountable for fund utilization as per the sanction. Re-appropriation of funds can be undertaken only after approval of BIRAC, within the same Budget Head (Non-Recurring or Recurring).

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. A letter of authorization by the Head of the Academia for acceptance of the Grant-in-Aid under NBM in BIRAC format.
b. Opening up a No-Lien Account with a scheduled/nationalized Bank if recommended by BIRAC.
c. MoU with collaborator(s) (if applicable)/letter of support from contributors.
d. Commitment to comply with Clinical Research Validation and Management Framework (CRVMF).
e. Commitment to obtain all applicable environmental authorizations.
f. Inclusion of qualified environmental / EHS engineer in the team for implementation of Environment and Health Risk Management Plan (EHRMP) and comply with

Environmental Management Framework (EMF) requirements during all stages. Requirements on Environmental aspects may be found at http://www.birac.nic.in/webcontent/emf.pdf

g. Adhere to the Project Risk Management Plan during all stages of execution.

6. Program Monitoring Mechanism

Project Monitoring Committee (PMC)

All funded proposals must have their own Internal Monitoring Committee/Internal Project Review Committee which should meet regularly and its minutes should be filed appropriately for review.

The funded proposals shall also be monitored and mentored regularly by a Project Monitoring Committee (PMC) constituted by PMU-NBM, BIRAC for each project. The PMC is responsible to monitor the progress of the Project in conformity with the outputs, milestones, targets and objectives contained in the Agreement. Audit of the projects if warranted may be carried out.

Based on monitoring and assessment of progress the foregoing PMC will recommend:

a. Release of next instalment or part release thereof by BIRAC
b. Revision of project duration
c. Closing or dropping or modifying any of the components of the Project within the overall approved objectives, budget and timelines
d. Additional mentoring to overcome any technical problem faced in the Project implementation
e. Any other measure/s that will be deemed reasonably necessary for effective discharge of its duties and/or achievement of aims and objectives of proposed work

7. Reporting of Progress

a. On Successful completion of each Milestone, the applicant will be required to submit a detailed Milestone Completion Report (MCR) as per the prescribed format.
b. The MCR will be assessed by the PMC for its completion. On recommendation of the PMC, the next Milestone fund will be released.
c. The Applicant will have to submit a duly certified Statement of Expenditure (SoE) and Utilization Certificate (UC) on every 30th September and 31st March within a month of closure of the accounts for the respective half year till completion of the Project duration.
d. Format for MCR including Technical completion report, Utilization Certificate and Statement of Expenditure will be made available as per requirement.
e. The Applicant will have to submit compliance to the Project Risk Management plan.

8. Funding Mechanisms

Project budget must be milestone-based. Funding will be awarded for maximum of 03 years and depending on the objectives. Fund disbursements will be subject to the project team attaining the committed milestones. The primary applicant and the proposed collaborator(s) should specify their respective budgets and their corresponding milestones. The funds will be

disbursed to them separately subject to the achievement of milestone/s and satisfactory reporting of progress.

Allowable Costs:

Allowable costs may include but not limited to the following:

- **Non-Recurring:** Purchase of Laptops/desktops/tablets, proprietary software, servers, sim cards, laser printer, photocopier, scanner, weighing scale, refurbishment, furniture, CCTV, cold storage (-80ºC, -20ºC, refrigerators), temperature monitoring system, data loggers, centrifuges, UPS, AC.

- **Recurring:**
  - **Database**: Servers, relevant journal and market reports subscription.
  - **Manpower**: Administrative/HR executive for field office, study coordinator, study investigator, data manager, pharmacist, QA staff, nursing staff, GIS manpower, Census manpower, Station manager, statistician, project manager, lab technician, phlebotomist, field workers.

    IT manpower – Software developer/tester and technicians as applicable

  - **Consumables**

    Clinical consumables - thermometer, stethoscope, sphygmomanometer, USG gel bottles, USG thermopaper, stadiometer, measuring tapes, wipes, sanitizer, tissue roll cotton roll, alcohol (ethanol), disinfectant, etc.

    Lab consumables - Centrifuge tubes, culture bottles, ice buckets, laboratory trays, vacutainer needles, vacutainers, microcentrifuge tubes, pipettes, pipette tips, cryovial container box, sample collection vials, syringes, cannulas, needles, kits, sample transportation packing/bags, microtiter plates, cuvettes, pH testing paper or pH testing probe, microslides, slide boxes, paraffin, petridishes, loops, Bio-specimen collection containers, test tube rack, etc.

    Safety gear - disposable masks, shoe covers, disposable gloves, labcoats, Eye Protection, eye goggles or face shield, etc.

    IT accessories - computer accessories, software, printer cartridge, data logger, tablet bag, SIM cards (with data)

    General Stationary including subject material
    Communication expenses, scientific publication relevant to the funded project
    Subject reimbursement for participation
    Ethics Committee fees

  - **Travel:** This may include local travel for staff for community engagement**,** investigator travel to field/site, meeting within the cluster, to BIRAC for review meetings and

presentations, internship travel (domestic or international) (only for training participants), Vehicle rental and fuel charges

- **Contingency and Overheads:**
  - Insurance: Accidental
  - May include rentals including rentals for guest house, rentals for servers, utilities like AC, telephone bills, electricity bills (only for field office functioning as per RFP 2 & RFP 3)

Non-Allowable Costs:

- Construction work
- Outsourcing for preparation of reports of any nature.
- Any Litigation/ Opposition/ Infringement cost.
- Any legal fees outside the purview of allowable cost.
- Any fees/ charges related to existing collaborations for individuals or organizations.
- Any other cost as recommended by the SAG/ TAG.

9. Screening and Proposal Evaluation Criteria

a. **Proposal Merit:**

- Does the LoI approach align with the objective of RFP?
- Does the LoI/Proposal demonstrate preliminary experience which will be useful for the proposed scope of work?
- Has the applicant provided an adequate description of the existing manpower and infrastructure to understand their present capabilities?
- Are the objectives, activities and milestones well defined in the proposal?

b. **Team/Applicant:**

- Is the applicant/collaborator(s) competent to ensure effective conduct of the proposed work?
- Does the team have relevant capabilities and appropriate experience for the same?
- Has the applicant provided letters of support/approvals from the appropriate statutory authorities they would like to engage with during the different stages of execution of the proposed work?

c. **Implementation and Infrastructure:**

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

proposal?

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

Note: We welcome potential applicants contacting the mission before submitting applications to clarify any questions or discuss their ideas with us. Kindly submit the Letter of Intent and if shortlisted please submit the full proposal also at least a few days before the deadline.

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

Email: technical.birac@gov.in

For RFP 1: Dr. Madhvi Rao, Senior Programme Manager, PMU- National Biopharma Mission. **Email:** nbm1@birac.nic.in

For RFP 2, RFP 3 and RFP 4: Dr. Shikha T Malik, Programme Manager, PMU- National Biopharma Mission. **Email:** nbm2@birac.nic.in

SECTION III - Details of the RFP

RFP 1: To establish Clinical Trial Networks (CTNs) for hospital-based trial in specialties of Diabetology, Ophthalmology, Rheumatology and Oncology.

A. Background

As one of its objectives, National Biopharma Mission (NBM) provides support to advance development of Indigenous Biosimilar products while in parallel strengthening the capacity and infrastructure required for development of these products and thereby ensuring launch of affordable biosimilars at the earliest in Indian market. Towards this NBM is supporting Indian Biotechnology academia and companies in preclinical and clinical development of Biosimilar products.

In reference to the clinical development of Biosimilars one of the needs identified by Biotech companies is the challenge in accessing trained and equipped clinical trial sites in the country. It is expected that about 10-15 Biosimilars will be required to be tested against the innovator in head to head clinical trials each year for the next few years. For testing any one biosimilar typically 200-300 patients are recruited in each trial to test the efficacy in the primary indication of the Biosimilar. Presently, the Indian Biotech companies are facing numerous challenges in identifying adequate number of clinical trial sites which have the required infrastructure, capacity, trained manpower, harmonised processes and background data on disease incidence at their respective sites and access to disease registries, at institutional, local, regional/state, and national levels.

Considering the limited capacity of Indian hospitals in handling regulatory compliant multiple clinical trials it is anticipated that delay in conduct of clinical trials can impact the development timelines of biosimilars and thereby delay launch of affordable biosimilars for the Indian population. Based on the portfolio of products being supported National Biopharma Mission is proposing to support establishment of respective CT networks of hospitals. Considering the success of the "***National Cancer Grid"*** it is anticipated that each speciality network over time can follow the model of "***National Cancer Grid"*** for its future course.

B. Objective

To establish CT networks so that each CT network has multiple sites accessible to Indian biotech companies for conduct of clinical trials for testing Biosimilars/ Biologicals. As CT network will have multiple sites, all sites in the network are expected to develop harmonised processes, each site will establish basic infrastructure required for conduct of clinical trials of that speciality, will have registered ethics committee. Common IT system across sites on registry data of patients will allow pooling of data by end of 02 years of funding. In addition, each site should have access to NABL accredited lab (either in house or through external collaboration) for haematology/biochemistry/ immunology profiling.

C. Technical Scope of the Proposal

The following respective specialty CT network is expected to provide Indian Biotech companies access to all the sites in the network for conduct of clinical trials.

- Diabetology
- Ophthalmology
- Rheumatology
- Oncology

D. Screening and Evaluation Criteria

A particular speciality CT network needs to identify sites which would work together and apply to National Biopharma Mission as one CT network giving the required details of each site.

Each specialty Network (Diabetology network or Ophthalmology network or Rheumatology network or Oncology network) should have at least 6 sites with each site having the following attributes

1. Respective Specialty being practiced in the hospital. Specialty wise diagnostic set-up is required for respective therapeutic area. e.g. for oncology, radiology setup with study related specifications and expertise, ultramodern diagnostic equipment in ophthalmology with super specialties like retina specialist, glaucoma, etc.
2. Appropriate infrastructure of the hospital in terms of number of beds and other facilities like uninterrupted electricity, pharmacies with temperature control and log and Intensive Care Unit and emergency department with critical care professionals to handle emergencies for enrolled patients, either trial-related or otherwise.
3. Inclination of each site Investigator to be part of meaningful research and time availability. It is critical that the Investigator of each site does not have too many trials on their hands at any given point in time, so as to be able to give individual attention to each study, the patients, and the trial conduct as well as overall responsibility of the study team as a whole.
4. Declaration from the Head of the institution to provide for adequate dedicated constructed space (~ 2500 sq ft) for subject counseling, consenting, recruitment activities, pharmacy and accredited laboratory sample collection facility. Additionally, central storage and archival facility to be available in the hospital.
5. Access to NABL accredited lab either in the hospital or in vicinity.
6. In a network at least one site should demonstrate expertise in conduct of research studies/ clinical trials/studies. Qualified, experienced and interested team of Investigators/Co-investigators, physician, coordinators, nurses, lab technicians and field workers having experience and specialization relevant to the therapeutic area who is prepared to guide other inexperienced sites in the network. An established Clinical Trials Unit will be an advantage.
7. Functional Ethics committee at each site (institutes with ECs registered with DCGI to be preferred) with appropriate frequency of meeting. Availability of EC Chairman, contact person and required quorum. (Some sites may have additional committees such as Scientific or additional review committees and should be accordingly mentioned in the application)

8. Access to a large patient pool with pre-existing patient databases and registries being an added bonus. Yearly (and/or monthly) OPD and in-patient records, including procedures and treatment statistics.

Each CT network should have the following attributes between its proposed sites:

1. Reasonable representation of private and public hospitals sites in the network with at least one third of the sites being public hospitals.
2. Representation of sites from as many diverse geographies of the country as possible (North, West, central, South, East and north-east India)
3. CT networks with mix of experienced and new sites (approximately one-third of the sites should be new in the network proposed who have not done regulatory submission clinical trials in the past)
4. Proposal to develop basic minimum patient data registry through common IT software or data collection tool.

E. Budget

The budget for establishing one network is capped at 1600 lakhs for 03 years. The final approved budget will consider the number of sites proposed in each network.

F. Expected Outcome

The year wise expectation from each site in the network is as described below:

End of Year 1

1. Recruitment, training of Manpower for establishing systems for conduct of clinical trials and providing at least 3-years contract to recruited manpower to ensure continuity
2. Development of essential Standard Operating Procedures which will be required for conduct of clinical trial (List mentioned below) to be harmonised across all sites so as to have as similar processes as possible
3. Training of recruited manpower and existing faculty team on GCP and development of SOPs and cross training between sites of the network. Online training portals may be used to ensure ICH-GCP, Indian regulatory requirements, Audio-video Consenting, Source documents, SAE reporting process related training documents etc.
4. Assessment of training imparted to evaluate both trainer and trainee performance.
5. Identify vendor for establishing common IT systems for sharing of data of registries data, Installation of the software for data collection and harmonizing systems across sites and development of plan for developing a registry of few diseases in questions
6. Development of patient database/registry plans to access patient specific population from the immediate and wider catchment areas. Identification of catchment area, specific institutes and doctors, as well as designated feeder sites.
7. Publication of the collated registry data of all sites
8. Installation of the refrigerator, back-up of refrigerator and temperature monitoring systems with well-defined systems

9. All sites in the network will undergo third-party audit for review of the systems and processes before release of grant for second year
10. Annual meet of all the sites and cross training of the recruited manpower as required
11. Calibration and standardization of the equipment of clinical trial site at regular intervals, with the meticulous maintenance of records. Annual maintenance contracts.

End of Year 02

1. Initiation of registry work across all sites as per the submitted plan
2. Identification of a NABL accredited lab and forming systems for sample transfer from hospitals and receiving at the lab ensuring GCLP compliance for each site in the network
3. Standardization of local laboratory reference ranges – at most of the sites, the reference ranges are updated upon change in reagents.
4. Establishment of dedicated pharmacy with required systems of temperature monitoring and access to Pharmacy
5. Establishment of dedicated and adequate archives/record keeping area or third party archival facility
6. Evidence of reaching out to Indian Biotech companies expressing interest and ensuring audit of their systems from Indian CRO's or Biotech companies
7. All sites in the network will undergo third-party audit for review of the systems and processes before release of grant for third year
8. Publication of the collated registry data of all sites.
9. Reach out to Indian Biotech companies so as to identify potential clinical trials of Biologicals which can be done at respective sites.

End of Year 03

1. Continue to compile data from all collaborating institutes on the registries and publish collated data of all sites
2. Initiate clinical trial for an Indian Biotech company at the site for regulatory submission

**SOPs at each site to be harmonised in each network*

- Informed consent process
- Setting up and maintenance of Site master file
- Preparing for monitoring visit, audit and inspection
- Hiring of staff and Delegation of responsibilities
- Study staff training
- Collection and Handling of biospecimens
- Receipt, storage and accountability of Investigational Product
- Quality Management systems
- Study Participant Retention
- Calibration of Instruments
- Communication with Ethics Committee
- Documentation & Record keeping
- Documents storage and archival

- Management of Adverse Drug Reactions / Events
- SAE management and reporting

Initiative for Strengthening Clinical Trial Capacities for conduct of Community based Vaccine trials (Phase I/II/III Human Clinical Trials)

Background:

One of the objectives of National Biopharma Mission (NBM) is to strengthen vaccine product development capabilities to a level that will be globally competitive. Towards fulfilling this objective NBM is:

- Supporting Indian vaccine companies developing new and novel vaccine candidates
- Supporting independent viral and bacterial GCLP compliant labs to conduct clinical immunogenicity studies during human clinical trials
- Supporting formation of translational research consortia between hospital sites and research labs for diseases of Dengue and Chikungunya.

In continuation towards the above-mentioned efforts another key area identified by NBM is to strengthen field-based clinical trial capabilities for late-stage vaccine efficacy trials. The new and novel vaccine candidates being supported under NBM are for Dengue and Chikungunya diseases. Since, the primary efficacy analysis in Phase III trials is expected to be the number of Dengue cases of any serotype in vaccinated and control subjects, planning of such trials depends on reliable estimates of disease incidence and input of accurate incidence data from as many geographical zones as possible. In addition, as with all new vaccines, it is unknown how long the measured protection against Dengue/ Chikungunya will last. Therefore, prolonged monitoring as well as post-licensure studies, will be expected to be done to measure long-term safety and efficacy, including whether there is any waning of protection over time. The Phase III clinical trials may also have exploratory efficacy objectives like measuring disease attack rates, hospitalizations, severe disease, medical visits, costs. etc.

Keeping in view the above requirements of identifying the study sites and the ability of each study site to ensure long term follow-up of vaccinated and control subjects it is important to have field sites with reliable estimates of disease burden, access to all age groups of target population, ability to follow-up each enrolled subject for long term follow-up, ability to do cluster based randomized trials if required, complete mapping of private and public health service so as not to miss any disease case, access to accredited labs etc.
The Biopharma mission therefore proposes to address this need through the following two initiatives:

1. Estimate Disease Incidence in all age groups in existing DSS/DHS/DDESS* sites in the country to complement the ongoing efforts of Indian Council of Medical Research (ICMR) and prepare the sites for conduct of GCP complaint vaccine clinical trials. (**RFP 2)**

2. Establish new DSS/DHS/DDESS* sites within the country to have complete geographical representation of potential trial sites and to study epidemiology of Dengue and Chikungunya in different age-groups at these sites. (**RFP 3)**

**Demographic Surveillance System/Demographic and Health System/Demographic, Development and Environmental Surveillance System*

Through this effort NBM aims to establish Clinical Trial Sites for field-based studies. Such sites once developed would further be available for conduct of other vaccine trials such as RSV, Influenza, specific target population studies like the Maternal immunizations etc. as and when needed. This would positively impact the clinical development timelines of products (esp. vaccines) and thus their cost and availability in the country.

RFP 2: **To study epidemiology of Dengue & Chikungunya in different age-groups at existing DSS/DHS/DDESS* site(s) and to further prepare the sites for conduct of GCP compliant field-based clinical trials**

**Demographic Surveillance System / Demographic and Health Surveillance / Demographic, Development and Environmental Surveillance System*

A. Objective:

The objective is to undertake community-based studies to estimate incidence of Dengue & Chikungunya at existing **DSS/DHS/DDESS* sites**. All sites selected through the call are expected to follow a common study protocol to estimate the incidence of Dengue and Chikungunya through an active surveillance study. In addition, the sites are expected to explore factors influencing community's participation in vaccine trials, and building capabilities to ensure adherence to ICH GCP and Indian GCP guidelines. The sites will also be linked with the Translational Research Consortia funded under National Biopharma Mission for potential scientific research collaborations.

B. Technical Scope of the Proposal

The grant would be provided to the applicant for a period of 03 years to:

(a) Study the epidemiology of disease of interest i.e. Dengue & Chikungunya (Year 1 to Year 3)

Conduct active surveillance studies to study disease incidence in the 03 age groups; 1-5 years, 5-18 years, and >18 years, baseline seroprevalence in the population and calculate accurate attack rates and disease burden, seasonal variability, age and gender disease incidence and elucidate strain specific seroprevalence in the healthy population after seeking Ethics committee approval. The laboratory accessed should be NABL accredited and sample collection, storage and shipment processed should be well defined.

(b) Understanding of the factors influencing willingness of community participation in Dengue / Chikungunya vaccine trials (Year 2)

To understand community perceptions, awareness and behaviour towards participation in future Dengue & Chikungunya vaccine trials, recruitment potential retention challenges and community need assessment.

(c) Build capacity for conduct of GCP compliant clinical trials (Year 3)

The sites will ensure site preparedness for future conduct of clinical trials by: developing systems establishing processes for implementing clinical trial procedures, having the required infrastructure and building capacity through training. Systems and tools to ensure GCP compliance will be developed. Procedures related to storage of

Investigational products (IP), clinical supplies, biological samples and other activities including randomization, blinding, adverse event monitoring, quality systems in accordance with GCP and GCLP compliance will be established.

(d) Publication of epidemiology data (Year 2 & 3)

C. Screening and Evaluation Criteria

1. Access and availability of demographic data of the DSS/DHS/ DDESS site (denominator for calculation of incidence).
2. Evidence of local permissions from state and/ or district authorities for prior engagement activities with the community (to be provided as evidence).
3. Evidence of functional Field office with basic infrastructure and staff.
4. Demonstrate access to an existing secondary health care centre/Medical college with in-patient admission and diagnostic facilities.
5. Ethics Committee review mechanism.
6. Experience in conducting community-based longitudinal/ cross-sectional surveillance studies.
7. Experience of collaboration with multiple stakeholders (academia, government, non-profit organizations, and community advocacy group, clinical researchers, funders, physicians).
8. Applicant units having well-trained staff with capabilities for community outreach / community-based research.
9. Access to GCLP compliant laboratories for sample collection, handling, processing, storage & testing and validated diagnostic tests under the NABL scope for case confirmation of Dengue and Chikungunya.
10. Existing Data collection, management and analysis capabilities.

D. Pre-requisites for submitting full proposal if shortlisted in screening

While submitting full proposal, the applicant should provide the following details (and documentary proof wherever applicable):

1. Experience and current capabilities pertaining to:

- Access and availability of demographic data of a healthy cohort in a geographically defined area.
- Human resource, facilities and infrastructure for conducting community-based research activities
- Local Govt. permission letters (eg. MoU with state govt., permissions from district health authorities) for prior activities done in the local population.
- Outline of active surveillance epidemiology study feasible to be conducted in the population. This may include a brief on research plan including clearly defined objectives

and methodology, sample size, Community engagement and outreach plan and Data Management plan and the lab to be accessed.

2. Letters of support/approvals from the appropriate statutory authorities they would like to engage with during the different stages of execution of the proposed work.

NOTE: DSS sites already being supported by ICMR for similar activities will not be eligible to apply under this call.

E. Budget:

The budget for one site is capped at 650 lakhs for 03 years.

F. Expected Outcome:

Year-wise expected outcome is as follows:

Year 1 to Year 3:

- Dengue and Chikungunya Epidemiological data in the cohort as per the common protocol across all sites selected to be funded under NBM.
- Needs Assessment and Understanding of the factors influencing willingness of community participation in Dengue/Chikungunya trial.
- Processes established for use of NABL accredited labs and
- Mapping of all health providers in the site and establishing systems to obtain health related data for the population of the site.

Year 3:

- A well-established clinical trial site with required infrastructure including but not limited to access to NABL accredited laboratory facilities, trained research team, infrastructure for IP & sample storage, document archival capacity, access to hospital for admissions and quality management systems/ tools to execute GCP complaint clinical trials at the DSS site. This capacity at site will be established in the third year only if the site was judged as satisfactory after the first-two years performance.

RFP 3: **Establish new DSS/DHS/DDESS* sites within the country to have complete geographical representation of potential trial sites and to study epidemiology of Dengue & Chikungunya in different age-groups at these sites.**

**Demographic Surveillance System / Demographic and Health Surveillance / Demographic, Development and Environmental Surveillance System*

A. Objective:

The objective of this grant is to establish a population based geographical cohort towards having **DSS/DHS/DDESS* sites.** The size of the cohort to be equivalent to or higher than 01 Block or 50,000 population. After establishing the cohorts in the first two years the site is expected to study epidemiology of Dengue and Chikungunya in different age-groups at these sites. The sites will also be linked with the Translational Research Consortia funded under National Biopharma Mission for potential scientific research collaborations.

B. Technical Scope of the Proposal:

(a) Establish a new DSS/DHS/DDESS site (Year 1 and 2)*

Within the first two years, the unit will study the detailed demography of the proposed cohort of healthy population (equivalent to or higher than 01 Block or 50,000 population.). This includes demographic variables of age, cohort, sex ratio, marital status, household size / type of family, residency status / migration, and mortality data. In addition, socio-economic status markers, including education, employment / annual income, household wealth and place of residence will need to be collected. The software tool will guide on collection of other related datapoints like geospatial, meteorological and air quality etc.

(b) Study the epidemiology of Dengue & Chikungunya in different age-groups at the established site (Year 3)

In the third year the sites which would have successfully completed establishing a DSS/DHS/DDESS site will receive funding for studying epidemiology of Dengue and Chikungunya through a common protocol being followed at other sites. Conduct active surveillance studies to study disease incidence in the 03 age groups; 1-5 years, 5-18 years, and >18 years, baseline seroprevalence in the population and calculate accurate attack rates and disease burden, seasonal variability, age and gender disease incidence and elucidate strain specific seroprevalence in the healthy population after seeking Ethics committee approval. The laboratory accessed should be NABL accredited and sample collection, storage and shipment processed should be well defined.

(c) Publication of demographic data (Year 3)

C. Screening and Evaluation Criteria

1. Access to an existing secondary health care centre or district hospital or medical college with in-patient admission and diagnostic facilities in close vicinity.
2. Presently ongoing community-based activity through field office and or permission from local administrations (eg. state govt. or district health authorities) for the proposed ***DSS/DHS/DDESS*** site.
3. Institutional Ethics Committee review mechanisms.
4. Mechanism for surveillance of target population.
5. Proposed *DSS/DHS/DDESS* site to have access to medical college or tertiary care institute or secondary health institute.
6. Applicant site(s) has access to NABL accredited clinical laboratories for sample collection, handling, processing, storage & testing, or access to validated diagnostic laboratories for case confirmation of Dengue and/or Chikungunya;
7. Good documentation practices processes in place for Data collection, retrieval and storage.
8. Linkages with ICMR/ DBT institutes
9. Existing Data collection, management and analysis capabilities
10. Dengue/ Chikungunya Seroprevalence data of the local population.

D. Pre – requisites for submitting full proposal

While submitting full proposal, the applicant should provide the following details (and documentary proof wherever applicable):

1. Applicant PI's experience in conducting epidemiological studies and / or surveillance.
2. Detailed plan for building the DSS/DHS/ DDESS site.

E. Budget

The budget for one site is capped at 450 lakhs for 03 years.

F. Expected outcome

At the end of the three-year grant period, the applicant will demonstrate

1. An established ***DSS/DHS/DDESS site*** with demographic and socio-economic data by the end of two years.
2. Epidemiology data on Dengue and Chikungunya in the established site.

RFP 4: To Establish data management platform: An IT platform for community-based data collection, analysis and reporting.

A. Objective:

To develop a Comprehensive Software for Demographic Surveillance Sites for **collecting and storage of population-based data collected in a paperless manner for a large number of variables repeatedly over time**. The application will be a **web-based and android based data entry application** that may store a database of:

Minimum requirement:

- Collection of Demography data and Demographic events (e.g. change of household head, death, change in marital status, pregnancy outcome/birth, pregnancy registration and migration)

In addition, the following variables may be captured in the database:

- **Socio cultural-economic and demographic variables**
- **Other new projects** that will be commissioned from time to time at these surveillance sites.

B. Technical Scope

B.1.To manage the Demographic Surveillance System in a paperless manner on a server. The designer/ platform should ensure the following but not limited to:

1. **Common Tasks**: The Common Tasks module should allow performing common functionalities in the application, such as login, forgot password, dashboard, and updating user Profile.
2. **Masters**: The Masters should allow managing locations, such as country, state, district, block, village, sector, and language and timing duration for the census data.
3. **Line listing:** Creation of line listing of the households/parcels in the surveillance site to be developed.
4. **Creating Baseline, census and update and update rounds**
5. **Nature of the built structure and their corresponding details:** Details of residential, non-residential and mixed structures, details of the individuals registered and options for viewing the household details should be there.
6. **Project Management:** The Project Management section should allow to create/manage the projects embedded in surveillance area.
7. **Form Designer:** Electronic Data Collection (EDC) should have a designer module through which case report forms and questionnaires can be designed according to different study designs: cross-sectional, cohort, case-control, clinical trials etc. and configure the database accordingly.
8. **Automate entire workflows:** The submission of form to the supervisor and finally to the

server should be triggered by the complete automation sequence.

9. **Follow up visit:** EDC should allow case follow up visit automatically based on the study protocol.
10. **Visit setup:** EDC should allow to set-up studies with fixed or predefined visit structure for longitudinal study designs.
11. **Real time validation checks:** EDC should allow users with no programming expertise to configure simple or complex validation checks through and easy to use web interface.
    - Validation rules
    - Dependencies and piping
    - Autofill
    - Calculated field

12. **Offline and online data entry platform**
13. **Create users, delegate rights and data collection points:** It should allow the admin of software to create users and user groups and give them access to studies, dashboards, forms, data and more.
14. **Quality Assurance:** EDC should allow the user to automate data quality process.
15. **Dynamic Form Activation:** Form activation should allow the user to customize the study database to display specific data entry forms based on values entered in trigger fields. User can design the study to display different forms depending on the treatment allocated to the subject, activate or hide specific forms based on variable.
16. **Data Extraction:** EDC should allow the user to extract data through a powerful data extraction module.
17. **Reports:** The Reports module should allow the admin to generate reports on various demographic data and the project data available for the population.
18. **Other features**
    - Form library
    - Question library
    - Audit logs, GPS capturing
    - Powerful design features like popups, click/upload photo, upload files and more
19. **GIS Integration:** Software should have mechanism to integrate demographic, and other collected data with geospatial mapping system.

B.2. Data Analysis

1. **Data Collation**: EDC should allow case data to be collated together from all sites.
2. **Data Analysis**: Data Analysis components to be built-in the software in consultation with Data Manager (or Biostatistician) as per the requirement of the site.

C. Screening and Evaluation Criteria

1. Availability of an existing data collection and management tool which can be deployed quickly at the sites.
2. Team Strength (Software developers-android and web, testers)

3. Previous experience of software development.

D. Pre – requisites for submitting full proposal

Already designed software being used by atleast one user.

E. Budget

The budget for this application is capped at 250 lakhs for 03 years.

F. Expected Outcome

1. The software should have features that provides dynamicity to register new projects, modify existing projects and able to introduce new variables and forms as required using the web-based/Android based data entry formats. The software should be ready for installation at different sites and data to be stored in central server.
2. Provide support of installing and maintaining the software through dedicated manpower at 6 sites across the country.
3. Continuous data back-up on a different server.

Data Ownership:

a. Each site will own the data collected at their site.
b. Data collated from all sites will be submitted to the Department of Biotechnology (DBT), Govt. of India and owned by DBT and not by the software developer.
c. Through a publication policy agreed by all sites data may be published as per the understanding/agreement between the sites.