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

Implementing Agency:

Biotechnology Industry Research Assistance Council (BIRAC)

(A Government of India Enterprise)

Co-funded through World Bank Loan Assistance

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Section 1: About the program

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)

Implementing Agency:

Biotechnology Industry Research Assistance Council (BIRAC)

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.

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 this sector in the country, including isolated centers 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.

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.

To aid in preparing a blueprint for building such a Program, DBT conducted multiple consultations with relevant stakeholders (composing of senior leaders and renowned experts across Government of India, industry and academia) that helped in understanding specific needs and gaps for product development, further aided in prioritization of the focus areas, outlining other requirements and structuring of this Program.

Envisioned Impact of the Program:

The Program is unique in that it leverages on effective utilization of existing indigenous potential, resources and infrastructure; creates a global network of experts/mentors/advisors to partner for enhancing product innovation in India; provides a non-competitive platform for engaging diverse stakeholders and ensures effective governance and project management through national-international networks.

The impact of the Program would be apparent across the product development value chain as:

- Development of specific affordable products would be enable de-risking and accelerated product development with increased success rates, reduced cost of development and faster uptake by the public health agencies;
- Building of accessible facilities would lead to decreased cost and risk during early stages of product development, with higher probability of converting research into products leading to decrease in investment and operational cost required during early stages of development;
- Building robust clinical trial network would aid in efficient clinical trial design decreasing redundancies and resource wastage, while increased awareness about clinical trials and regulatory pathways and ensure reliable and robust clinical validation of products ensuring safety of Indian population;

- Consortia would provide platform for development of innovative technologies that could assist in efficient and improved product development leading to enhanced product-oriented discovery and translational research;
- Bridging the talent gap in the ecosystem will create high-end work force for product development and aid in able staffing of the facilities and thereby enable efficient product development. It would also empower generation entrepreneurs and trainers, building scientific leadership in the country;
- Aid in enhanced academia-industry interlinking and providing increased opportunities for academia to translate knowledge into products and technologies through setup of TTO's would promote industry-academia collaborations and strengthen existing biotech clusters.

From an overall socio-economic perspective, this Program would impact beneficiaries ranging from academia, entrepreneurs, large industry, service sectors, SMEs and the public at large. From a social stand point, it would improve health-care system by providing new and targeted products and affordable solutions for current health needs. Also it would create a sustainable ecosystem that enables job creation and provides an environment for skilled talent to thrive and grow. This Program would also lead to increase in market capitalization of the country in terms of products (goal is to of capture 5% of global biopharmaceutical market from the current share of 3%), enhanced outsourcing capabilities, decreasing dependency on imports, leading to an IP driven bio-economy.

Program Design:

The Program would bring multiple elements together on the same platform by engaging with partners (government, academia and industry), providing strong governance structures, harnessing of individual strengths across the biopharmaceutical value chain, generating newer funding mechanisms and providing access to experts at different stages of development that would result in efficient product development. It would incorporate both incremental and non-incremental developmental approaches. The program will have 5 major components under 2 categories. Which are as follows:

1) *Development of specific affordable products:*
   Leveraging on resources available in India acceleration of three types of products would be facilitated:
   i. Biotherapeutics
   ii. Vaccines &
   iii. Medical devices (including diagnostics)
2) *Technology transfer and skill development.*
   i. *Establishment and capacity building of TTOs*
   ii. *Training and skill development*

Separate RFPs will be issued for each of the above five components

Section 2: Applications and evaluation processes:

1. Eligibility Criteria (Who can apply):

- **Legal eligible Proponents**

  - The proposals can be submitted by:
    - Solely by an Indian Company or
    - Jointly by an Indian Company and National R&D Organizations and Institutions; or
    - By a Consortium of Indian Companies along with National Research Organizations etc.
    - 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

- 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.

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 sanction 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)

2. Proposal Submission Methodology (How to apply):

The Proposal can be submitted online as per the required format. The website will provide detailed user guide in order to facilitate the online proposal submission.

Process for submitting the proposals online is detailed below:

- Log on the BIRAC (http://www.birac.nic.in)
- If you are a registered user, log-in using the credentials, else you need to register your company with by clicking on New User Registration.
- In case of new user registration, a computer generated password would be sent to the email-id provided at the time of registration. The password can be changed later.
- Once you login, you would be navigated to the page displaying RFP link.
- Click on the RFP on i3 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.

Company User Registration is open round the clock.

Online Proposal Submission can be done only during an active call. (Advertisement for Call for proposals is released in all national dailies and some biotechnology related magazines. Intimation of an active call is also displayed on the BIRAC and DBT websites)

Proposal Format

Proposal Outline

The Proposal should contain the following:

1. Applicant Details
2. Proposal Details
    - Overview
        - Objectives
        - Goals
    - Current Status and Justification
        - Key Challenges facing the sector
        - Rationale for the approach (any other strategies, reason for selecting proposed strategy,)

        - Background and currently available information (stage of development, preliminary data, studies conducted, patents details (if any)
        - Regulatory Clearances/Approvals (if any)
        - Patent Details (if any)
        - Alternative strategies considered
    - Research Approach/Strategy
        - Description of Approach (Summarize the special features in the environment and/or resources that make this application strong or unique)
        - Description of the Activities
        - Monitorable deliverables and Outputs
    - Team Details
        - Proposed partnership and roles (team composition, project sites/partner description, defining role of each partner)
        - Organizations credentials, its current capabilities, proposal's alignment with its mandate, previous expertise
        - A summary of Senior/Key Persons followed by their Biographical Sketches
    - Workplan and Timelines (PERT Chart)
    - Implementation arrangements/management
3. Appraisal
    - Impact assessment and the uniqueness of the proposal (economic and social impact)
    - Risk Assessment
4. Proposed Budget and justifications
5. Documentary Evidence Required:
    - Formal agreements/ MoUs with other key facilities/ suppliers

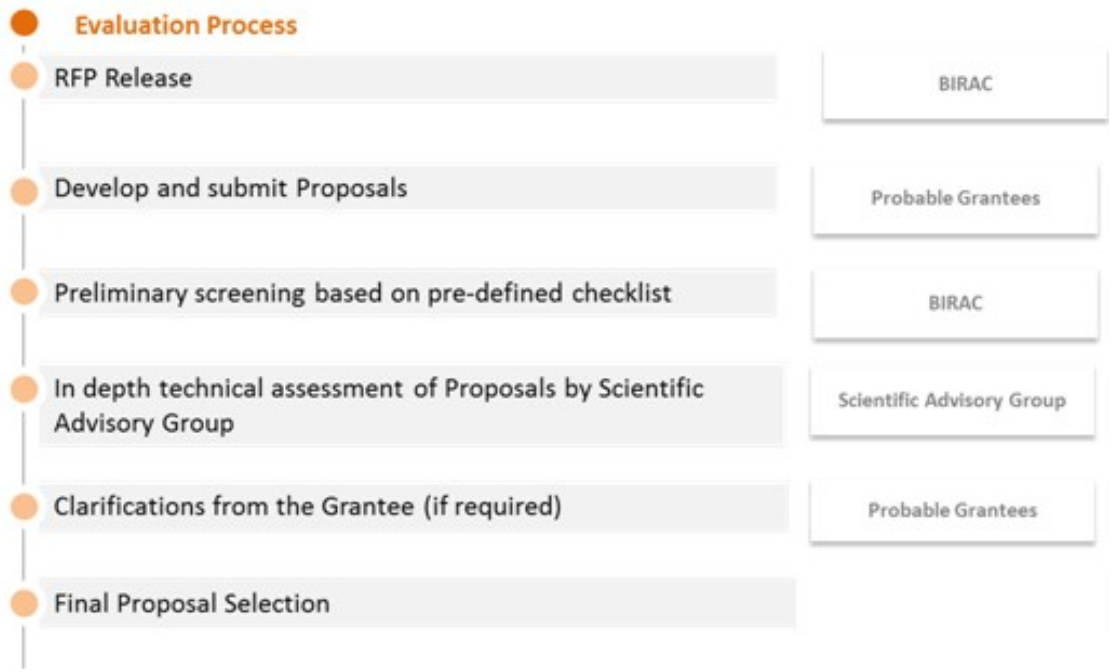
Any other due diligence

3. Evaluation Methodology

Full proposals will be sent to the Scientific Advisory Group for review. Information (including "personal data") provided in the Proposal will be used to process and evaluate the Proposals and to administer grant support, for the purposes of audit and evaluation and to monitor the fairness and trends in application decisions. Reviewers will be checked for conflicts of interest and sign confidentiality agreements. Information may also be shared with selected third parties for the purposes of independent audit, evaluation and assessment of activities. Some of the individuals, organizations and third parties with whom the information may be based outside of India. All personal data will be stored and used by or on behalf of

DBT/BIRAC in accordance with the Acts and confidentiality norms.

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.



4. Evaluation criteria

I. Screening and Preliminary review of the Proposal:

- Completeness of the Proposal: All the components duly filled (details in section 4) with appropriate documentation
- Basic eligibility:
  - Legal requirements
  - Aligned with the call objectives and requirements (detailed in Requirements in Section 3)

II. The Scientific Advisory Group will review based on the following parameters:

- **Approach and Methodology**

Ethical, scientific, scholarly, and financial standards in the promotion, design, conduct, evaluation and reporting of research.

1. Clarity of the research question.
   - Writing style that facilitates understanding of the plan
   - Objective/goals and reasoning clearly presented
2. Clarity of rationale for the research approach and methodology.
   - Appropriateness of the research design.
     - Best strategy chosen and alternative approaches considered
     - Well-integrated, well-reasoned
   - Appropriateness of the research methods
     - Consistent with the research design and best for achieving the desired research outcomes
   - Feasibility of the research approach

        - Project has clear and realistic plan, timeframe, work plan, budget, benchmarks
    - Literature review and preliminary data (If available) relevant to study design/research plan.
3. Anticipation of difficulties/risks that may be encountered in the research and plans for management.

- **Intellectual Property (if applicable)**
    1. Is there any background IP?
        - Relevance of the background IP for the proposed project
    2. Possibility of generating foreground IP
    3. Does the applicant have freedom to operate

- **Impact**

1. Potential for a significant contribution to the improvement of people's health in India and the world and/or to the development of more effective health services and products.
2. Appropriateness and adequacy of the proposed plan for knowledge dissemination and exchange - publication, dissemination amongst users , product related/commercialization

- **Organization credentials**

1. Qualifications of the applicant(s), including training, experience, demonstrated potential and independence (relative to career stage).
2. Experience of the applicant(s) in the proposed area of research and with the proposed methodology.
3. Expertise of the applicant(s), as demonstrated by scientific productivity over the years (publications, books, grants held, etc.). Productivity should be considered in the context of the norms for the research area, applicant experience
4. Appropriateness of the team of applicants (if more than one applicant) to carry out the proposed research, in terms of complementarity of expertise and synergistic potential.

5. Funding Release and Program Monitoring Mechanism

6. Key Dates

Call Opens on	**15th November 2017**
Call closes on	**15th December 2017 at 23.59**

7. Contact Information

Further information Contact Head NBM, Email: technical.birac@gov.in

Section 3: Detailed Request for Proposals

3.1: Biotherapeutics

RFP 1: Biosimilar – Product Development

Background:

Global efforts to develop bio-therapeutics (therapeutic proteins and monoclonal antibodies) have given us many novel and effective products that have enormously improved human health with more than 135 bio-therapeutics being use in various indications. They offer an attractive solution in comparison to small molecule with longer circulating half-life, high target specificity and ability to induce the immune system thereby providing successful solutions against medical conditions that had no effective treatments till recently. Yet their exorbitant cost makes them inaccessible to the Indian population e.g. a full one-year course of Herceptin treatment for breast cancer costing about $70,000, advocating the need for cost effective solutions.

Biosimilar are a cost effective alternative to this, with a huge market potential (large number of blockbuster biologics, mostly mAbs, worth $100 billion will be going off-patent by 2020). India with proven capabilities in this sector (more than 50 biosimilars being developed by 27 manufactures) has the business opportunity to capture the global market and increase its share from **3% to 5%** in next 5 years.

Objective:

To support development of biosimilars (therapeutic proteins and monoclonal antibodies) that are currently under development by the industry and bring them closer to the market in 5 years and simultaneously develop an ecosystem that would spur innovation to develop novel products.

Scope of RFP:

This call seeks proposals to accelerate development of cost effective, safe and efficacious biosimilars of monoclonal antibodies and therapeutic proteins for cancer, rheumatoid arthritis and diabetes.

The Call will ***not*** fund activities related to:

- Filing of Registration to CDSCO;
- Commercialization;
- Setting up large scale manufacturing facilities;
- Fundamental/Basic research

Mechanisms of Support through the call

- Direct Funding of product development activities through various stages including, preclinical development, production of early phase clinical grade material and human clinical trials.
- Access to the following affordable services and solutions developed through other calls of the i3 program:

- A GMP-compliant Cell Line Repository providing access to well-characterized cell lines (mammalian, microbial)
- A cGLP compliant facility for bio therapeutic characterization and validation.
- A Process Development Laboratory to enable development of manufacturing process
- A GMP compliant CMC facility for manufacturing of regulatory compliant preclinical and clinical trial lots

- Access to a group of Global and National experts from industry and academia for:
  - Development of Product Development Plan
  - Guidance and support during different phases of product development
  - Creation of strategies and plans for clinical trial plans/designs and engagement of an enriched study population
  - Development of a regulatory strategy

Requirements from the Applicant for the RFP

The applicant can be an industry or an academic institute with established linkages with a manufacturer. However, the Applicant must fulfill the following criteria prior to submitting the Proposal:

- They should have a biosimilar candidate for cancer, rheumatoid arthritis and diabetes with established biological activity and provide all supporting data for the same as a part of the proposal
- They must provide details of proposed activities and success criteria across all stages of development:
  - Proof of concept establishment
  - Pre-clinical activities- e.g. Requisite standardized assays and their expected end points that would be essential for conducting preclinical analysis
  - Manufacturing plan including expression systems, technologies being considered production, formulation details and success criteria parameters like (e.g. productivity, Purity, stability, possible Cost of goods, Scale of production etc.)
  - Clinical Trials – Clinical Development plan and Study documents as per ICH GCP
- They must delineate discrete goals, milestones, and criteria that can be used to evaluate progress during different stages of development.
- They should have freedom to operate as related to IP, including consent from others where applicable
- They should provide letters of support/agreements for 5 years with any third party they would like to engage with during the different stages of product development for which support is being sought for under this call.
- They should provide work plan for the 5 years.

RFP 2: Process Development Laboratory

Background:

The continuous increase in the number of approved bio therapeutics suggests that therapeutic proteins, mAbs, and their derivatives, will continue to be the focus of the biopharmaceutical industry for years to come. With longer circulating half-life, high target specificity and ability to induce the immune system, bio therapeutics offer an attractive solution in comparison to small molecules. Yet their exorbitant cost makes them inaccessible to the Indian population.

Although there have been vast improvements in capability to manufacture, characterize, and stabilize them, there are still challenges to be overcome. MAbs have high effective dose as compared to other drugs and require availability of large quantities of the product with quality, cost and time efficiency to meet market demand. Maintaining desired quality attributes as per regulatory standards, while reducing time to market and sustaining cost effectiveness is a critical hurdle.

Objective:

To establish a Process Development Laboratory that would enable development of cost effective manufacturing process of bio-therapeutic products to help accelerate their development. .

Scope of the RFP

This call seeks proposals by applicants for establishing a Process Development Lab for bio-therapeutic products like biosimilars, therapeutic proteins etc. The Laboratory to be set up would have:

i. **The ability for Cell line development and creating a Master Cell Bank (MCB) -** Generation of a stable monoclonal antibody/therapeutic protein producing cell line.

ii. **The ability for Development of Preliminary Analytical Methods** for **i**dentification of critical process parameters and development of analytical methods for quality assessment of the process and product.

iii. **The ability for Process Development and Optimization upto 200l scale –** Optimize and streamline a process that delivers reliable and efficient product yields

iv. **A team of professionals that can support the industry to: -**

a) Conduct robust 'Develop-ability Assessment' or 'feasibility assessment' for state of readiness for process development of molecules that have established proof of concept.
b) Develop a Process Development plan in collaboration with the selected CMO/industry-partner/CMC facility
c) Defining a Target Product Profile (TPP) of the candidate
d) Proposing specifications and define the regulatory compliant release criteria and critical quality attributes (CQA), for late stage manufacturing
e) Conduct on-site GMP audit of the CMOs/CMC Facility
f) Enable linkages with CMOs/CMC Facility for late stage manufacturing and provide technology transfer support

Mechanisms of Support through the call:

- Direct funding for a period of 5 years for establishment of the lab including infrastructure setup, equipment acquisition and human resources
- Access to the following affordable services and solutions developed through other calls of the i3 program:
    - A GMP-compliant Cell Line Repository providing access to well-characterized cell lines (mammalian, microbial)
    - A cGLP compliant facility for bio therapeutic characterization, and validation.
    - A GMP compliant CMC facility for manufacturing of regulatory compliant preclinical and clinical trial lots

Requirements from the Applicant for the RFP

The applicant can be an industry or an academic institute. However the Applicant must fulfill the following criteria prior to submitting the Proposal:

- They should be proficient with relevant upstream and downstream manufacturing processing technologies, process parameters setting and appropriate controls
- They should have demonstrated capabilities in translating the molecule from proof of concept to clinical stages and early stage manufacturing through cell line development, assays development and optimization of processes
- They must have knowhow and ability for guiding regulatory compliances and product licensure
- They should have an experience in assessing and engaging with CMO/CROs
- They should have preferably demonstrated capabilities of being a service provider, ability to manage multiple clients and develop linkages with industry
- The applicant should be committed to out license and tech transfer developed processes and analytical assays to i3 facilities and partners at affordable costs.
- The applicant must delineate discrete goals, milestones, and criteria that can be used to evaluate the facility work-plan during the 5 year grant period.
- The applicant should provide letters of support/agreements for 5 years with any third party they would like to engage for the purposes of the work under this call.
- They should provide work plan for the 5 years.

RFP 3: Chemistry, Manufacturing, Control Units:

Background:

Inherent challenges in advancing novel products from basic discovery through the preclinical-to-clinical translation process include a complex technological landscape requiring expensive specialized facilities and demanding regulatory requirements. Chemistry, Manufacturing, and Controls (CMC)[1] help expedite early development by utilizing scientific and regulatory expertise to craft a streamlined program for the manufacturing and testing of novel products. In addition to providing the appropriate information to regulatory authorities, CMC oversight identifies and manages issues to reduce costly delays and setbacks and ensure development remains on track.

Objective:

The aim of the program is to establish a GMP compliant CMC facility that can manufacture regulatory compliant preclinical and clinical trial lots of biosimilar and novel monoclonal antibodies; conduct analytical assays .

Scope of the RFP

This call seeks proposals by applicants who are interested in establishing a GMP compliant CMC Unit(s) as Contract Service Facility to accelerate development of preclinical and clinical trial lots of biosimilar and novel monoclonal antibodies.This facility shall be responsible for:

Facility Details:

- Product manufacturing for preclinical and clinical studies inclusive of:
  - Process optimization & standardization
  - Appropriate testing of in process parameters like cell growth, fermentation, harvesting, inactivation, purification, stability processing and detoxification etc.)
  - Characterization of manufacturing processes in detail including the nature and performance of the specific equipment used for every step of the manufacturing process
- Method validation as per ICH guidelines (ICH Q2(R1))
- Stability and safety studies for evaluating production cells (e.g. through gene copy number estimation, consistency of expression, stability of the genetic markers under the conditions of propagation; and ensuring cell lines are free from adventitious agents etc.);
- Product testing for characterization, meeting with specifications for product release and quality control.
- Providing Technical assistance and support to Indian industry through a team of professionals for**:**
  - Product Licensure in Compliance with Indian and Global Regulations

[1] Chemistry, Manufacturing and Controls (CMC) as defined by the USFDA includes activities related to chemistry (product characterization, product release and stability testing), manufacturing (manufacturing facility, utilities, process equipment and materials, manufacturing personnel, manufacturing process) and controls (in-process controls, product specifications, product expiration dating, documentation, batch record review, auditing).

- Develop a regulatory strategy and support preparation of related filings, e.g. pre-IND, IND (India, USA and International)

- Preparation of regulatory dossiers as per relevant ICH guidelines for CMC submission (ICH Q8, Q9, Q10) including:
  - Information to assure the identity, quality, purity, strength and stability of the drug product
  - Information on controls including process controls, consistency, and specifications, product expiration dating, documentation, batch record review
  - Information on manufacturing including details of manufacturing facility, utilities, process equipment and materials, manufacturing personnel and manufacturing process

Mechanism of Support through this call

- Direct funding for strengthening existing facility for use as a Contract Service Facility including infrastructure setup, equipment acquisition and human resources
- Access to the following affordable services and solutions developed through other calls of the i3 program:
  - A GMP-compliant Cell Line Repository providing access to well-characterized cell lines (mammalian, microbial)
  - A cGLP compliant facility for bio therapeutic characterization and validation.
  - A Process Development Laboratory to enable development of manufacturing process

A MoU will be signed for the use of this facility by the Partners of i3 program and/or other start ups / researchers supported by the Government.

Requirements from the Applicant for the RFP

The Applicant must fulfill the following criteria prior to submitting the Proposal:

- They should have an existing facility for manufacturing of bio therapeutics (therapeutic proteins and monoclonal antibodies)
- They should have demonstrated capabilities in conducting studies for product safety, stability, characterization, and setting up assays for product specification and release.
- They should have proven experience in documentation and preparation of regulatory dossiers and product licensure.
- They should have demonstrated capabilities of being a service provider.
- The applicant must delineate discrete goals, milestones, and criteria that can be used to evaluate the facility work-plan during the 5 year grant period.
- The applicant should provide letters of support/agreements with any third party they would like to engage for the purposes of the work under this call.
- The existing facility will have to create a separate governance model for the facility to be used as a Contract Service Facility.
- They should provide work plan for the 5 years.

RFP 4: cGLP validation facility for Bio therapeutics

Background:

Biopharmaceuticals (mAbs and vaccines) development is a time taking and resource intensive process (8-10 years for a product to reach market and estimated cost of $800 million per NME product) with high rate of failure due to lack of efficacy and safety in later stages of development (FDA data shows 50% failure for Phase III products due to lack of efficacy and 30-40% due to safety).

To address this 'lagging science of product development' it is important to consider provision of integrated solutions that could enable an accelerated proof of concept establishment, critical evaluation and validation of products.

Objective of the Facility:

To establish a cGLP facility for characterization and validation of bio therapeutics (therapeutic proteins and monoclonal antibodies).

Scope of the RFP:

- This call seeks proposals by applicants who are interested in establishing a cGLP facility for characterization and validation of bio therapeutics in a Contract Service Facility. This facility shall be responsible for:
- Bio-analytical characterization of bio therapeutics using state-of-the-art technology to assess:
  - Physicochemical characterization like primary and higher order structures, post-translational modifications, molecular mass determination and intentional chemical modifications
  - Purity, impurities and contaminants determination
  - Aggregation studies
  - Stability studies
- Functional assessment of bio therapeutics by:
  - Binding affinity estimation
  - Breadth & potency assessment by antibody neutralization
  - Effector function estimation

Mechanism of Support through this call:

- Direct funding for establishment / strengthening of existing facility including infrastructure setup, equipment acquisition and human resources
- Access to:
  - A GMP-compliant Cell Line Repository providing access to well-characterized cell lines (mammalian, microbial)
  - A Process Development Laboratory to enable development of manufacturing process
  - A GMP compliant CMC facility for manufacturing of regulatory compliant preclinical and clinical trial lots
  - Novel technologies and assays developed at the Translation Research Consortia

- **A MoU will be signed for the use of this facility by the Partners of i3 program and/or other start ups / researchers supported by the Government.**

Requirements from the Applicant for the RFP

The applicant can be an industry or an academic institute. However, the Applicant must fulfill the following criteria prior to submitting the Proposal:

- They should have demonstrated capabilities for Bioanalytical characterization and Functional assessment of bio therapeutics
- They must have the requisite space and infrastructure for platforms for this assessment:
- They should have capabilities of data management and analysis (assay readouts, mass spec data analysis etc.)
- The applicant must have human resources trained in building and operational management of a cGLP environment
- It would be preferable if they have demonstrated capabilities of being a service provider
- The applicant must delineate discrete goals, milestones, and criteria that can be used to evaluate the facility work plan during the 5 year grant period.
- The applicant should provide letters of support/agreements with any third party they would like to engage for the purposes of the work under this call.
- They should provide work plan for the 5 years.

RFP 5: Cell line Repository

Background

Access to well characterized cell-lines is one of the prominent issues faced by manufacturers and entrepreneurs developing biopharmaceuticals products. Currently cell lines for use in India either have to be ordered from cell banks overseas (that have challenges like prohibitive shipping costs, time delays and customs issues); bought from companies (with high cost of licensing fees and royalties) or are sourced from other academic labs (risk of misidentification and purity).Hence it becomes critical to establish a central cell repository of global standard that specialize in the authentication, production, preservation, and secure distribution of biological materials.

Objective

To create a GMP-compliant Cell Line Repository for providing low cost access to academia and manufacturers of cell lines (mammalian, microbial) and expression systems that are tested, validated and well-characterized.

The repository is expected to stimulate biopharmaceutical product development by encouraging innovators and manufacturers, through the easy availability of high-quality, reliable cell lines to develop novel products that could otherwise not be done due to a lack of access, high cost and other legal and IPR issues.

Scope of the RFP

This call seeks proposals from applicants who are interested in establishment of a GMP compliant Cell Line Repository. The repository shall be on a Contract Service Model and responsible for:

1. Acquiring, maintaining and storing cell lines and expression systems that could be used for assay development and manufacturing of products. It is critical for the 5 years of this grant period that the repository have the cell lines and expression systems that may be needed for diseases like Dengue, HPV, Pneumococcal & other emerging viral infections; cancer, diabetes and rheumatoid arthritis. These should include (but not limited to):
    - Mammalian cell lines (e.g. CHO cell based cell lines, NS0, HEK, Sp2/0, GS (---/---), Per.C6);
    - Microbial cell lines (e.g. E. coli (BL21), S. cerevisiae, Pichia pastoris)
    - Expression systems (e.g. CMV promoter enhancer, DHFR negative cell lines, GPEX Technology)

2. Conduct quality control testing and characterization of the cell lines and expression systems in compliance ICH regulatory guidelines (ICH Q5D) such as:
    - Authentication (STR profiling; isoenzyme analysis or sequence-based barcoding; cytogenetic analysis);
    - Phenotypic characterization (viability, cell morphology, doubling time, receptor status, protein secretion);
    - Purity (cells are free of adventitious agents primarily mycoplasma, bacteria, and viruses)

3. Cataloguing and providing regulatory compliant documentation of each stored cell line/expression system (including information but not limited to name, typology, karyology, morphology, origin, properties, culture characteristics, immunological profile, cytogenetic analysis etc.

Mechanism of Support for the call:

- Direct funding for establishment / strengthening of existing facility including infrastructure setup, equipment acquisition and human resources
- Access to the following affordable services and solutions developed through other calls of the i3 program:
  - A cGLP compliant facility for bio therapeutic characterization and validation.
  - A Process Development Laboratory to enable development of manufacturing process
  - A GMP compliant CMC facility for manufacturing of regulatory compliant preclinical and clinical trial lots

Requirements for the RFP:

The applicant can be an industry or an academic institute. However, the Applicant must fulfill the following criteria prior to submitting the Proposal:

- They must have linkages for acquisition of cell lines and development of expression systems
- They must have experience and/or knowledge in regulatory compliant acquisition, handling, testing and characterization of cell lines and expression systems
- They must have requisite space and infrastructure such as:
  - Multiple freezers (vapor-phase liquid nitrogen freezers, mechanical freezers, cold rooms etc.)
  - Freezer failure back-up
  - Laboratory space
  - Separate space for storing mammalian and microbial cell lines
- They should have capabilities for cataloguing and data management
- They should have demonstrated capabilities of being a service provider
- The applicant must have human resources trained in building and operational management of a GMP environment
- The applicant must delineate discrete goals, milestones, and criteria that can be used to evaluate the facility workplan during the 5 year grant period.
- The applicant should provide letters of support/agreements with any third party they would like to engage for the purposes of the work under this call.
- The applicant should provide tentative cost of characterized cell lines and expression systems as a part of the proposal
- They should provide work plan for the 5 years.

3.2 Vaccines

RFP 1: Novel Vaccine candidates for HPV, Dengue and Pneumococcal

Background

Vaccines are one of the most cost-effective means available for managing infectious diseases. However, vaccines that are available for prevention or control of diseases with the greatest impact are often not designed with the developing country context in mind. These vaccines often confer short-lived immunity resulting in multiple re-vaccinations, display poor efficacy or safety profiles and have limited capacity to protect against multiple serotypes.

Additionally, novel vaccine discovery and development is plagued with challenges like lack of understanding of the precise antigens needed to elicit protective immunity due to genetic variation; inability to predict immunogenicity, efficacy, reactogenicity or safety and knowledge of factors that would enable generation of long-lived protective immune responses. Gaps in availability of validated assays, accessibility to well characterized cohorts for conducting clinical trials; unclear regulatory pathway for novel vaccines further contribute to delays in novel vaccine development.

Cervical cancer is the fifth most common cancer in humans, the second most common cancer in women worldwide and the most common cause of death due to cancer in the developing countries. With limitations of current screening and treatment procedures, vaccination is considered to be the best means of HPV Management.

Pneumonia remains a major killer of children under five with India having the greatest number of pneumococcal deaths in children aged 1–59 months. WHO and United Nations Children's Fund (UNICEF) have also prioritized reducing child mortality due to pneumonia by 2025.

WHO and the Indian Academy of Pediatrics Committee on Immunization (IAPCOI) has further recommends offering HPV and Pneumococcal vaccine to all who can afford the vaccine. Though there are vaccines currently available in the market, their high cost makes them unaffordable to large section of the Indian population. Hence there is a need to develop cost-effective indigenous vaccine against HPV and Pneumonia.

Objective:

To facilitate accelerated development and commercialization of promising novel vaccine candidates of **HPV, Dengue, Pneumonia**.

Scope of the RFP

This call seeks proposals by applicants that have vaccine candidates for **HPV, Dengue, and Pneumonia** in development and are interested in seeking support in accelerating its development.

This call will ***not*** fund activities related to:

- Development of new adjuvants, formulations.
- Filing of Registration to CDSCO;
- Commercialization;

- Setting up large scale manufacturing facilities;
- Fundamental/Basic research

Methodology of Support through this call

- Direct Funding of product development activities through various stages including, preclinical development, and production of clinical grade material and early phase human clinical trials.
- Setting up of a Product Development Unit (PDU) that would bring together a group of Global and National experts from industry and academia for
    - Development of Product Development Plan and Target Product Profile
    - Guidance and support during different phases of product development
    - Creation of strategies and plans for clinical trial plans/designs and engagement of an enriched study population
    - Development of a regulatory strategy
- Access to the following affordable services and solutions supported developed through other calls of the i3 program:
    - GCLP compliant facility for vaccine characterization and validation in clinical stages of development
    - Translation Research Consortia for:
        - Access to novel assays
        - Conduct of Challenge/protection studies in Animals

For the purpose of this RFP, "vaccine candidate" is defined as a candidate for which proof-of-concept data have been obtained, and "preclinical development" is defined as all activities beyond lead candidate identification.

Requirements of the RFP:

The applicant can be an industry or an academia with established linkages with a manufacturer. However, the Applicant must fulfill the following criteria prior to submitting the Proposal:

- They should have a vaccine candidate with established proof of concept established with preliminary data on immunogenicity and protective response. The applicant must provide all supporting data for the same as a part of the proposal
- They must provide details of proposed activities and success criteria across all preliminary data on stages of development:
    a. Proof of concept establishment
    b. Pre-clinical activities- e.g. Requisite standardized assays and their expected end points that would be essential for conducting preclinical analysis
    c. Manufacturing plan including expression systems, technologies being considered production, formulation details and success criteria parameters like (e.g. productivity, Purity, stability, possible Cost of goods, Scale of production etc.)
    d. Clinical Trials – Clinical Development plan and Study documents as per ICH GCP
- They must delineate discrete goals, milestones, and criteria that can be used to evaluate progress during different stages of development.

- They should have freedom to operate as related to IP, including consent from others where applicable
- They should provide letters of support/agreements for 5 years with any third party they would like to engage with during the different stages of product development for which support is being sought for under this call
- They should be willing to develop a Product Development Unit facilitated by the Program Management Team
- They should provide work plan for the 5 years.

RFP 2: Novel and complex vaccine candidates for other diseases of high burden and Priority in India

Background

Vaccines are one of the most cost-effective means available for managing infectious diseases. However, vaccines that are available for prevention or control of diseases with the greatest impact are often not designed with the developing country context in mind. These vaccines often confer short-lived immunity resulting in multiple re-vaccinations, display poor efficacy or safety profiles and have limited capacity to protect against multiple serotypes.

Additionally, novel vaccine discovery and development is plagued with challenges like lack of understanding of the precise antigens needed to elicit protective immunity due to genetic variation; inability to predict immunogenicity, efficacy, reactogenicity or safety and knowledge of factors that would enable generation of long-lived protective immune responses. Gaps in availability of validated assays, accessibility to well characterized cohorts for conducting clinical trials; unclear regulatory pathway for novel vaccines further contribute to delays in novel vaccine development.

Emerging infections are a potent threat to public health security. Intriguingly most of these are viral in origin; thus highlighting the potency of viral threat in an ever-changing ecosystem of the world. Several diseases have evolved at the turn of the 21st century. Avian influenza virus A H5N1 infection spiraled into a global pandemic in 2009, due to mutations in highly infectious H1N1 strain. The outbreak directly affected tourism, service sector, retail, trade, transport, entertainment, agriculture, pig farming and international economy. While chikungunya which was first recorded in Kolkata in 1963 remerged in 2006 after a gap of 32 years and caused an explosive outbreak affecting 13 states in India and causes an annual economic loss of 391 million rupees. The spread of the pandemic echoes the need for preventive measures, ensuring robust health care systems and development of effective biomedical tools e.g. vaccines which shall help to respond beyond the spatial and temporal limitations.

Objective:

To facilitate accelerated development and commercialization of promising novel vaccine candidates.

Scope of the RFP

This call solicits proposals by applicants to accelerate development of novel vaccine candidates for diseases of high burden and high priority in India (excluding Dengue, HPV and Pneumococcal).

This call will ***not*** fund activities related to:

- Development of new adjuvants, formulations.
- Filing of Registration to CDSCO;
- Commercialization;
- Setting up large scale manufacturing facilities;
- Fundamental/Basic research

Methodology of Support through this call

- Direct Funding for vaccine development activities including preclinical development and early phase human clinical trials as required.

- Experts from industry and academia will provide advanced mentorship for
    - Development of Product Development Plan and Target Product Profile
    - Guidance and support during different phases of product development
    - Creation of strategies and plans for clinical trial plans/designs and engagement of an enriched study population
- Supported projects will have access to the following affordable services and solutions developed through other calls of the i3 program:
    - GCLP compliant facility for vaccine characterization and validation in clinical stages of development
    - Translation Research Consortia for:
        - Access to novel assays
        - Conduct of Challenge/protection studies in Transgenic/Humanized Mice and Non-Human Primate Models

For the purpose of this RFP, "vaccine candidate" is defined as a candidate for which proof-of-concept data has been obtained, and "preclinical development" is defined as all activities beyond lead candidate identification.

Requirements of the RFP:

The applicant can be from industry or academia, however, the Applicant must fulfill the following criteria prior to submitting the Proposal:

- They should have a vaccine candidate with established immunogenicity and protective response as proof of concept. The applicant must provide all supporting data for the same as a part of the proposal
- Preclinical research alone, without clear feasible and realistic plans for progressing to development of vaccine candidate is not considered responsive to this particular announcement.
- They must provide details of proposed activities and success criteria across the stage/s of development for which funding is requested.
- They must delineate discrete goals, milestones, and criteria that can be used to evaluate progress during different stages of development
- They should have freedom to operate as related to IP, including consent from others where applicable
- They should provide letters of support/agreements with any third party they would like to engage with during the different stages of product development for which support is being sought for under this call

3.3 RFP for Medical Devices and Diagnostics

About the RFP - Critical Medical device Technologies

Background:

The Indian healthcare industry is growing at a tremendous rate and simultaneously going through transformation across the continuum. With the approval of National Health Policy 2017 by the Government of India, healthcare expenditure intends to increase to 2.5% of gross domestic product (GDP) and India embarks on a planned approach to bridge the healthcare divide while maintaining industry competitiveness.

The medical device sector represents 9% of the overall Indian healthcare industry. The Indian medical device sector is worth approximately USD 5.5 Billion and is growing at 15% CAGR. Indian medical devices market is the 4th largest in Asia and in the list of top 20 in the world. The global medical devices market has been growing exponentially and Indian companies have also been capitalizing on their indigenous capabilities. Despite significant progress, there are certain challenges such as import dependency and unsuitable devices that have been designed for use in industrialized countries. The medical device market is dominated by imported products, which comprise of around 75% of total sales.

This advocates for a critical need to channelize efforts towards promoting the medical device sector and focus on development of innovative and affordable medical devices and diagnostics relevant to the Indian public health needs, making it one of the key focus areas of the Program

Indian government is making serious efforts to uplift domestic manufacturing of medical devices, the i3 program can give boost to the efforts of BIRAC and GoI towards “Make in India” initiative.

Purpose

- To support product development of critical medical device technologies that address Indian health needs
- To address affordability by lowering the cost of development
- Long term goal of increasing global market capitalization
- Streaming the medical device development process by:
    - Providing accessible facilities and technologies
    - Enhancing relevant talent

Objective of the RFP

The objective of the Program would support development of the following:

- Development of critical medical device technologies that are currently under development by the industry and bring them closer to the market in 3 years.
- Development of core technologies which will be platform technologies and can be used in various products segments leading to development of indigenous medical devices.
- Development of an ecosystem that would spur innovation to develop novel products.
- Development of Shared Infrastructure

Scope:

- This call seeks proposals to accelerate development of critical medical device technologies that has high relevance in India
- The focus is on generating critical technologies in medical device sector with high market potential, better product profiles and greater cost effectiveness than current products in market.
- This call will support the various stages of a critical technology development including, proof concept establishment, preclinical development, product manufacturing and human clinical trials.

Technical Scope of Critical Medical Device Technology Development

Applicant would need to evolve a minimum of 2 core technologies supporting the medical devices for which grant has been applied for:

Sl. No	Product Segment	Medical Device Segment	Associated Core Technology for R&D
1	Laboratory/Diagnostic Analyzers	Bio-Chemistry Analyzer (Automatic)/Hematology Analyzer (5 Part Differential)/Electrolyte Analyzer/Blood Gas Analyzer	1. Hyperspectral Imaging; 2. Cytometric Glass; 3. Flow sensor based blood gas detector 4. Electrodes development with membrane integration-
2	Cardiac Care	Balloon Catheters Pacemakers	1. Dilatation Balloon soldering technology 2. Hydrophilic coating on polymer catheters for endoscopy

3	Diagnostic Imaging (non-ionizing)	Ultra-sonography CTG Monitor MRI	1. Piezoelectric crystals 2. Beam forming/bending technology 3. Data Acquisition Systems (DAS) 4. Image Processing 5. Magnets for 1.5 Tesla MRI
4	Diagnostic Imaging (ionizing)	X-Ray CT Scan C-Arm	1. X-ray tube (Rotating Anode (gears, should reach 11000 rpm in 2-3 sec without lubricant) 2. CT scan tube up to 2 MHU. 3. Data Acquisition Systems (DAS) 4. Beam forming/bending technology 5. 16 bit dynamic flat panel detectors 6. Glass and Vacuum brazing 7. Liquid Crystals 8. High Frequency Generator 9. Bi directional couplers 10. Image optimization software 11. Bearings technology with high precision 12. TFT arrays 13. Static detectors 14. Transformer for 16 slice 150 KW CT 15. Collimators 16. Detector Array 17. CCD image sensor 18. Backlit CMOS sensors 19. Scintillators 20. Fluorescence filters (C-Arm) 21. Slip rings (CT)

5	Neonatal care	Incubators Neo-natal ventilator Pulse-oximeter	1. IR based ETCO2 monitoring 2. Precision measurement of blood based parameters, specially in low values 3. Paramagnetic sensors for FIO_2 monitoring 4. Non-invasive Bilirubin measurement 5. Trans Cranial Doppler
6	Ventilation	High Frequency Ventilators	1. Console panel for high fidelity measurements 2. Respiratory sensors 3. FEV monitoring 4. O_2 sensors 5. Oxygenator for Heart Lung Machine 6. Humidifier
7	Renal Care	Dialysis Machine Membrane Technology	1. Hollow fiber concentrator for dialyzer 2. HME filter 3. Continuous Renal Replacement Therapy (CRRT) circuits 4. Pumps for Dialysis Machines
8	Endoscopy	Endoscope Laparoscope Gastroscope	1. Optics and electronics 2. Lens 3. Cold source (LED Based) 4. Polymer catheters for guide wire 5. Hydrophobic and hydrophilic filters 6. Embedding of Optics and Electronics, 7.CCD Wafering, 8. Medical grade Bi -directional Coupler 9. Lenses: Dicing Systems and Crystal Growth
9	Non-Cardiac Implants	Un-cemented hip joints	1. 316 LVM (Alloy)

		Spinal implants	2. Ceramic rod 3. UHMWP(Ultra High Molecular Weight Polyethylene) 4. Bone glue 5. Bone cement (Poly methyl Methacrylate)
10	Molecular Biology	Advanced Diagnostic Devices using Bio-markers, sequencing technologies	1. Microscopic lenses 2. Micro positioners (with resolution of 1-2 microns) 3. Whole Slide Scanners 4. Actuators (between 2 cells) 5. Micro Arrays 6. Mass Arrays 7. Gene Arrays 8. Fluorescence nucleotides 9. Mass spectrometer 10. HLA typing with respect to luminux based sequencing

The following will not be supported under this call

- Projects focusing on technology/process development with no preliminary data and based only on hypothesis
- Products not having application in the Medical Device industry

Mechanism of Support

Support provided to candidates selected in this call will comprise of:

- Direct funding of R&D activities- Funding provided would be dependent on the current stage of development and the proposed activities to be conducted.

- Access to a group of experts from industry and academia with expertise in Medical Device discovery, development, clinical validation and trial, delivery experts, Indian health care delivery systems experts, regulatory experts, IPR and legal experts. They would aid in:

- scientific and technical guidance towards implementation of the components and their activities including development of Product development Plan for products
- identifying specific areas support (for example technologies, infrastructure, finance, advisory, trainings etc.) that would act as catalyst for component success
- identify issues and difficulties at an early stage that potentially slow down implementation of the related project activities and provide timely and practical advice to avoid them
- aid in adoption of new perspectives, new skill sets and facilitate training and linkages with other national and global experts

Support will also be provided to candidates selected in this call to access **the following Scientific Facility:**

- Optics
- Integration Facility for Scintillators
- Molding and Coating Facility
- Implants coating and molding
- Extrusion Facility
- General Safety (Mechanical, Radiation, Electrical and Acoustics) and Electro Magnetic Compatibility Testing Facility (EMI-EMC)
- 3-D printing and Rapid Prototyping Facility (Collagen, Cell pat, Polymers, Biomaterials)
- Gamma Irradiation Facility
- Tube manufacturing Facility
- Bio-material Testing Facility
- Metal Molding Facility