Request for Proposals (RFP)

- **Enabling Indigenous Development of Technologies for Affordable biomanufacturing**
- **Biotherapeutics and Therapies**

Under

NATIONAL BIOPHARMA MISSION

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)

Through Implementing Agency

Biotechnology Industry Research Assistance Council (BIRAC)

(A Government of India Enterprises)

Table of Contents

Section I - Program Overview - NBM

This is an Industry-Academia Collaborative Mission For Accelerating Discovery Research To Early Development For Biopharmaceuticals - "Innovate in India (i3) Empowering biotech entrepreneurs & accelerating inclusive innovation", also referred to as National Biopharma Mission (NBM).

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 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").* Biotechnology Industry Research Assistance Council (BIRAC) setup by DBT is the Implementing Agency of *i3* Program (Program co-funded by World Bank loan) managed through a dedicated Program Management Unit (PMU).

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

RFP Area

Enabling Indigenous Development of Technologies for Affordable Biomanufacturing

RFP 1: Development of Affordable Serum-Free, Chemically Defined Media (SF-CDM) and Feed Supplements for Biopharmaceuticals.

RFP 2: Development of Affordable Chromatography Resin for Protein Purification

RFP 3: Development of Filtration Systems, Process Accessories and/or Storage Devices for Affordable Biomanufacturing

RFP 4: Develop IT Platforms for Quality Management System in Biopharmaceutical Industry

RFP Area

Biotherapeutics and Therapies

[1] *For further details of the Program, see the National Biopharma Mission Document*

RFP 5: Development of Bio-betters and biotherapeutics

RFP 6: Development of Antibody Drug Conjugates (ADCs)

RFP 7: Development of CAR-T therapies.

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

1. Application Timelines

Key Dates

Call Opens	**31st October 2019**
Last Date of Submission	**26th December 2019 (5:00 PM)**

2. Application Guidelines and Process

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

Process for submitting the proposals online is detailed below:

a. Go to BIRAC's website or Go the URL: https://www.birac.nic.in/nbm/
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 proposal.
d. Further details on 'How to Submit a Proposal' 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 company/organization by clicking on New User Registration.
g. In case of new user registration, a computer-generated link will be sent to the email-id provided at the time of registration to generate a password.
h. Once you login, you will be navigated to the proposal submission page under NBM link.

Instructions:

a. Applicants are advised to fill-up and submit their applications early without waiting for the last date in order to avoid any last-minute contingencies. The system stops accepting applications automatically after **5:00 PM** of the last date of 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 proposals with essential supporting materials provided as uploads.
c. Requests for changes in the proposal 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 your application, budget and organization are in compliance with the eligibility criteria provided. Proposals for projects that do not meet the eligibility criteria and/or do not directly respond to the call area will not be reviewed, regardless of their quality. You are strongly encouraged to contact BIRAC if you are unsure about the eligibility or responsiveness of your project.
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 in connection to the proposed technology, background IP, collaborations, outsourcing, consultancy, joint ventures, consortium partnerships, IP licensing, technology transfer, material transfer etc. should be provided at the time of proposal submission.
h. Risk management proposal for the project should be submitted after scrutiny of the execution aspects of the project.

3. Evaluation Methodology

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

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

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

4. Eligibility Criteria

Who may apply?

The proposals can be submitted:

- Solely by Indian Company / LLP/ Non-profit organizations/ Society/ Trusts/ Foundation/ Associations/ Government entities/ Institutes/ R&D Organizations/ which is a legal entity OR
- Jointly by Indian Companies/ Non-profit organizations / LLP/ Society/ Trusts/ Foundation/ Associations/ Government entities/ Institutes/ R&D Organizations/ OR
- By a consortium of Indian Company/ Non-profit organizations/ LLP/ Society/ Trusts/ Foundation/ Association/ Government entities/ Institutes/ R&D Organizations/
- Indian Start-up companies in collaboration with Industry/Academia/research institutes/ are specially encouraged to apply.

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.

Limited Liability Partnership:

A limited liability partnership is defined as one which is incorporated under the Limited Liability Partnership Act 2008. Minimum half of the persons who subscribed their names to the LLP document as its Partners should be Indian citizens. [Indian Citizens do not include Person of Indian Origin (PIO) and Overseas Citizenship of India (OCI) holders].

Relevant documents for submission in the application:

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. Either incubation agreement; or letter of intent in favour of applicant, issued by Incubation centre (which states that the incubation centre is willing to give facilities to applicant for the project applied for)

Companies: -

a. Incorporation certificate
b. Latest Share holding pattern as per BIRAC format only (For formats go to https://www.birac.nic.in/nbm/cms/page/resources and click Formats), certified by external CA and verified from MCA/ ROC records
c. Details regarding in-house R&D facility, if any, or Incubation agreement
d. Audited financial details of last three financial years (i.e. 2016-17, 2017-18, 2018-19), if applicable
e. Copy of passports of the shareholders (in support of 51% eligibility criteria) or self-declaration of citizenship attested by a gazetted officer

Limited Liability Partnership: -

a. Incorporation/Registration certificate.
b. Partnership deed; or list of subscribers which states that minimum half of the partners are Indian citizens.
c. Copy of passports of Indian partners/subscribers or self-declaration of citizenship attested by a gazetted officer.
d. Research mandate/ details regarding in-house R&D facility, if any, or Incubation agreement.

e. Audited financial details of last three financial years (i.e. 2015-16, 2016-17, 2017-18), if applicable.

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, or Incubation agreement.
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.
b. Details regarding in-house R&D facility, if any, or Incubation agreement.
c. CA certificate (supporting the fact that half of the members of the society are Indian citizens)

Trust

a. Trust deed.
b. Details regarding in-house R&D facility, if any / Incubation agreement.
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 / Incubation agreement.
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.

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 and/or A Board Resolution from the Company Partner for acceptance of the Grant-in-Aid under NBM
b. Opening up a No-Lien Account with a scheduled/nationalized Bank
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, prior to the commencement of product development activities
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 https://www.birac.nic.in/nbm/uploads/2019/08/emf.pdf

g. Adhere to the Project Risk Management Plan during all stages of execution
h. Submission of documents related to conveyance of interests in the background technology/IP

6. Program Monitoring Mechanism

Project Monitoring Committee (PMC)

All funded projects must have their own Internal Monitoring Committee/Internal Project Review Committee.

The projects 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.

Based on the foregoing PMC will assess and recommend:

a. Release of next instalment or part release thereof by the 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 time-frame
d. Mentor(s) to overcome any technological problem faced in the Project implementation
e. To advise on issues related to securing of IPR
f. To advise on any other matter as referred to it by BIRAC and/or otherwise reasonably necessary for effective discharge of its duties and/or achievement of aims and objectives of proposed Scheme

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 budget will be released
c. The Applicant will have to submit a duly certified Statement of Expenditure for every 30th September and 31st March
d. Format for MCR, Utilization Certificate and Statement of Expenditure will be made available as per requirement
e. Compliance to the Project Risk Management plan

8. Funding Mechanisms

Project must be budgeted on a milestone basis. Funding will be awarded for maximum up-to 3 years depending on the objectives. Fund disbursements will be subject to the project team attaining the proposed milestones. The primary applicant and the proposed collaborators should specify their quantum percentage and their corresponding milestones. The funds will be disbursed to them separately subject to the achievement of milestone and reporting of progress

a. ***allowable costs include***

- *Personnel*: All personnel working for the development of the product *only* are allowed to claim costs. Researchers and PIs who receive a salary from the host institution as permanent or fixed term staff members may NOT claim salary reimbursement from BIRAC grants
- *Technology Consultants*: These may include both national and/or foreign consultants who provide a service and capability that is not available among the project partners. Preference should be given to national service providers
- Equipment and accessories for the project including cGMP and clean room facility.
- Supplies and consumables for the equipment to be engaged for the project
- Travel & accommodation: Must be directly related to the execution of the project or travel related to seeking technology transfer
- Institutional overheads (maximum 8% of recurring budget)
- IP protection (Project related) – Upto Rs 2 Lakhs

b. ***Non-allowable costs include***

- Purchase or construction of a building/ space/ land
- Rental costs for space
- Recruitment costs for staff
- Attendance at conferences
- Legal fees

9. Intellectual Property

- The applicant team should have freedom to operate as related to IP, including consent from others where applicable.
- Intellectual Property developed under the BIRAC funding through this grant will be owned by and will be the responsibility of the applicant (unless stated otherwise).

10. Evaluation and Decision-Making Criteria

a. **Proposal Merit:**

- Does the proposal's approach align with the objective of RFP?
- Does the proposal demonstrate preliminary work of the identified product which will be useful for the proposed scope of work?
- Has the Primary applicant provided an adequate description of the existing manpower and infrastructure to understand their present capabilities?
- Are the objectives, activities and milestones well defined?
- Does the proposal identify project objectives with the Mission's mandate?

b. **Team/Applicant:**

- Is the Primary applicant competent to ensure effective conduct of the proposed work?
- Does the applicant team have relevant capabilities and appropriate experience for the same?
- Has the collaborations established have adequate technical expertise and background experience to achieve the objective of the RFP.
- Does the applicant have any prior regulatory experience?

- Has the applicant provided letters of support/agreements with any third party they would like to engage with during the different stages of product development?

c. **Implementation:**

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

d. **Business Strategy:**

- Has the applicant provided any market surveillance details for the said product?
- Has the applicant provided any details on cost effectiveness of the product vis-à-vis existing products in the market?
- Has the applicant considered affordability on account of availing the Mission's funding?
- Has the applicant identified any specific clients or business opportunity for the product after development?

e. **Budget Estimates:**

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

Note: We welcome potential applicants contacting the mission before submitting applications to clarify any questions or discuss their ideas with us. Kindly submit the application at least a few days before the deadline to avoid proposal rejection due to non-alignment with the scope of RFP.

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

Dr. Mirage Singh, Programme Manager, PMU- National Biopharma Mission

Email: nbm5.birac@nic.in

Phone: 011-24362107

Section-III

RFP AREA: ENABLING INDIGENOUS DEVELOPMENT OF TECHNOLOGIES FOR AFFORDABLE BIOMANUFACTURING

RFP 1: Development of affordable serum-free, chemically defined media (SF-CDM) and feed supplements for biopharmaceuticals.

Objective:

To develop indigenous capabilities for manufacturing and supply of affordable serum-free, chemically defined media (SF-CDM) and feed supplements for mammalian cells utilized in upstream manufacturing of biopharmaceuticals.

Technical Scope:

Applications are being sought for development and manufacturing of serum-free, chemically defined media for CHO or any other mammalan cell line platforms used for biopharmaceutical production. Media should be free of animal components. The scope of the activities under this call are:

- Development of serum and protein hydrolysate free, chemically defined media with animal origin-free concentrated feed supplements (combinations consisting of components such as amino acids, vitamins, glucose, trace elements, growth factors, hypoxanthine/thymidine, ADCF lipids, ADCF cholesterol etc.) and study the effect on parent cell line behaviour in terms of metabolic activity and growth.
- Validation of the optimized media formulation by: 1) Establishing reproducible growth profile, optimum cell density and cell viability of parent cell line 2) Reproducibility in terms of substrate and metabolite profiling 3) test for adventitious agents as per guidance outlined by the regulatory agencies (US Food and Drug Administration and the International Conference on Harmonisation (ICH Q5A), TGA Australia.
- Scale-up and commercial manufacturing of cell culture media & feed supplements for which early phase development studies are already established.

Expectation from the applicants:

The proposals may be submitted for early phase development or upscaling of technology or both

1. **Early Phase Development**

- Should employ design of experiments (DOE) strategy for media formulations to demostrate comparable or better growth kinetics and metabolic profile of a parent cell line in comparision with other commercially available media.
- The applicant team should have basic laboratory set up to support sterile lab scale production and be able to study the substrate and metabolic profiling during the growth analysis of parent cell lines.
- Spent media analysis for changes in amino acid and water-soluble vitamin levels, glucose/lactate, and selected lipids and cations to support continuous media development.

- Consistency should be demnostrated with at least three batches upto 2 L scale in bioreactor.
- The parent cell line used in early phase development studies should be a validated cell line (certified cell line)

2. Upscaling of technology

- The applicant team should have completed early phase development and appropriate supporting data should be submitted.
- Applicants team should form collaboration to support sterile media manufacturing and testing (end-user industry such as biopharmaceutical manufacturer) to validate the technology. Industry with sterile media manufacturing capabilities should be the primary applicant for such proposal.
- Applicant team having serum free media and supplements' manufacturing capacities such as blending, dried/liquid packing along with scale-up of selected media formulation, cell culture lab to assess the medias/feeds at bioreactor level. Support will be provided for strengthening such capabilities.
- Applicant team should have required built-up area to set-up clean room for blending and strilization of media.
- Demonstrate consistency of media composition and performance with parent cell lines/ recombinant protein producing cell line at a maximum scale of 50 L bioreactor.
- Data on growth kinetics and metabolic profile of a parent cell line in comparison with conventional media along with spent media analysis should be generated.
- Validate the media in commercial setting and ensure manufacturability, reliability and quality standard as per ISO 9001, ISO 13485 and 13408 certified processes and according to current good manufacturing practices (cGMP).

3. Instructions for the applicant team

- Applicants team should provide a detailed work plan, milestones and deliverables with appropriate timelines and letters of support/agreements with any third party they would like to engage with during the different stages
- Applications, if submitted with an academia/industrial collaborator, should demonstrate how the partnership will rapidly move the proposal towards the end goals/deliverables with clearly defined roles of each partner.
- Engaging with overseas experts/industry is encouraged provided that the manufacturing of the final product will be primarily in India. However, funding will only be provided to the Indian partner.

RFP 2: Development of affordable chromatography resin for protein purification

Objective:

To support indigenous technologies towards design and development of protein purification matrices for affordable and efficient purification of biotherapeutics (antibodies, antibody variants and oher therapeutic proteins). This may include but not limited to the development of

- Affinity and selective affinity chromatography resins (e.g. Protein A based affinity chromatography)
- Ion-exchange resins
- Mixed mode resins
- Hydrophobic resins
- Size exclusion chromatography resin

Technical Scope:

Applications are invited for indigenous development of affinity and selective affinity chromatography resins, ion-exchange resins, mixed mode chromatography, hydrophobic resins and size exclusion chromotography resins that can be utilized in monoclonal antibody and therapeutic protein purification. The scope of the activities under this call are:

- Development of protein purification resin by using exisitng or novel ligand, base matrix or conjugation chemistry. Early phase developmental studies to be established by comparing its performance and stability with commercially available resins.
- Demonstrate the resin quality by using the mAbs or proteins developed by industry/academia partner and studying the parameters by following procedures but not limited to: Static and dyanmic binding capacity, leachables, Host Cell Protein (HCP) levels, elution profiles at lab scale in comparison with commercially available resins. In addition, ability of the resin(s), particularly ion-exchange and/or mixed mode resins, to remove/reduce viral contaminants (through viral reduction studies using MMV and MuLV) should be demonstrated.
- Proposed technology should have high translational potential with a clear path for continued development for commercial use. The resin(s) should be suitable for cGMP manufacutring and reliable supply for use should be demonstrated

Expectations from the Applicants:

- The products of this research should be developed and validated with clear commercial potential such that they are ready to be transferred to industry for efficient and effective manufacturing of biotherapeutics. To ensure that technologies being developed are high-quality, align with industry standards and are comparable to current technologies in market, this RFP encourages a partnership structure expected to bridge gaps in investigator knowledge and ensure development of technologies with commercial potential.
- The applicant team should have a basic laboratory set-up to carry out the chemistry for ligand and base matrix synthesis/modifications (immobilization of ligand and prototype resin preparation)
- The applicant team is expected to have the necessory background experience in polymer chemistry, protein purification techniques. Team demonstrating the relevant experience through publications and patents will be preferred.

- The applicant team should have lab scale chromatography capabilities for assessment of developed resins in comparison with commercially available resins.
- Applicant team must have have access to CHO cell upstream production capability (expected yield for mAbs 0.5-1 gm/L) to test resin performance i.e, static and dyanmic binding capacity, leachables (such as protein A), HCP levels, elution profiles at lab scale in comparison with commercially available resins, either alone or in collaboration.
- Applicant team with proposals for early phase development studies should demonstrate the background experience and necesorry collaborations for testing and validation.
- Applicant team with proposals for upscaling of technology for commercial supply with completed early phase development study (supporting data required), Industry should be the principal applicant with capabilities for cGMP manufacturing and large scale validation of technology. Support will be provided for strengthening of the capabilities for large scale validation and commercial manufacturing.
- In collaborative proposals, team should demonstrate how the partnership will rapidly move the proposal towards the end goals/deliverables with clearly defined roles of each partner.
- Detailed work plan, milestones, deliverables, timelines and success parameters should be provided
- Engaging with overseas experts/industry is encouraged provided that the manufacturing of the final product will be primarily in India. Funding will only be provided to the Indian partner.

RFP 3: Development of filtration systems, process accessories and/or storage devices for affordable biomanufacturing

Objective:

To develop indigenous capabilities for manufacturing and supply of affordable biomanufacturing process accessories/devices for filtration, purification and storage bags for, biopharmaceutical solution including media and buffer, product intermediates, final drug substance and drug product formulation /blending and fill finish

Technical Scope:

Development of filtration devices, process accessories and compatible single use disposable bags for storage of in-process and bulk drug substances and drug product during manufacturing of biotherapeutics. The scope of the activities under this call are:

- Filtration devices such as depth filtration for clarification of conditioned media during harvest.
- Sterile filtration devices, pre-filtration and crossflow membrane-based cassettes and systems solution devices for ultrafiltration and dia-filtration during manufacturing process.
- Filtration devices for virus clearance.
- Polymer based sterile storage bags (5 mL to 50 L) for compatible storage of biologics and buffer. This include necessary aseptic connector, in-line filter wherever necessary, provision of sampling, harvesting and connection/tubing for final fill finish
- Design must enable standard and customizable fitting to linings in biomanufacturing.
- Establishing the quality attributes of the technology and demonstrating clear improvement, in terms of cost-effectiveness, with comparable quality with other commercial products available in the market
- Validation of the technology to ensure suitability for cGMP production of biotherapeutics like testing for compatibility through stability studies, proper lining ensuring minimal leachable and extractables, filter integrity testing, sterility, strength, temperature & pressure rating, minimum mixing volume, maximum yield output (minimum hold up volume) etc. in comparison with other commercial products.

Expectations from the Applicants:

- The products of this research should be developed and validated with clear commercial potential such that they are ready to be transferred to industry for efficient and effective manufacturing of biotherapeutics. To ensure that technologies being developed are high-quality, align with industry standards and are comparable to current technologies in market, this RFP encourages a partnership structure expected to bridge gaps in investigator knowledge and ensure development of technologies with commercial potential.
- Applicant team should focus on development of new material of construction (MOC) or modification of existing materials for these technologies/devices. MOC should be compatible with the drug substance and drug product as per the regulatory norms for leachable and extractables.

- It is expected that the applicant team has basic laboratory set-up to carry out the research in designing, assembly and prototyping.
- Applicant team should have experienced manpower in designing and prototyping.
- Applicant team with proposals for early phase development should demonstrate the background experience and necesorry collaborations for testing and validation.
- Applicant team should have access to built-up area for setting up clean room assembly and sterilization area.
- Applicant team with proposals for upscaling of technology for commercial supply with established early phase development study (supporting data required), Industry should be the principle applicant with capabilities for cGMP manufacturing and large scale validation of technology.
- Applicant team should have manufacturing capabilities such as heat sealing, moulding, final assembly, packaging and sterilization for commercial supply. Strengthening of these capabilities will be supported for commercial manufacturing.
- Proposed technology should have high translational potential with a clear path for continued development to move into manufacturing facility for biotherapeutics.
- Detailed work plan, milestones, deliverables, and success parameters should be provided.
- Proposal should demonstrate how the partnership will rapidly move the proposal towards the end goals/deliverables with clearly defined roles of each partner.
- Engaging with overseas experts/industry is encouraged provided that the manufacturing of the final product will be primarily in India. However, funding will only be provided to the Indian partner.

RFP 4: Develop IT platforms for quality management system in biopharmaceutical Industry

Objective:

To seeks proposals from an applicant team with experience in software development to develop solutions for a strong quality management system. The aim is to develop economical, single purchase and multiple user software (s) for biopharma Industry.

Technical Scope:

- Proposals are invited to develop software solution to provide
  - An electronic lab note book to record and maintain experimental data as per ALCOA++ principles with following features but not limited to
    - User friendly software which allows creation of experiments for easy traceability.
    - Software should allow data entry in the form of word, excel, powerpoint, PDF and various image formats. Experiment can be recorded in a formattable template and experimental data can be exported in the form of a PDF file.
    - Should be compatible with windows 7 and afterwards operating system and can be connected to cloud computing.
    - Should have features for electronic review and signature of the experimental data as per the guidelines of USFDA part (11)
  - A laboratory Information management system for commercial manufacturing keeping track of events such as sample numbering, online tracking, results generated with below mentioned features but not limited to
    - Lab project and sample management including accessioning and barcode generation. Software should generate chain of custody including location with electronic signature.
    - Integration with laboratory instruments and applications allowing import of instrument result files for quality assessment of the samples.
    - Software should have features for Instrument calibration and maintenance, Inventory and equipment management, product specification management, data analysis as per the contemporary LIMS software features.
  - An automated data-back up software solution system to provide data back-up including metadata and audit trails with following features but not limited to
    - Secure changes in an attributable manner and generates an automated back-up from any analytical data system.
    - Completely automate the databack -up system and stores document in secure location. Review and downloading of the documents is done as user attributable manner.
    - Supports Windows operating system from windows 7 onwards and windows server 2016
    - Supports databases such as SQL server 2016 and 2017, Oracle 12 c R2 server and oracle 12c R2 client.
- Software development team need to provide a broad design of software functioning as per the current regulatory requirements such as USFDA 21 CFR (11), ICH Q8-Q10 and GAMP5.

- Software developed should have multiple users' login and one-time license provisions. Annual updated versions of the software should be provided at user requirement.
- Software system must provide equivalent or better functionalities for regulatory compliance at lower prices in comparison to the commercially available softwares.

Expectations from the Applicants:

- Applicants must submit application either solely or in collaboration.
- Applicant team should have strong background in software development. Applicants having experience in developing software for life-science industry will be preferred.
- Applicant team must have experts in the team or establish collaborations to bring in necessary know-how about the biopharmaceutical product development and requirement of quality management systems.
- Applicant team should have required Infrastructure and experienced manpower relevant to RFP objective.
- Applicant team must ensure cost-effective licences for software usage by Indian biopharmaceutical Industry and academia.
- Detailed work plan, milestones, deliverables, and success parameters should be provided
- Engaging with overseas experts/industry is encouraged provided that the manufacturing of the final product will be primarily in India. Funding will only be provided to the Indian partner.

RFP AREA: BIOTHERAPEUTICS AND THERAPIES

RFP 5: Development of Bio-betters and biotherapeutics

Objective:

To enable early stage development of Bio-betters and biotherapeutics such as antibody fragments (Fab, Fv, scFv etc.), nanobodies/camelids and monoclonal antibodies against existing validated therapeutic targets.

Technical Scope:

- This call seeks proposals for early stage development of:
  - Bio-betters including antibodies and therapeutic proteins
  - Antibody-based biotherapeutics including monoclonal antibody and antibody fragments (monospecific, bispecific), Nanobodies/Camelids.
- These candidates should be against validated drug targets for which there are products currently available in market (Indian or Global).
- The drug candidate being developed should have substantial improvement over marketed products. The areas of improvement could be improved specificity, efficacy, potency, half-life, immunogenicity, reduced toxicity and side effects as compared to existing therapeutics.
- The applicant could provide proposal for either of the following stages of development:
  - Discovery and development of antibody-based biotherapeutics and bio-betters against validated targets up to early phase development.
  - Product development up to pre-clinical and clinical stage of development for which early phase development is already established.

Expectations from the Applicant

- The applicant team must have relevant technical experience in the development of monoclonal antibodies, antibody-based biotherapeutics, or bio-betters or recombinant proteins demonstrated through publications and patents.
- It would be preferable if the applicant have relevant experience in early stage product development and translation of candidates from early phase development to preclinical and clinical stages of development
- The applicant must provide substantial justification for the products being considered such as:
  i. Market potential of the current product including current molecules in market and pipeline for the same target
  ii. Uniqueness of the technology, including technical advantage over existing bio-therapeutics
  iii. Public health demand and disease justification in context in Indian scenario
- The Applicant must provide data/research plan to justify the current stage of development such as (but not limited to)
  i. For the proposals for early phase development:
     - Tools used for discovery such as phage libraries, hybridomas, recombinant clones etc.

- Proposed methodology for biobetter development, types of modification and targeted quality attribute.
- Affinity characterization studies
- Established functional assays

ii. For proposals up to preclinical/clinical development (as applicable):

- Product characterization and bio-comparability data, both in vitro and in vivo, with respect to the existing therapeutic molecule to demonstrate improvement.
- Established analytical methods
- Details of processes, quality, consistency at small scale
- Characterization data of cell banks as per ICH guidelines.
- Amino acid sequence to establish identity
- Stability data of drug substance and drug product
- Preclinical and initial toxicology studies' data (if available)
- Quality attributes

- The Applicant team must provide a detailed workplan of the scientific activities across all stages of development. Milestones, deliverables, success parameters should be clearly defined to evaluate progress during the different stages of development. Anticipated risk and risk mitigation strategies should be identified and described
- Applicant team should provide letter 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
- The data generated as an outcome of this awarded grant through this call should be in compliance with regulatory guidelines for product development and suitable for submission to RCGM and CDSCO for seeking relevant approvals
- Applicants are required to conduct and manage their research results such as products and other material developed by BIRAC funding in a manner that enables (a) the knowledge gained during the project to be promptly and broadly disseminated, and (b) the intended product(s) or technology is made available and accessible at reasonable licensing fee/royalty terms to manufacturers who intend to develop affordable products within India.

RFP 6: Development of Antibody Drug Conjugates (ADCs)

Objective:

To enable development of Antibody Drug Conjugates (ADCs) against validated targets.

Technical Scope:

- This call seeks proposals for the development of:
  - Biosimilar Antibody Drug Conjugates or
  - New Antibody Drug Conjugates (ADCs)

  Proposals may also be submitted for Drug conjugates with proteins and peptides. Proteins and peptides selected for drug conjugation should be against validated targets and fulfil functional requirement to develop an ADC.

- New ADCs can be developed as a combination of already marketed or new antibodies and cytotoxic drug e.g.:
  - An already marketed (in India or globally) antibody conjugated with known cytotoxic drugs
  - An already marketed (in India or globally) antibody conjugated with new cytotoxic drugs which are highly potent and biologically active in nature
  - A new antibody against therapeutically validated target in combination with known or new cytotoxic drugs which are highly potent and biologically active in nature
- The new ADCs being developed should attempt to have substantial improvement over its unconjugated therapeutic counterparts (both Immuno & Chemo therapies) with better efficacy and acceptable safety.
- The applicant could provide proposals for either of the following stages of development:
  - Discovery and development New Antibody Drug Conjugates (ADCs) for early phase development.
  - Product development up to pre-clinical and clinical stage of development for which early phase developmental studies already established for biosimilar and new ADCs

Expectations from the Applicant:

- The applicant team should have relevant technical experience in Antibody development and research, recombinant protein expression and purification, chemical conjugation of biological molecules with active drugs and other moieties such as PEG and other proteins/peptides demonstrated through publications and patents
- It would be preferable if the applicants have relevant experience in early stage product development and translation of candidates from early phase development to preclinical and clinical stages of development
- The applicant must provide substantial justification for the ADCs being considered such as
  i. Market potential of the current product including current molecules in market and pipeline for the same target
  ii. Uniqueness of the technology, including technical advantage
  iii. Public health demand and disease justification in context in Indian scenario

- The Applicant must provide data to justify the current stage of development such as (but not limited to):

  i. **For the proposals on early phase development**
  - Target validation with data to show that target has capability for internalization upon antibody binding
  - Data to show that selected antibody binds to the target, and the drug is cytotoxic at small quantities.

  ii. **For proposals up to preclinical/clinical development:**
  - Details of conjugation methodologies including stability of linkers
  - Data to show key Quality attributes like payload, residual drug, potency of drug and mAb, linker stability
  - Data to show functional activity of ADCs through In-vivo assays.
  - Product characterization and bio-comparability data (in case of biosimilars ADC)
  - Established analytical methods
  - Details of processes, quality, consistency at small scale
  - Stability data of drug substance and drug product
  - Preclinical and initial toxicology study data (if available)

- The applicant must provide a detailed workplan of the scientific activities across all stages of development. Milestones, deliverables, success parameters should be clearly defined to evaluate progress during the different stages of development. Anticipated risk and risk mitigation strategies should be identified and described.
- Applicant should provide letter 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
- The data generated as an outcome of this awarded grant through this call should be in compliance with regulatory guidelines for product development and suitable for submission to RCGM and CDSCO for seeking relevant approvals
- Applicants are required to conduct and manage their research results such as products (ADCs) and other material developed by BIRAC funding in a manner that enables (a) the knowledge gained during the project to be promptly and broadly disseminated, and (b) the intended product(s) or technology is made available and accessible at reasonable licensing fee/royalty terms to manufacturers who intend to develop affordable products within India.

RFP 7: Development of CAR-T therapies.

Objective:

Support indigenous technologies towards design and development of CAR-T cell therapy against cancer and other diseases with high burden in India.

Technical Scope:

The applications are being sought for supporting indigenous development for chimeric antigen T cell receptor therapy approachess for cancer and diseases of high burden in India. The applicant having existing Chimeric Antigen Receptor T-cell construct (CAR construct) against validated target will be considered for funding for activities including but not limited to:

- **CAR-T development**
  - Preclinical *in vivo* toxicity and therapeutic efficacy studies
  - Clinical Trial studies for products with established early phase development studies into a reproducible and safe therapy for patients with leukaemia, lymphoma or any other cancer or disease of high burden in India
- Support may be given to expansion or refurbishment of an existing cell culture lab/sterile area to a GMP manufacturing unit dedicated to CAR T-cell production and propagation
- Support may also be given for cGMP facility for production of retrovial and lentiviral particles (VLPs) for commercial supply.

Expectations from the Applicants:

Applicants must submit applications either solely or in collaboration. Applicant is expected to develop strong cooperation with, academia, indutry, patient organisations, policymakers, public health experts and regulators, to bring in their diverse expertise for fulfilment of the project.

- The applicant team should have access to patients in hospital and a apheresis/blood collection site at the hospital for collection of samples.
- The applicant team should have a demonstrated experience of molecular biology, cell culture processes, immunological techniques and GMP facility operation.
- Applicant team should have access to the basic infrastructure and equipment for carrying out the proposed work (e.g, clean rooms, deep freezers, flow-cytometer and RT-PCR, centrifuge, plate washers, homogenizer etc.)
- Applicant should have access to cGMP grade ancillary genetic modification reagents, such as retroviral and lentiviral vectors, media, etc.
- Relevant supporting data should be provided along with the proposal
- The production and quality control of vectors for genetic modification should meet the requirements of current guidelines for gene therapy products
- The applicant should be able to conduct quality control of CAR-T cell products with a full range of tests on quality, safety, and effectiveness, based on relevant guidelines, either alone or in collaboration.
- An understanding of relevant regulatory/ethical requirements is expected as per the stage of the project

- For production of clinical grade material, researchers should have a good and standardized quality management system for production of materials, including risk assesment of their use, auditing of suppliers, and quality testing.
- In collaborative proposals, team should demonstrate how the partnership will rapidly move the proposal towards the end goals/deliverables with clearly defined roles of each partner.
- Detailed work plan, milestones, deliverables, and success parameters should be provided
- Engaging with overseas experts/industry is encouraged provided that the manufacturing of the final product will be primarily in India. Funding will only be provided to the Indian partner.