Request for Proposal (RFP)

Globally Accessible and Cost-Effective Novel Antibodies

Background

Few biomedical innovations over the past three decades have been as commercially successful and offer as much promise as antibodies. The current market is estimated to be $ 95 Billion, with 6 of the top 10 selling drugs in 2017 being antibodies; each generating revenue > $6 billion. India has made significant strides in the antibody market, focussed on the biosimilar space with 36 antibody products in market. India, with antibody market valuated at $2.7 B market (2018), is considered as one of the global leaders for biosimilars, alongside European Union, United States, South Korea and China.

However, the impact of antibodies, including biosimilars, is currently limited to high-income countries and private insurance markets. Exorbitant cost of antibodies makes them inaccessible in the vast majority of LMICs. Biosimilars, at best, are only ~30% cheaper than novel antibodies. Additionally, both novel antibodies and biosimilars face critical delivery challenges such as dose administration, need for chain logistics, formulations requirements that limit their uptake. Antibodies and their biosimilars in market target only few diseases such as cancer and inflammatory disease, whereby they have the potential to address major diseases afflicting India and prevent ~78 thousand million DALYs.

At present, India has only skirted with the 'tip of the iceberg' of antibody potential through its foray into biosimilars. By investing in the novel antibody space, India will create a unique opportunity to capitalize on a $200 billion global antibody market by 2023 and propel the transformation of antibodies into a viable public health option for the global South. This will require India to spearhead a multi-pronged effort in developing newer and better antibodies that not only align with India's disease needs but are also affordable and accessible to the people who need them the most.

Given the above, the Department of Biotechnology is establishing an initiative to spur discovery and development of novel antibodies against diseases that are particularly relevant in Indian context and would ensure that these products are accessible and affordable to the target population.

On recommendation from experts, three diseases - Antimicrobial Resistance (AMR), Human Immunodeficiency Virus (HIV) and Snakebite Envenoming (SBE) were prioritized as focus areas for this initiative. The prioritization was done on basis of (i) India's disease burden and potential for public health impact, (ii) use of antibodies to address those diseases and (iii) India's research and product development capabilities for those diseases.

In a process to fulfil the ambition of this initiative, Department of Biotechnology (DBT) in collaboration with Biotechnology Industry Research Assistance Council (BIRAC) invites full proposals in the area of Drug Development.

Introduction of DBT-BIRAC Joint call:

In order to tap the huge potential of novel antibody as immuno-therapeutics, the Department of Biotechnology, Government of India has announced this Joint call with the Biotechnology Industry Research Assistance Council (BIRAC) on **"Globally Accessible and Cost-Effective Novel Antibodies"**. This DBT-BIRAC joint call will focus on the three prioritized areas as mentioned above and will leverage the funding expertise of both the organizations. This initiative focuses on nurturing collaborations between academia, industry and LLPs to enhance their capabilities and competencies for developing novel antibodies for AMR, HIV and SBE.

Aim of the DBT-BIRAC Joint Call:

The Department of Biotechnology aims to discover and develop cost affordable, globally accessible novel antibodies against Antimicrobial Resistance, HIV and Snakebite Envenoming, while harnessing and strengthening India's antibody innovation ecosystem. To enable the above, the Department of Biotechnology plans to establish **Novel Antibody Development Partnership Program** in each of the disease focus areas.

Applications are hence solicitated from academic institutions/research labs/start-ups/industry to establish disease focused Novel Antibody Development Partnership Program for discovery and development of novel, cost affordable, globally accessible antibodies.

Research Objective

Novel Antibody Development Partnership Program aimed at discovery and development of novel, cost affordable, globally accessible antibodies would be established for:

- Human Immunodeficiency Virus (HIV)
- Snakebite Envenoming (SBE)
- Antimicrobial Resistance (AMR)

Each Novel Antibody Development Partnership Program will be a consortium that will bring in new knowledge, next-generation technologies and hands-on development expertise to discover and advance a specific novel antibody product, while simultaneously ensuring strengthening of Indian capabilities by establishing local Centres of Excellence and technology platforms.

Scope of the Call

This Call would support collaborative proposals that combine complementary and synergistic research strengthsfor establishment ofNovel Antibody Development Partnership Program aimed at development of novel antibodies.

- Each proposal for Antibody Development Partnership Program should be submitted for a consortium focussed on only one disease area i.e. either Antimicrobial Resistance, HIV or Snakebite Envenoming.
- The goal of the consortia is to discover a novel antibody and establish its proof of concept.
  In case a novel antibody has established proof of concept, the product development plan could also include studies for conducting Phase I, II or II/III clinical trials[1].
- Each consortium should comprise of all the capabilities for discovery and development of novel antibodies. Itshould have capabilities to access pathogen samples and host/infected samples, capabilities to understand the pathogen structure and host immune responses, a platform for antibody isolation (pioneering at least one discovery methodology), capabilities to validate, characterize and (if required) engineer antibodies. Further it

[1]For the purposes of registration, a clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiological procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc. https://www.who.int/topics/clinical_trials/en/

should have capabilities for pre-clinical evaluation (in-vivo/animal studies), assessing the molecules suitability for manufacturing and cloning in manufacturing grade cells.

Requisite Components of the Antibody Development PartnershipProgram

i. ***Access to samples:***Of(i)circulating and geographically diverse viral, venoms or drug-resistant bacterial strains (as applicable) and (ii) infected/immunized patients or animals samples (serum, plasma, PBMCs etc.).
ii. ***Capabilities for understanding specific pathogen/toxin:***Should have capabilities for understanding specific pathogen/toxin with goal to develop antigenic baits for isolation of antibodies and neutralizing assays for antibody characterization.Shouldutilize technologies like Electron microscope (EM), X-ray crystallography, next-generation sequencing for pathogen/toxin characterization, proteomic and transcriptomic studies,ornext generation technologies like -omics approach, CRISPR, AI for the same.
iii. ***Capabilities for Antibody Discovery:***With established platform technology to isolate and discover antibodies. The platform technology can range from *in vitro* display technologies (e.g. phage, yeast, mammalian cell and cell-free), single cell sorting, to use of humanized mouse.
iv. ***Capabilities for in-depth molecular and functional characterization of the antibodies:*** Should have capabilities for extensive characterization of antibodies such as (i) molecular characterization like primary and secondary structure determination, post translation modifications, epitope mapping, aggregation, stability (ii) functional characterization through invitro assays for assessment of binding, neutralization, potency, effector functions.
v. ***Capabilities for antibody engineering:*** Should have capabilities for optimizing and engineering antibodies such that the antibodies are suitable to be developed as a commercial product. Engineering can be done to increase their efficacy/potency, safety, stability, breadth and half-life.
vi. ***Capabilities for conducting developability assessment:*** Should have assays established and validated for assessing aggregation and, chemical and physical stability to ensure that antibodies discovered are suitable for further manufacturing.
vii. ***Access to regulatory compliant animal facility***: For conducting toxicology, and pharmacokinetics/pharmodynamics evaluation of antibodies in small animals &non-human primates.
viii. Access to manufacturing grade cell lines, and capability for cloning lead antibody candidates in a manufacturing grade cell lines for further technology transfer to industry for further manufacturing

Not within the scope of the call:

- Individual projects with limited R&D value
- Consortia focused on diseases areas other than the prioritized diseases in the scope
- Proposals focusing only on knowledge generation or blue-sky research without product-oriented research
- Establishment of a new biorepository
- Proposals restricted to training component only cannot qualify for the support.

Expectation from the Applicants:

- The primary applicant for this call is mandatorily an Indian entity
- Consortia can comprise of Academia, company, LLP (based on Eligibility Criteria mentioned in the section below). Global collaborators can also be engaged in the partnership.

- Primary applicant and all the collaborators should have prior experience in the relevant disease, technology or other respective areas demonstrated through prior publications and data published from their respective labs/ institutes. In case capabilities do not exist, the plan should include pathway for building capacities for the same. But, preference would be given to applicants with established capabilities.
- Primary applicant and all the collaborators should have relevant assays, infrastructure and equipment to conduct the research activities. In case capabilities do not exist, the plan should include pathway for acquiring and establishing the same. But, preference would be given to applicants with established infrastructure.
- If a Global collaborator is being engaged within the consortia, a counterpartIndian entity should also be identified that would be trained and strengthened by the Global collaborator over the period of the grant, so that the capabilty gaps in the country would be addressed.
- A PI/Co-PI within the consortia should be the coordinator of the consortia. The role of coordinator would be:
    - Planning, development, implementation and management of the consortia. Coordinator will coordinate with all the other partners ensuring effective implementation and management of the overall consortium's scientific activities.
    - Ensuring that the expenses presented by unit partners correspond with the activities agreed by the unit partners
    - Submit regular reports and other documentation on behalf of the Consortium

Eligibility Criteria

1. Eligible Organizations

➢ The Primary Applicant organization could be:

- Academia in India having a well-established support system for research:
    - Central/State Govt. Institutions of Higher Education
    - Private Institutions of Higher Education
    - Research institutes, universities, medical schools, IIT's and other engineering institutions, other recognized research laboratories in the public sector and not-for-profit institutions.
    - The institution must be recognized by DSIR as a Scientific and Industrial Research Organization (SIRO), if outside public sector.

- 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 selfdeclaration 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. RFP for enabling indigenous development of technologies for affordable biomanufacturing, biotherapeutics and therapies Page 8 of 25
e. Audited financial details of last three financial years (i.e. 2015-16, 2016-17, 2017-18), if applicable.

- Other collaborating organizations of the partnership can be Academia, company, LLP (based on terms mentioned above). (**Note:** International collaborating organizations can not be the primary applicant)**.**

2. Eligible Individuals-Principal Investigator(s)

Scientists working in Universities/Academic Institutions/National Laboratories/Industries & Non-Profit Organizations with necessary facilities and strong scientific background in the proposed area as the Principal Investigator(s) are invited to develop an application for support.

Funding Criteria

Project must be budgeted on a milestone basis. Funding will be awarded for 5 years, subject to the project team meeting agreed milestones. The primary applicant and the proposed partner can specify their quantum percentage and their corresponding milestones. The funds will be disbursed to them separately subject to the achievement of milestone and reporting of progress.

Allowable costs include:

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

Non-allowable costs:

- Purchase or construction of a building
- Rental costs for space that is owned by the institutions participating in the project

- Recruitment costs for staff
- Attendance at conferences
- Institutional overheads on funds that are being "on-granted" to consortium partners
- Purchase of office furniture.

Terms of Award

- ***Human Subjects:***

Before any funds can be expended for in-country research activities in a foreign country, the grantee institution must show evidence of compliance with Indian regulations for the conduct of research involving human subjects. Additional information on Indian requirements can be found in the Revised ICMR National Ethical Guidelines for biomedical and health research involving human participants (https://www.icmr.nic.in/sites/default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf)

- ***Intellectual Property:***

  - The investigators/institutes shall follow the detailed instructions on technology transfer and Intellectual Property Rights (IPR) as given at Annexure-I.

Mode of Submission:

Proposals need to be submitted in the prescribed format, clearly stating **"Globally Accessible and Cost-Effective Novel Antibody-based Immuno-therapies"** through online: **http://dbtepromis.nic.in/pi/loi.aspx**. PDF version of the proposal should also be send to Dr. Vinita Chaudhary, Scientist 'E', DBT: vinita.chaudhary@nic.in . Subsequently, two hard copies should also be sent to: Dr. Vinita N. Chaudhary, Scientist 'E', Department of Biotechnology, Block- 2, Room No.704, 7th floor, CGO Complex, Lodhi Road, New Delhi – 110003.

Below mentioned are the steps to submit Proposal

1. Open dbtepromis.nic.in website
2. Sign in into your account
3. Click on Login as PI button
4. PI user interface page will open
5. Now copy paste the link https://dbtepromis.nic.in/pi/frmOpenCallList.aspx

Proposal Outline

Each application must include the following components and activities

1. Biographical Information for proposed Project Leader and any other key personnel; including:
   - Name, degree, and current position title;
   - Education/training and field(s) of study;
   - Relevant research experience; and
   - Current research support including the % effort already committed for currently funded projects.
2. Description and plan for establishing a Multi-Disciplinary Team:
   - Describe the nature of the multidisciplinary team
   - Role and expertise of each partner

- In case of Global collaborator, justification for collaborative work outside the country, clear work plan and role of the Indian and Global partners respectively
- Provide Letters of Support as the proof of the same.

3. Justification of prior experience and capabilities:
   - Provide details of prior experience, capabilities in the relevant disease, technology or other respective areas by providing prior publications and data published.
   - In case capabilities need to be build, provide plans for building the same.
4. A description of the Program, Leadership & Resources:
   - Describe the institutional environments that are or would be relevant to the effective implementation of the proposed program.
   - Describe available resources, such as clinical and laboratory facilities, participating and affiliated institutions and units, geographic distribution of partners and trained resources.
   - Resources available to complete the work, including sources of human samples, and any samples to be obtained from an independent clinical study (if obtaining samples or other resources from an independent source, include a letter from the director of the independent study confirming the availability of the samples or resources)
5. Product Development Plan for development of at least one antibody:
   - A detailed description of the proposed work that includes the central hypothesis(es) or research question(s), specific aims, experimental approaches and sample size calculations offering adequate statistical power
   - Describe and provide rationale for the planned disease and isolation technology. Depending on the state of molecule, the product development plan could include strategies for Phase I, II or II/III clinical trials.
   - Inclusion of work plan indicating work to be done in India and globally (if applicable) respectively to address the objectives proposed
6. Training and Capacity Building Component:
   - In case of Global collaborators, describe a plan for training of new investigator(s) and capacity building in country.

Evaluation process:

Proposals will be evaluated by Technical Expert Committee and final recommendations will be communicated to the participants.

Evaluation criteria:

Proposals will be evaluated based on the following criteria:

a) Scientific Merit:

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

b) Team/Applicant:

- Is the Primary applicant competent to ensure effective conduct of the proposed work? Does the primary have substantial background published research to demonstrate adequate experience for the disease area/platform?
- Does each unit Investigator have relevant capabilities and appropriate experience to the same?

- Are the team roles and responsibilities, governance and organizational structure clearly defined?

c) Implementation:

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

d) Partnerships and Stakeholder Engagement:

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

f) Cost Estimates:

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

For any queries please contact:

Dr. Sundeep Sarin, Adviser, DBT:**sundeep@dbt.nic.in**

Dr. Vinita Chaudhary, Scientist 'E', DBT:**vinita.chaudhary@nic.in**

Timeline:

Call opens: **21st November, 2019**

Call closes: **29th February, 2020**