

Establishing preclinical models for Drug discovery

RFP Document

2023

1. Introduction

The maximum treatment therapies fail during translation of results from preclinical models to humans due to deficiency of robust preclinical models. Generating meaningful and predictive results preclinically requires alignment of the model systems that mirror the patient context. Animal models have many facets that mimic various disease conditions in humans like systemic autoimmune diseases, rheumatoid arthritis, epilepsy, Alzheimer's disease, cardiovascular diseases, Atherosclerosis, diabetes, etc., and many more. In doing so, the ability to conduct both forward translations, (the process of implementing basic research discoveries into practice), as well as reverse translation, (the process of elucidating the mechanistic basis of clinical observations), greatly enhances the ability to develop effective treatments.

For testing the lead molecules/ NCE/drug repurposing etc. researchers are either dependent on preclinical models from abroad or compromise on doing the studies with available model. There is need of relevant pharmacological models which may predict the intended therapeutic indications

2. Objective

The objective of this request for proposal (RFP) is to establish preclinical disease models (In-vitro/In-vivo) for screening new drugs, NCE, natural compounds, vaccines etc. Robust models would be developed which would be able to offer insights into the multifaceted pathophysiology of diseases relevant to India. The developed models should be ready to be offered as a service-based platform, which researchers/ Industries across the country may access to get their molecules tested.

In view of above, a landscape report was prepared by BIRAC and main objective of the report was to prioritize the disease areas of the country based on prevailing disease burden, Existing drug-specific pipelines, contractual Research organizations, Phase I clinical trial units and repositories/library on NCEs, biologics and bio-active molecules in the country.

Detailed methodology was chosen to prioritize the diseases. According to the method opted, 19 diseases out of 130 were identified by applying high level filters. As a result of priority process which was based on two key parameters i.e. Disease potential and Impact on community, top ten (10) indications were identified and detailed reports were generated. In addition to the scoring, a high level semi-

qualitative assessment among the 10 prioritized indications yielded top three key indications which were Chronic Kidney Disease, Chronic Obstructive Pulmonary Disease and Head and Neck Cancer.

The top 10 prioritized indications as per Indian Scenario are:

1. Acute Ischemic Stroke (Metabolic disorder)
2. Breast Cancer (Oncology)
3. Chronic Kidney Disease, (Diseases and conditions that cause chronic kidney disease include: Type 1 or type 2 diabetes)
4. Chronic Obstructive Pulmonary Disease, (Lung disease)
5. Coronary Artery Disease (Metabolic disorder)
6. Head and Neck Cancer (Oncology)
7. Human immunodeficiency virus infection (Infectious Disease)
8. Migraine
9. Tuberculosis (Infectious Disease)
10. Type 2 Diabetes (Metabolic disorder)

Robust models which could offer innovative insights into the multifaceted pathophysiology of unmet diseases relevant to India will be useful which may further be expanded as a service-based platform model, where researchers/ Industries across the country may access to get their molecule tested.

Therefore, there is a need for developing preclinical models in some of the prioritized areas as mentioned in scope of call (below).

3. Scope of the call:

The Scope of the current call is to generate robust preclinical models and their validation in the following areas.

- **Metabolic Disorders**
- **Infectious Diseases**
- **Auto immune disorders**
- **Genetic and rare diseases**
- **Neurodegenerative diseases**
- **Oncology**

Models	Types
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In-Vitro models/tools	<ul style="list-style-type: none"> • Generating Immortalized cell lines including iPSC cell lines from patient specific diseases • Cell based assays and High throughput screening assays • Organoid models • High-throughput Humanized 3D bioprinted models • Organ on chip models • Development of Indigenous viral/non -viral vectors for disease induction and validation
In-Vivo models	<ul style="list-style-type: none"> • Transgenic, knockout induced models for Indicated disorders • Humanized models

4. Expectation from the applicant:

- Investigators should be proficient and have a prior expertise in the R&D subject matter of the proposed area in developing preclinical models
- As a part of model development experience, applicant should be able to demonstrate expertise and provide the following in the relevant area:
 - Patents/Publication/Products and processes commercialized or in Pipeline which reflects the experience in animal model development
 - To demonstrate the superiority of the proposed model over available models
 - To provide the details of commercial viability of proposed model over the existing ones if any.
 - To possess/have access to a readily available facility/infrastructure required to fulfil the objectives of the proposed studies and later to be able to extend to a service model. The use of model must be justified in terms of specific need and relevance to human pathology in accordance to existing ethical rules.
- The experimental protocol should be clearly exposed, particularly regarding the number of animals, technical protocols, the procedure time, elements of follow-up, different endpoints that will be analyzed (clinical, biochemical, histological, biological) and most importantly validation protocol with details of drugs to be tested. A detailed timeline should be provided. Budget should take into account for the entire studies which has been proposed. Experimental structure and conditions must be appropriate and achievable milestones properly defined and scheduled should be envisaged.
- The applicants are encouraged who may demonstrate capabilities of being a service provider in the areas relevant to the proposal and ability to manage multiple clients.
- Grantee should be able to provide their model for services even after the

completion of project and plan of the business model and services charges (subsidized) to be provided along with the application. Once the model is ready for testing, a committee may be constituted along with BIRAC representation to decide on subsidized rates to company and academia, parameters on which molecules will be tested and services to be delivered.

- As a service provider, the applicant will be expected to have a fee-for-service governance model in place. Detailed governance model and differential pricing fee structure to be submitted
- The applicant must delineate discrete goals, milestones, and criteria that can be used to evaluate the work plan and sustainability.
- 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.

5. Administrative Eligibility

Proposals can be submitted by the stake holders (Academia or Industry) individually or in collaboration with each other. The entities who are the applicants or the collaborators shall be evaluated for eligibility criteria for which details are as below-:

- a. Academia (Public or Private Research Institute, University) having a well-established support system for research. The institute should have been established in India and have NAAC/ UGC/ AICTE or any equivalent recognition certificate or any other Public/ Government supported organization. The applicant must be a full time, permanent faculty of the applicant entity. The applicant can apply either: 1. Individually, or 2. Jointly with academic and/or industrial partner
- b. Company (Start up, Small, Medium or Large) incorporated under the Companies Act, 2013 having a minimum of 51% of the shares of the Company to be held by Indian Citizens (Indian passport holders), preferably with some (documented) commercially successful track record in relevant field.
- c. Limited liability Partnership (LLP) incorporated under the Limited Liability Partnership Act, 2008 having a minimum half of the persons who have subscribed their names to the LLP document as its Partners should be Indian citizens
(NOTE: The applicants should have adequate in-house facility /permanent facility to address the project implementation (which shall be evaluated during the proposal evaluation)).
- d. Application can be submitted by any of the above entities (a - c) either singly or in collaboration.

The below mentioned documents would be required for the Stake holders where ever applicable

(Academia/Industry or both)

- a) Scanned copies may be uploaded along with CA certified shareholding, Registration certificate, copy of self-attested Passport copy of the PIs (applicant and collaborators), establishment or incorporation documents and other relevant documents
- b) Applicant and Collaborator can submit Letter Of Intents (LOI), Memorandum of understanding (MOU) or support letters as scanned copies executed on relevant Letter Heads to show the mutual arrangements. Detailed signed MoU would be needed before the project is sanctioned.
- c) Board Resolution requirement can be substituted by resolution signed by MD/CEO/ COO along with any other executive Director or Company Secretary. Letter of Authorization requirements shall be considered adequate if signed by the Head of the Institution/ Head of the Department/ Principle Investigator / Dean of the Institute.

6. Application Process

- A request for proposal document will be published on BIRAC's website. Proposals will be sought through an open call through BIRAC's on-line platform.
- Proposals submitted in hard copy or those submitted after the call closure will not be accepted.

7. Selection Process

- a. The screening of the proposals will be a uniform evaluation process for all the applications received under the call. Submitted proposals will be screened for administrative eligibility internally by BIRAC. Eligible proposals will be considered for further screening
- b. The Program Advisory Group (PAG) and Apex committee will be constituted for evaluating the proposals. The PAG will meet through videoconferencing or in person to screen and perform the evaluation to shortlist the proposals further, primarily on their technical relevance. Preliminary technical evaluation process will be decided by BIRAC based on total number of applications submitted. Post shortlisting, detailed presentation (as per the format given) including objective, methods, deliverables, and budget will be made by applicant to the committee.
- c. PAG is empowered to recommend the proposals for funding seeking grant of ≤ 100 Lakhs (less than or equal to 100). PAG is empowered to recommend proposals for funding seeking grant of ≤ 500 Lakhs (less than or equal to 500 Lakhs) for site visit.
- d. PAG is empowered to recommend the proposals for funding seeking grant of ≤ 500 Lakhs (less than or equal to) post site visit. PAG is empowered to recommend proposals for apex consideration seeking grant of >500 Lakhs (more than 500 Lakhs) after site visit.
- a. BIRAC officers will update the site visit observations and recommendations

and PAG are empowered to recommend proposals seeking grant > 500 L (more than 500 Lakhs) for consideration of APEX.

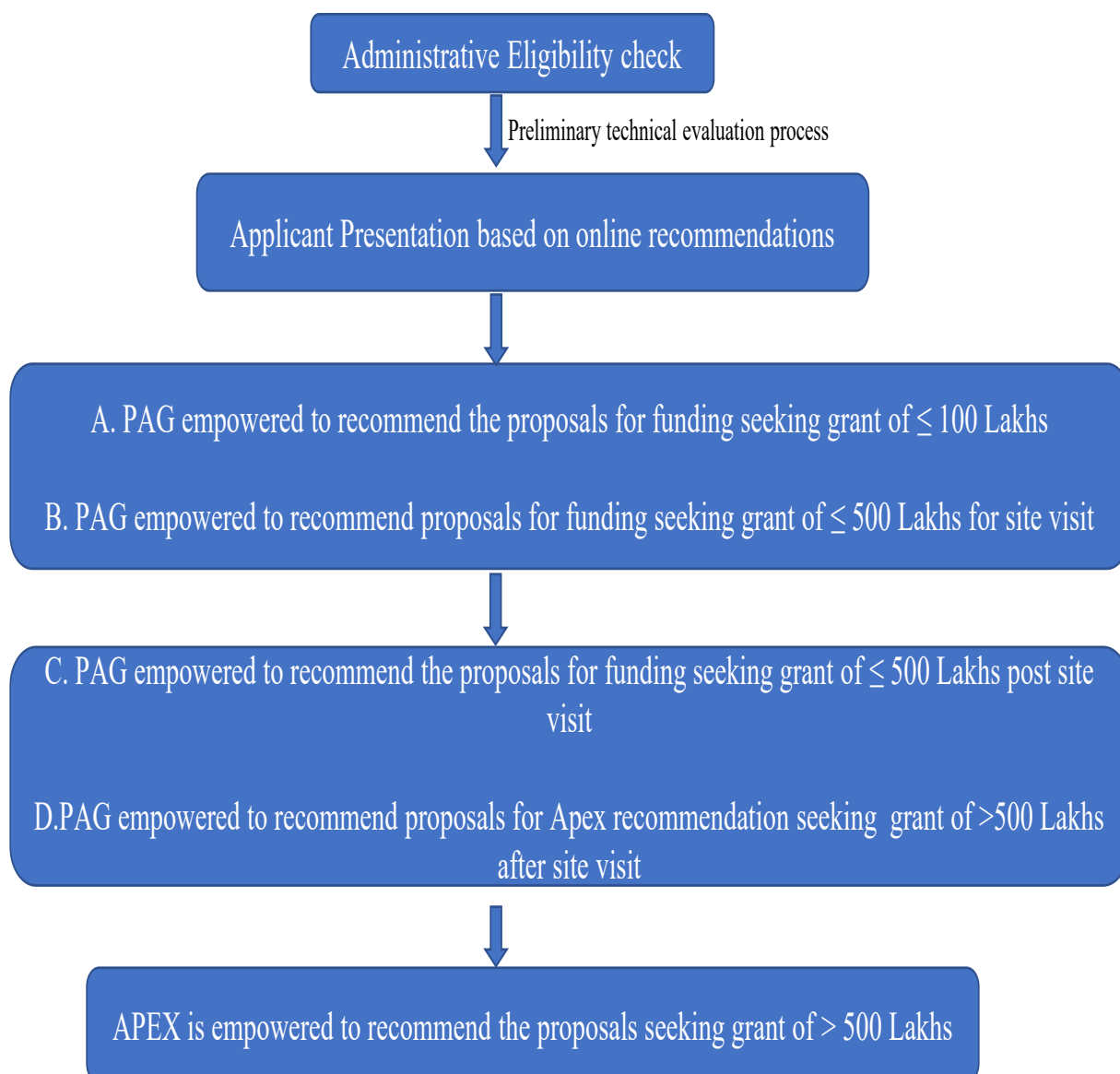
- b. The Apex committee will screen the shortlisted proposals for further review and recommendation for funding.

8. Sanction of Fund Support

- a) Site visits for Technical Due Diligence will be conducted for proposals seeking grant based on the recommendations of PAG committee. After the final recommendation, the applicant will have to revise the proposal based on the recommendations of the committee. The application will be proceeded further for financial concurrence, legal/IP concurrence and issuance of GRANT-IN-AID LETTER AGREEMENT (GLA) as per BIRAC norms. Financial Due Diligence will be done as per BIRAC norms.
- b) After successful execution of the above documents and fulfilment of other formalities, fund disbursement will be initiated by BIRAC.

9. Fund Disbursement

1. Financial concurrence will be done on the proposal as per the recommendations of the approving Committee.
2. For the academia the funds will be released in the existing organizational accounts. A no lien account will have to be opened for the project by the company. The expenditure done after signing of the GLA should only be included in the project. All expenditure should incurred as per the details mentioned in the GLA. The equipment list should strictly match with those given in the GLA. All expenses (for both BIRAC and company) are to be done out of the no-lien account only.
3. The release for academia and non-profit entities shall be processed with the existing organizational accounts.
4. The GLA shall have specific undertakings with regard to the accommodation towards the first release provisions of Company/ LLP as applicable.
5. The fund disbursement will be milestone based (the duration, milestone and fund release schedule may be changed based on very specific recommendation of the committee).



Preliminary technical evaluation process to be decided by BIRAC based on No. of application

The funds release percentage as per the duration of the project is as-:

Milestones	Project Duration	
	12 months	24 months
Signing of GLA and release of funds for completion of first technical milestone	30%	40%
First Technical milestone completion	60%	0.0%
Second technical milestone completion	0.0	50%
Third Technical milestone	NA	0.0%
Final submission of report	10%	10%
Projects with 12 months will have (2 technical milestone) and those of 24 months will have (3 technical milestone).		

- *However, duration, milestone and fund release schedule will be based on very specific recommendation of the committee.*
- *Any other funding assistance condition very pertinent to a Project shall be considered based on the recommendation of committee.*

10. Funding Process and Project monitoring and mentoring

1. The funding will be in form of Grant-In-Aid letter assistance.
2. The Grant-in-Aid assistance support (hereafter referred to as Funding) will be subject to pre-acceptance of associated conditions and execution of Grant Agreement as prescribed by BIRAC
3. The fund allocation into different budget heads and break-up into milestones will be done as per the recommendations of the final approving committee
4. Outsourcing for activities to international labs may be considered if the facility to perform the same is not available in India.

Note: For industry, salary of Project coordinator and other manpower (Financial Clearance is required) may be included in the project cost in case they are not availing the same from any other source (as confirmed by self-certification).

11. Project monitoring and mentoring

- i. Review of progress: The projects sanctioned will be monitored/and mentored regularly by a PAG constituted by BIRAC. Site visits will be carried out subject to committee's recommendation comprising of domain area technical experts.
- i. Reporting of Progress: On Successful completion of each Milestone, the applicant is required to submit a detailed Milestone Completion Report (MCR) as per prescribed format. The progress is assessed by the committee for its completion based on presentation/report evaluation/ site visit. On recommendation of the PAG, the next Milestone budget will be released.
- ii. The Applicant has to submit a duly certified Statement of Expenditure for the Budget available for the specific milestone being reported upon.
- iii. The Fund Recipient shall submit the Utilization Certificate (UC) and Statements of Expenses (SOE) duly audited by a Chartered Accountant for the expenditure incurred towards the Project for every half year period, ending 30th September and 31st March, to BIRAC, within a month of closure of the accounts for the respective half year, in the format provided by BIRAC. The CA shall also certify that there has been no change in the shareholding pattern and if there is any change, the particulars shall be specified.
- iv. The Fund Recipient shall submit audited Annual reports along with the audited balance sheets and profit & loss accounts to BIRAC within seven months of the completion of the financial year ending 31st March till the completion of the Project Duration.
- v. The allowable cost includes the Recurring cost (Manpower, Consumables, Travel, outsourcing and contingency and Non-recurring component (equipment and accessories) not to be more than 30% of the total project grant. However, if a specific project has a requirement for non-recurring grant of more than then the same can be considered based on the recommendations of the committee. The non-

allowable costs include Civil construction work, Any Litigation/ Opposition/ Infringement cost, Overhead and Expenses related to company compliances

12. Governance, Monitoring & Reviewing

- i. The process implementation shall be governed by the funding agreement. The governance for projects implementation for all purposes shall be in terms of the respective agreement that will be entered between BIRAC and the Fund Recipient.
- ii. Review shall be conducted through the committees which will be formed for the projects. If need be, an online interaction/site visit shall be conducted during the course of the project or at completion.

13. Intellectual Property Governing Framework

A. SCOPE OF IP GENERATED DURING THE CONDUCT OF THE PROJECT

- a. The New Intellectual Property (IP) rights belong to the recipient of funds, in a jointmanner unless mutually agreed otherwise. Provided, this Project is not determined as a “Nationally Important Project” to be governed through specific „Order of BIRAC“. Such cases of “Nationally Important Project” shall have specific terms oflicensing, pricing or March-in-rights for the purposes of public interest/ demand ofGovernment of India.
- b. It is the responsibility of the Fund Recipients to protect the New Intellectual Property (New IP). They shall bear the expenditure involved in protecting the NewIP.
- c. **GLOBAL ACCESS**
The Fund Recipient(s) jointly and severally agree to conduct and manage the Project and the resulting products, services, processes, technologies, materials, software, data or other innovations (collectively, “Product”) and any IP that arises (New IP) in the manner that ensures “Global Access.”
Global Access requires that
- d. The knowledge and information gained from the Project be promptly and broadlydisseminated or published.
- e. Project Developments and/or New IP are made available and accessible at anaffordable price to people most in need within developing countries.
- f. In this regard, ensure Global Access in all present and future research and development agreements in a suitable form.

NOTE: For the purpose of this GLA, New IP means intellectual property generated during the conduct of the Project by the Fund Recipient(s), but excluding the intellectual property generated by the Fund Recipient(s) before execution of this GLA and any IP generated outside the scope ofthis GLA even during the term of this GLA.

14. Foreclosure and Termination

- i. In case, during the Project Duration, if it is found that the Project or any Project component is not likely to lead to successful completion, BIRAC may decide to foreclose the Project or the Project component as warranted. The decision of the BIRAC shall be final in all respects. The Fund Recipient shall submit detailed accounts of funds received and utilized. The Company shall immediately refund any grant-in-aid unutilized out of BIRAC's disbursements to BIRAC, BIRAC, at its discretion, allow deduction of, the future committed expenses to third party vendors on pro-rata basis according to the quantum of BIRAC's funding. If the Fund Recipient likes to continue the Project at its own cost, it would be able to do so without restrictions from BIRAC after complying with these provisions.
- ii. The fund recipients may, before the completion of the project, terminate the agreement by giving three months' notice in writing to BIRAC. BIRAC may also terminate the agreement by written notice in the event of committing breach of terms of the agreement and either not rectifying it to the satisfaction of BIRAC or not satisfying BIRAC about its inevitability within a Specified period. In the event of termination of the agreement, no further disbursement shall be made by BIRAC. The fund recipients shall be liable to return immediately the amount of Grant-in-aid already availed of from BIRAC with additional simple interest at the rate of 12 (Twelve) percent annum within 30 (thirty) days of termination of the agreement, Interest on the quantum of funding assistance shall accrue from the date of release of the Grant-in-aid assistance. In case of failure to repay, without prejudice to any other rights under the agreement, the amount can be recovered by initiating any procedure available in Law.
- iii. Breach of terms, unjustified delay in project progress, failure to bring own contribution, unjustified delay/ non-submission of UC/SOE/SOA, progress report as required for final closure etc. shall also be grounds for termination.

15. Extension in the duration of the project

Extension of projects is DISCOURAGED. Request for extension of project on account of Change in Coordinator/Principal Investigator, delay in purchase of equipment, hiring of manpower, submission of Milestone Completion Reports, Statement of Expenditure (SoE), Utilization Certificate (UC), or any other financial/technical document by the company/collaborator necessary for release of funds by BIRAC will NOT BE ENTERTAINED.

Request for extension of milestone/project can be considered (without any additional financial implications) only in selective cases where accomplishment of technical milestone is prolonged due to delay in securing regulatory approvals, or where the relevant committee feels that some

additional studies are needed to take the project to a logical conclusion/product development or due to any other technical reasons not envisaged at the time of submission of proposal. However, such request must be communicated to BIRAC at least TWO MONTHS before the scheduled date of completion of milestone/project with proper justification.

16. National Importance

The Projects that will be supported under this special call are to deliver and to give nationally important outcomes, in addition to the Global Access. Accordingly, every Project shall have a national/global commitment based on the expected results that will be part of the considered recommendations of the relevant Committee.

17. Call duration

The call for proposals opens on 20th/March/2023. The last date for proposal submission is 4th /May/2023 (5.00 P.M).

For any queries, please contact

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