Biotechnology Industry Research Assistance Council

(A Govt. of India Enterprise)

Special Call for Proposals
on
"Validation and Scale-up of Industrial Enzymes & Development and Characterization of Anti Snake Venom (ASV)"

(1st November – 15th December, 2017)

1. Call for proposals for Validation and Scale-up of Industrial Enzymes (under BIPP)

BACKGROUND:

Enzymes are applied in various fields, including technical use, food manufacturing, animal nutrition, cosmetics, medication, and as tools for research and development. At present, almost 4000 enzymes are known, and of these, many are used commercially. Some specific use of industrial enzyme in daily needs are

Textile – Enzymes are used for various textile wet-processing applications like desizing, bio-polishing, denim finishing, bleach clean-up, bio-scouring and de-wooling.

Leather – Enzymes are mainly used in soaking, unhairing, bating, degreasing and waste processing of leather industries.

Detergent - Enzyme detergents remove protein from clothes soiled with blood, milk, sweat, grass, etc. far more effectively than non-enzyme detergents

2-G ethanol - For biomass conversion, cellulases are key for the digestion of cellulose into glucose for fermentation into biofuels. For biodiesel, the enzymes lipase and phospholipase are the major players.

Pape and pulp – Enzymes help in deinking, bleaching, reducing viscosity, improving softness. Cellulase, xylanase, laccase and lipase are the most important enzymes that can be used in the pulp and paper processes.

Food and Beverage - Enzyme use instead of chemicals in the food processing industry generally creates superior products with improved yields in addition to reducing carbon footprint, energy consumption, and environmental pollution. Further, food enzymes account for low greenhouse gas emissions and less raw material wastage.

The biotech industry manufactures enzymes for a plethora of applications from food production to pharmaceutical drugs. Development and deployment of enzyme production to refine the existing chemical based systems is crucial for development of a sustainable bio based economy. Enzyme based process can deliver key advantages over synthetic chemical production methods, including the ability to reduce energy inputs, decreased use of metal-based catalysts, and completely selective access to specific products without unwanted side

products. Improving the production efficiency and cost of commercial enzymes poses significant challenges for industrial-scale fermentations. With the improved understanding of the enzyme production biochemistry, fermentation processes, and recovery methods, an increasing number of industrial enzymes can be foreseeable.

PURPOSE OF THE CALL:

Considering the above, proposals are invited to successfully tackle the validation/scale-up for the production of enzymes.

SCOPE OF THE CALL

Technologies/processes that have reached Early Validation stage and are ready for late stage validation/scale-up will be considered. The scope of the call will focus on cost effective, novel and innovative approaches for production of enzymes for leather, paper and pulp, 2-G ethanol, detergent, and textile applications:

- Scale up of process/technology
  - ✓ Scale of operation – 1000 – 10000 L
  - ✓ Efficiency of conversion – at least 50%
  - ✓ Enzyme concentration – at least 10 g/l

What the Project should encompass:

1. The developed enzyme should have applications in the manufacture of fine chemicals, bio-based polymers; the food and drink industry; industrial wastewater treatment or green conventional manufacturing processes.

2. A clear understanding of life cycle, environmental, and economic analysis for allowing direct comparison between bio-processes and their conventional chemical counterparts.

3. The enzymes developed should be resistant to heat, pressure or low pH when used in the production of chemical entities.

Proposals not falling within the scope of the call

1. Solutions that require long term development;
2. Proposals without proof of principle
3. R and D projects involving exploratory research and not resulting in any technology
4. Proposals based only on screening, collection or segregation of micro-organisms
5. Processes that are only slight improvements over existing approaches
6. Technology not established at lab scale

2. Call for proposals for developing novel tools/technologies/processes and product optimization/Scale up of "Anti Snake Venom"

(under SBIRI/BIPP/PACE)

BACKGROUND:

Snake bite is a common and frequently devastating environmental and occupational disease, especially in rural areas of tropical developing countries and is responsible for tens of thousands of deaths and disabilities every year. The World Health Organisation has added snakebite to the list of Neglected Tropical Diseases in 2009. India is estimated to have the highest snakebite mortality in the world. World Health Organization (WHO) estimates place the number of bites to be 83,000 per annum with 11,000 deaths. India therefore contributes to a significant proportion of global snake bite deaths. Although the full burden of human suffering attributable to snake bite remains obscure, hundreds of thousands of people are known to be envenomed and tens of thousands are killed or maimed by snakes every year. There are four species groups of snakes i.e. 'Big Four' are primarily responsible for the highest death rate from snakebite in any country in the world.

Snake venoms are the most complex of all natural venoms and poisons. Snake venom neurotoxins block/excite peripheral neuromuscular junctions by acting at various sites and bind to their receptors with high affinity, making reversal of paralysis by anti-venom implausible. Anti-venom, prepared by immunizing horses or sheep with venom from snakes is the only medically accepted remedy for systemic snake envenomation. Antivenom is derived by immunizing horses with snake venom in gradually increasing doses until the horse reaches a high titre of immunity to the venom. The horse's hyper-immune serum is then refined into antivenom. All Indian antivenom are polyvalent, that is, they are effective against all the Big Four common venomous snakes of India. However, the high cost of generating antibodies in horses and side effects, such as serum sickness, are bona fide problems.

There are growing indications from clinicians that anti-venom produced from venoms of the 'big four', mainly sourced from a particular region, may not effectively neutralize envenomation by the 'big four' and related species in other parts of the country.

There are some critical issues with ASV, the production of which started 100 years ago in India. The potency of the presently available ASV is less than what it was prior to 1950's. The main issues with ASV in actual clinical practice are species specificity, difficulty in availability, affordability and ideal storage conditions. One of the principal drawbacks of the immunotherapy is the issue of specificity. There is a huge species variation with current taxonomy identifying one, four and eight species of Russell's viper, cobras and kraits, respectively. So the variable composition and antigenic reactivity of the venom restricts the use of a particular ASV to a geographical area with relevant specificity. Venom variation, low potency, bites by other species could be responsible for the reported failure of polyvalent ASV in countering the venom effects in India.

Further there are various logistic, marketing and economic issues with the production and supply of ASV. Production in lyophilized form is costly, and there can be physiochemical changes in the product by lyophilization. The liquid form requires cold chain. The production of monovalent ASV is a costly affair. In India the monovalent ASV is not produced. However, it has been proposed that in developing countries, the production of ASV can be

sustained at affordable prices if cost efficient methods of production are kept in mind. There needs to be rapid technical advancement in production.

Identification of the snake is important in planning the treatment. Anti-venom is the only medically accepted remedy for systemic snake envenomation. Conventional clinical practice is to administer polyvalent ASV often causes severe anaphylaxis reaction in the victim, seen in up to 30 of the recipient's worldwide demanding secondary treatment. Acute pulmonary oedemas, cerebellar ataxia and uveitis an immunological complication are some of the complications following polyvalent serum. Though monovalent ASVs are available, lack of a proper diagnostic system preludes this opportunity. Many attempts have been made worldwide to develop species specific diagnostic kit based on antibodies, but have not found successful mainly because of inter-species cross reactivity to the crude venom as also the lack of sensitivity related to the small quantities in which venom is injected.

Considering to the importance of snake venom, it is necessary to evaluate the toxicity of protein components of snake venom. The Snake venom is extracted (milked) from different types of poisonous snakes. This extracted venom is stored in the form of lyophilised powder until its requirement for commercial production for anti-snake venom or for any research organization who want to carry research on snake venom. Snake venom is a very costly substance, but unfortunately we don't have any data whether the efficacy of venom is increasing or decreasing with respect to time. Snake venom should be remain active for approximately 5 to 7 years from the date of its extraction from snake. There is an immediate need of a facility to assure the efficacy of the venom going to be used for the production of the ASV, to assure the quality, safety and efficacy of the ASV and to assure that the quality of the ASV meets appropriate standards and is consistent.

PURPOSE OF THE CALL

Considering the above and other issues related to snake bite problem in India, BIRAC invites proposals for developing novel tools/technologies/processes pertaining to snake bite problem and product optimization/Scale-up on **"Anti Snake Venom".**

This call is to seek individual applications on either of the following:

1. Development of Novel and alternate ways of ASV production.
2. Development of new diagnostics kits for the identification of the snake biting species.
3. Characterization, evaluation and validation facility for ASV (Under BIPP, Category IV only).

SCOPE OF THE CALL

The scope of the call will focus on cost effective, novel and innovative approaches.

- The focus is on generating ASV with better product profiles and greater cost effectiveness than current products in market.
- This call seeks proposals to accelerate production of ASV with increased potency.
- This call will support the various stages of an ASV development including, proof concept establishment, preclinical development, product manufacturing and human clinical trials. Applicants may also request funds for production of clinical grade (manufactured Good Laboratory Practices (GLP) guidelines) ASV production.

What the Project should encompass:

The following are some of the indicative priority areas for submitting the proposals,

1. Production of Cost effective and improved quality of anti-venom.
2. New ways of producing ASV like Recombinant antibody based ASV production technologies.
3. Recombinant antibody based ASV for highly purified, well characterized, less allergic ASV having minimum variability.
4. Technologies for increasing the potency
5. Identification of herbal/peptide and small molecules for possible enhancement of available window for management.
6. Plant-made recombinant snakebite anti-venom antibody cocktail.
7. A pan-Asian anti-venom – with high potency anti-venom designed for several countries across the South Asian region, produce in large volumes and dispense in single dose.
8. An immunoassay for specific identification of the biting species/venomous snake bite in India (identification of venom toxins which are highly specific to the biting snake species, purification of these proteins and development of specific antibodies to these proteins.)
9. A diagnostic kit that would help differentiate venomous from non-venomous and also dry bites.
10. Development of bedside diagnostic kits for detection and quantification of poison for determining dose requirement of ASV.
11. Characterization , evaluation and validation facility for ASV

A product which has not been listed will also be considered if there is a proper justification. Applicants are encouraged to submit their proposals in collaboration with academic institute(s).

Proposals not falling within the scope of the call

1. R and D projects involving exploratory research and not resulting in any technology/product
2. Processes that are only slight improvements over existing approaches

Who can apply?

The proposals can be submitted under SBIRI/BIPP/PACE scheme of BIRAC

<u>Eligibility for SBIRI</u>

1. Solely by a Company incorporated under the Companies Act, 2013 *or*
2. Limited Liability Partnership (LLP) incorporated under the Limited Liability Partnership Act, 2008 *or*

3. Joint Ventures either in the form of Company/ LLP by any of the above entities jointly with other private or public partner(s) (Universities or Institutes).

Eligibility criteria for industry

- 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)
- Minimum half of the persons who subscribed their names to the LLP document as its Partners should be Indian citizens.
- Participating companies should have adequate in-house facility to address the project implementation aspects (which shall be evaluated during the site visit) OR Incubated with any of the recognized Incubation Facility.

Eligibility criteria for academic collaborator

- Public/private university/colleges in India
- National research laboratories
- Not-for-profit private research labs/societies/foundation

Eligibility for BIPP:

1) The proposals can be submitted:

- Solely by an Indian Company*
- Jointly by an Indian Company and National R&D Organizations and Institutions; or
- By a group of Indian Companies along with National Research Organizations etc.

* *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*

2) The Applicant Company should either:

i. Have adequate in-house facility to address the project implementation (which shall be evaluated during the site visit) or

ii. Incubated with any of the recognized Incubation Facility

Eligibility for PACE:

The scheme has two components as below:

i. *Academic Innovation Research (AIR)*

ii. *Contract Research Scheme (CRS)*

1. Academic Innovation Research (AIR):

The objective of Academic Innovation Research (AIR) scheme is to promote development of Proof-of-concept (PoC) for a process/product by academia with or without the involvement of industry

Eligibility Criteria for Academic Innovation Research (AIR):

1. ***Types of projects to be supported :***

Projects with well-established proof-of-principle leading to development of prototype of a product /technology of national relevance or commercial potential

(Basic/exploratory research, projects without well-established Proof of principle or with no or low commercial potential will not be supported)

2. Duration of project : up to 18 months *(BIRAC's Technical Expert Committee at its discretion may recommend for increased duration of the project depending upon the nature of the research study)*

3. Funding Support (Grant): Total cost of the project must not exceed Rs. 50 lakhs (*Non-recurring cost must not exceed 10% of the total cost)*

4. IPR : IP rights may be with academia alone, or jointly shared between academia and industry (if academia establishes PoC with industry) as per the understanding between the two partners

5. Who can apply?

(a) Under the scheme, academia (Public or Private Institute, University, NGO, or Research Foundation) having a well-established support system for research shall be the primary applicant. It can apply either:

(1) Individually, or

(2) Jointly with academic* and/or industrial** partner

* *For Public or Private Institute, University, NGO, or Research Foundation, proper registration/accreditation from a government body is mandatory*

** *Participating company (if any) should be registered under the Indian Companies Act, 2013 with at least 51% Indian shareholding i.e., 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)*.

(b). The applicant Company should have adequate in-house facility to address the project implementation or incubated with any of the recognized incubation facility.

B. Contract Research Scheme (CRS):

Contract Research Scheme (CRS) aims at validation of a process or prototype (developed by the academia) by the industrial partner

Eligibility Criteria for Contract Research Scheme (CRS):

1. ***Types of projects to be supported:***

Academia must have an established Proof-of-Concept (PoC) as evident by scientific data ready for validation by the industry in contract research mode

2. ***Duration of the project***

No time limit

3. ***Funding Support (Grant):***

Funding in the form of grant is provided to both academic as well as industrial partners. While funding is provided to the academia for In-House research which forms a part of validation of the Proof of Concept, funds are provided to the industrial partner for validation. There is no ceiling to the funding

4. ***IPR :***

Although the IP rights reside with the academia, the industry partner has first right of refusal for commercial exploitation of the New IP

5. ***Who can apply?***

(a) Academia* has to be the Primary Applicant with one or more partners of which at least one is a company**

* *For Public or Private Institute, University, NGO, or Research Foundation, proper registration/accreditation from a government body is mandatory*

** *Participating company should be registered under the Indian Companies Act, 2013 with at least 51% Indian shareholding i.e., 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)*.

(b). The applicant Company should have adequate in-house facility to address the project implementation (which shall be evaluated during the site visit) or incubated with any of the recognized incubation facility.

How to Apply?

Proposals under SBIRI/BIPP/AIR/CRS are required to be submitted online only. For submission of proposals, applicants need to register with BIRAC through "User Registration". Additional information on user registration and proposal submission are available online at BIRAC website at www.birac.nic.in.

No Hard Copy to be submitted. Proposals submitted online only would be considered.

Last date for Submission of Proposals: 15th December 2017

BIRAC will ensure maintenance of strict confidentiality of the proposals as per DBT norms.

For any queries, please contact:

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