Innovative R&D in Biotech Sector

Dr. Purnima Sharma

Managing Director

Biotech Consortium India Limited

New Delhi

ABOUT BCIL

Biotech Consortium India Limited

INCORPORATED : **1990**

PROMOTER : **Department of Biotechnology, Government of India & All India Financial Institutions**

Project Management	Consultancy	Technology Transfer	Certification Services
Biosafety	Information Services	IP Management	Human Resource Development

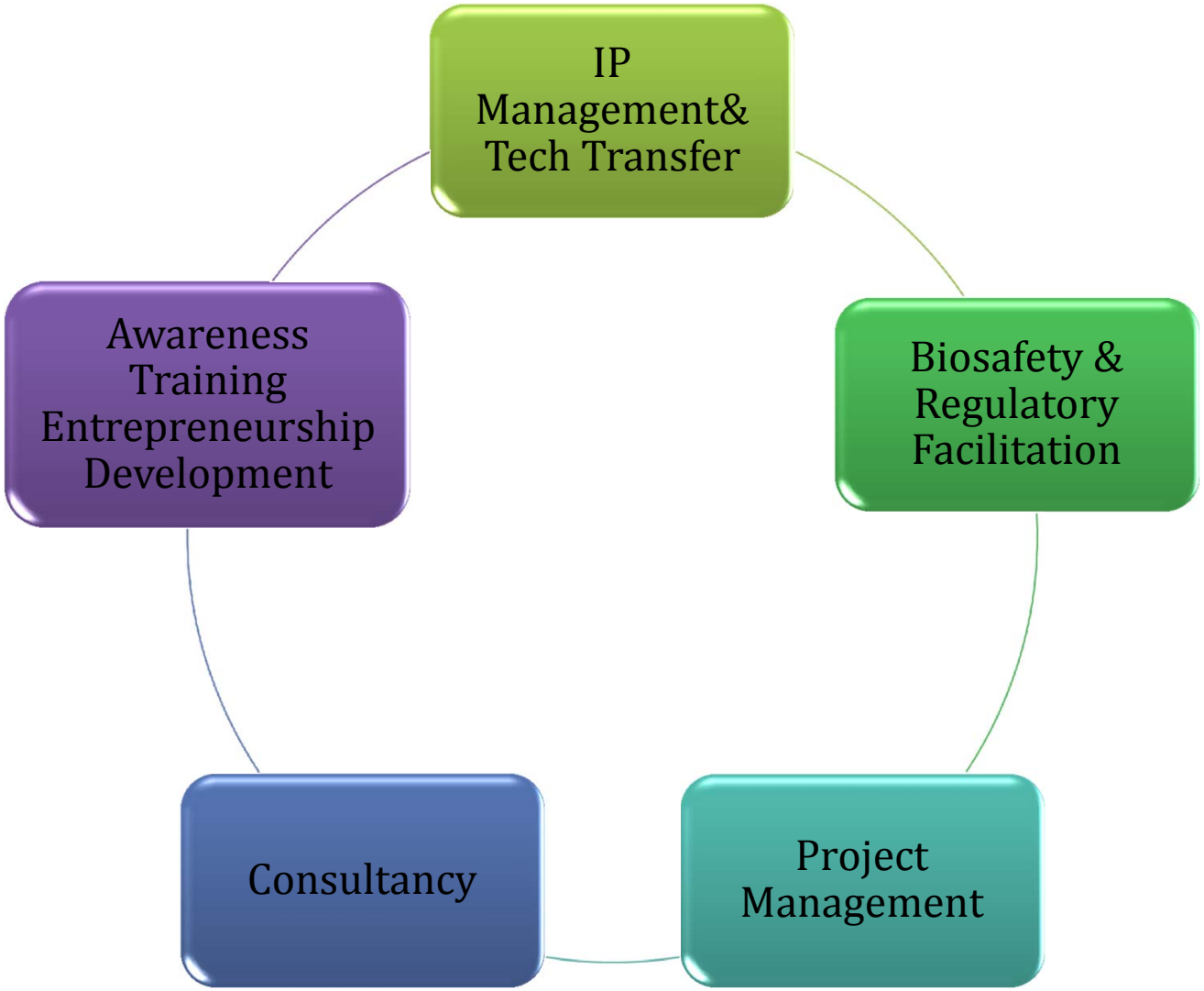
BOARD OF DIRECTORS

- **Secretary, Department of Biotechnology, Government of India/ Nominee.**
- **DG, Indian Council of Agricultural Research /Nominee.**
- **DG, Council of Scientific and Industrial Research/Nominee.**
- **Representatives of Financial Institutions (UTI, IFCI, IDBI).**
- **Individual Experts (Former Secretary DBT, Govt. of India & Former Director, CDRI, Lucknow).**
- **Directors from 2 Biotechnology companies.**

STRENGTHS OF BCIL

- Technically qualified team
- Extensive experience
- Equipped with latest Information Technology Tools
- State of the art patent and non-patent databases
- Extensive network with subject matter experts
- Extensive network with Biotechnology Industry

Services Offered by BCIL for Promoting Technologies & Innovation



BIRAC Vision-

"To Stimulate, foster and enhance the strategic research and innovation capabilities of the Indian biotech industry particularly SME's, to make India globally competitive in biotech innovation and entrepreneurship, for creation of affordable products addressing the needs of the largest section of society."

BIRAC Verticals

- **Fostering innovation and Enterprise Building:**
  - Fostering Innovation
  - Knowledge, Technology Mapping and Management
  - Technology Transfer, Licensing and Acquisition

- **Provide enabling services for promoting the innovation ecosystem**

- **Build Strategic Alliances – National & International**

How does BIRAC accomplish its Mission

Ensuring Entitlements

- Ignite new Ideas- Biotech Ignition Grant Scheme (BIG)
- Support early stage research for proof of concept validation – Small Business Innovation Research Initiative (SBIRI)
- Partnership with industry for high risk discovery led innovation research – Biotechnology Industry Partnership Programme (BIPP)
- Facilitating technology validation and development – Contract Research Scheme (CRS)

Empowering for Achieving Excellence

- Create world class quality Incubation space (Bio-incubators) for entrepreneurs and star-ups.
- Create common service facilities in public and private sector to serve the needs of Start Ups.
- Create Schemes that facilitate the acquisition or license of innovative technology and technology mapping for identifying patentable technology at national or international level.
- Create capacity in various fields required for successful Bio enterprises.

Biotechnology Ignition Grant (BIG) Scheme

Purpose:

Establish and validate of Proof of Concept

Encourage researchers to take technology closer to market through a Start Up

Target Groups:

Entrepreneurs from Academia or an Incubatee

(PhDs, Medical degree holders or Biomedical Engg. Graduates)

Support:

Grant-in-Aid limited up-to INR 50 Lakh
Mentoring and hand-holding

Supports up-to Proof-of-Concept stage

SBIRI

- **Launched: 2005**
- **Focus on SMEs and early stage R&D**
- **Funding available in Phases**
- **Phase-I easily extendable to Phase-II**
- **Provision for Grants and/or soft loans with easy repayment schedules**

SBIRI-
ELIGIBILITY REQUIREMENTS

- **An Indian Company**
  - Alone or
  - In collaboration with National Institutes/ Universities

- **JVs, Limited Partnership Firms**

•Registered under The Companies Act, 1956
•Minimum of 51% shareholding with Indians
•DSIR recognition/ IPR ownership on proposed work

SBIRI PHASE-I

Support for Early Stage Research Leads

PROJECT COST	SUPPORT	
	Grants –in-aid	Soft Loan (interest free)
Up to Rs 25 lakhs	80% of the project cost	---
Rs 25 to Rs 100 lakhs	50% of the project cost	---
Beyond Rs 100 lakhs	Rs 50 lakhs	Upto 50% of the amount by which the total project cost exceeds Rs 100 lakh (maximum Rs 50 lakh)

SBIRI PHASE-II

For Product & process development, validation studies, field trials, commercialization

Loan amount	Interest Rate (simple)
Upto Rs 100 lakhs	1%
up to Rs 10 crore	2%

SBIRI- PHASE I&II

- **If R&D and product development are simultaneously proposed**
- **Maximum of Rs 50 lakhs grant and soft loan up to 10 crores**

BIPP

- **Launched: December 2008**
- **An Advanced Technology Scheme**
- **Covers the entire spectrum of product development**
- **For all sizes of companies: Small, Medium and Large**

BIPP (Contd..)

- **Regular and special/need based calls for proposals throughout the year**
- **Varying models of grant and/or loans offered**
- **IP rights vested with the company**
- **Repayment**
  - **Loan: 10 equal half yearly instalments**
  - **Grant: 5% royalty for 5 years capped to twice the amount**

BIPP:
Categories & Type of Support

Category	Grant-in-aid	Loan (RoI)
I Products of high national and social relevance	√	√ (2-3%)*
II Products of high risk, high value IP	√	√ (2-3 %)
III Product evaluation & validation	√	√ (2-3%)
IV Major facilities around technology platforms	x	√ (5-6%)

** 2% - Upto Rs. 10 crores, 3% - >Rs. 10 crores*

BIPP - Eligibility Issues

Primary Applicant

Eligible	Ineligibles
• For Profit Company registered under **Indian Companies Act 1956** • Minimum of **51%** shareholding with Indians and/or NRIs	• Any entities other than registered company: **Proprietorship, Partnership, NPOs, NGOs, Trust, Society, Educational Institutes/ Universities, Any other**

Collaborating Organizations:

- Another registered company
- Institute/University
- Trust/Society/NGO

DSIR Requirements

- DSIR recognition for the in-house R&D lab **mandatory** for the primary applicant as well as for all company type collaborators
- In case, DSIR is unavailable, it is mandatory to have **applied to DSIR** before proposal submission
- **For incubatees**:
  - DSIR recognition of the incubator is considered as sufficient
  - Tenure of Incubatee with the incubator should be more than the proposal duration

Contract Research Scheme- CRS

Purpose:

Academia-industry interaction
Industry to validate process or partner for specific research

Leads should be at a level which provides sufficient data for Scale up/Validation:

- Exploratory validation of technology
- Small scale contract research resulting in generating several batches of process or multiple prototypes
- Large scale validation of prototype to commercial design

Target Groups-

Research institutes, Universities, Public funded research Laboratories, Governmental organizations, Research foundations
AND
Companies / industries

Company partner should have DSIR recognized R&D/Service unit(s)

Support:

- Funds for validation of PoC
- IP Services and Management
- Legal support: MTA, NDA, IP protection contracts, Licensing agreements

Bio-incubator Support Scheme- BISS

Purpose:

Strengthening and Up-gradation of the existing Bio-incubators and also to establish New World Class Bio-incubators in certain strategic locations.

Target Groups:

- Existing Bio-incubators across the country
- New Bioincubators

Support:

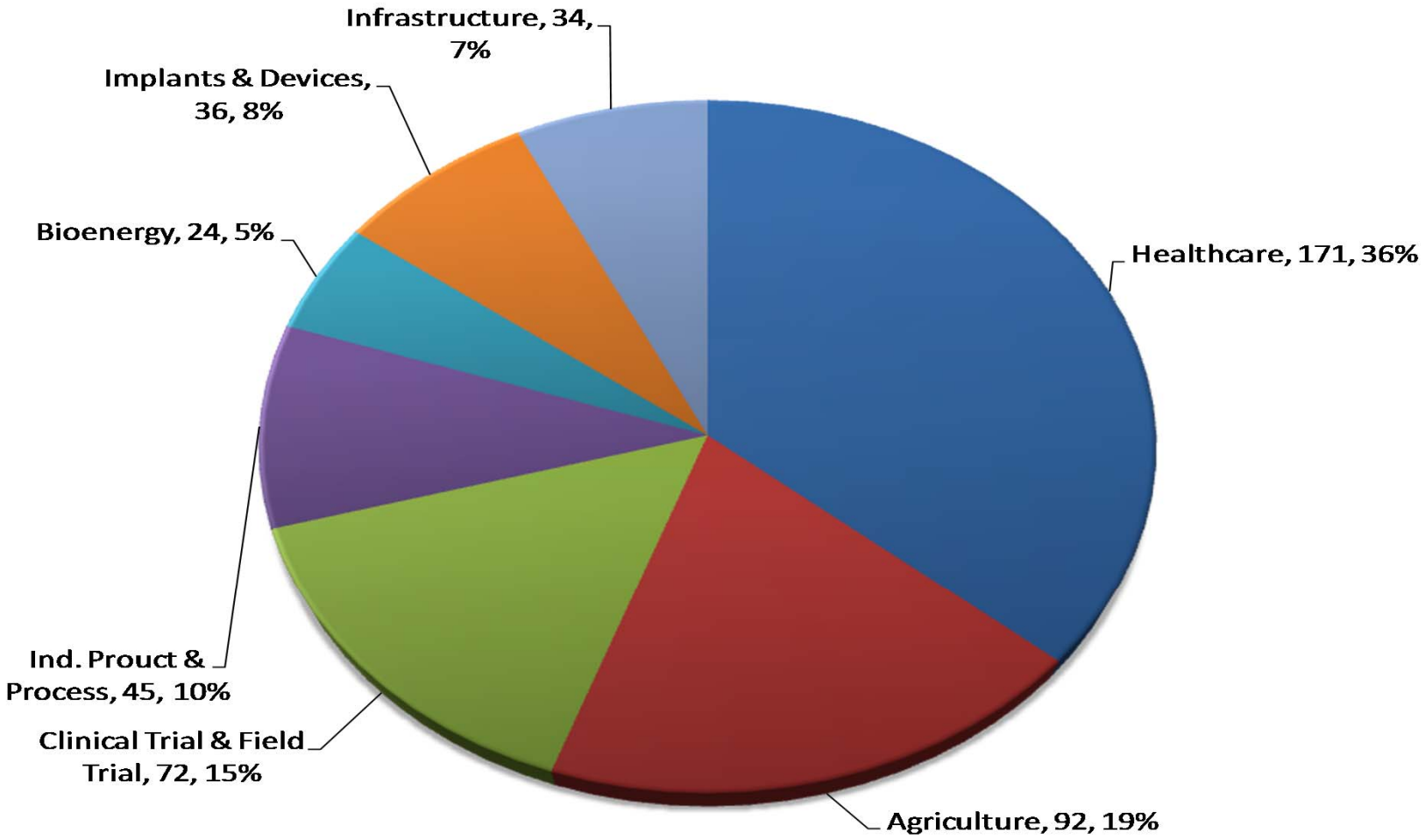
- Provide incubator space to Start-ups and Entrepreneurs.
- Provide access to a pool of special equipments in the Central Equipment Facility.
- Connect and facilitate Industry – Academia Interaction
- Provide enabling services and required mentorship for IP and Technology Management, Legal and Contract, resource mobilization and networking platform.
- Governance models would be cooperative or autonomous.

BIPP Overview and Key Elements of Effective Grant Writing

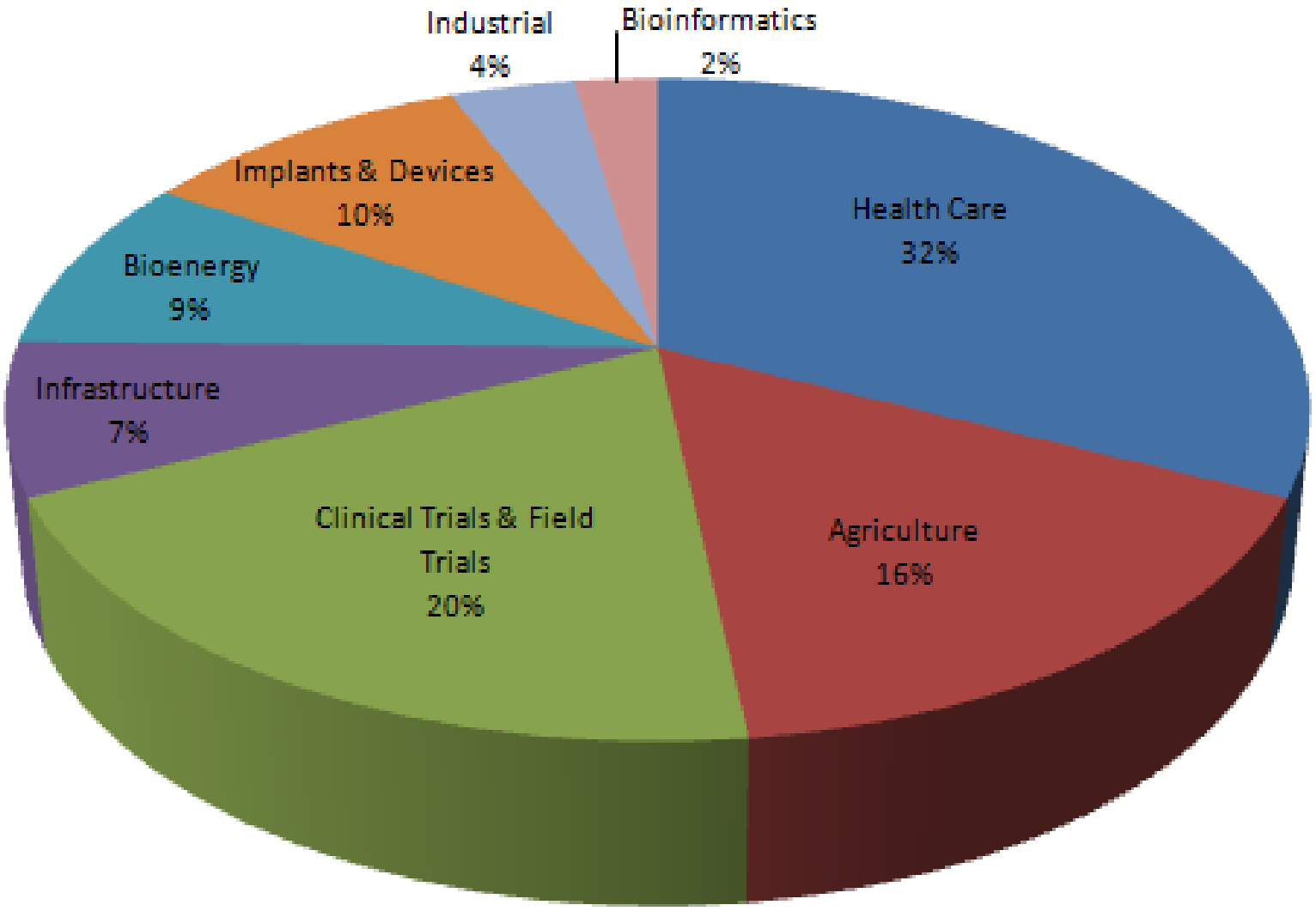
An Overview

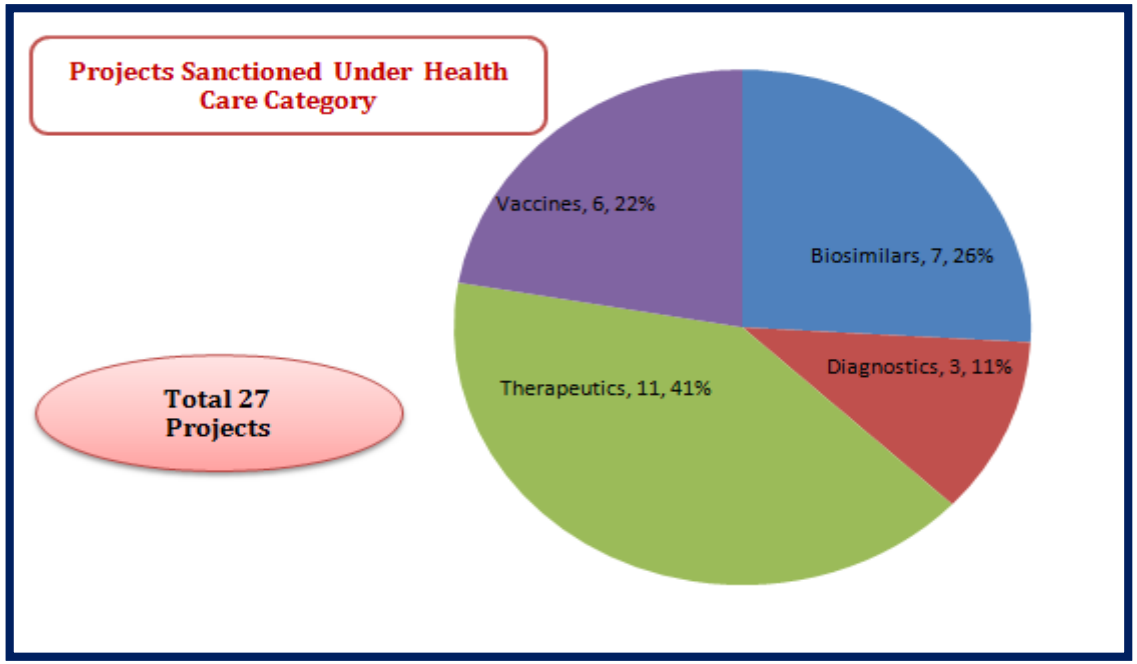
- Scheme Launched ---- **December 2008**
- Total Number of Calls--- **21 (till March 2012)**
  - Regular--- **10**
  - Special--- **11**
- Number of Projects Received --- **551**
- Number of Projects Approved --- **> 90**
- Total Budget Committed –-- **Approx Rs. 650 Crore**
  - Company Contribution–-- **Rs. 430 Crore**
  - BIPP Contribution--- **Rs. 220 Crore**

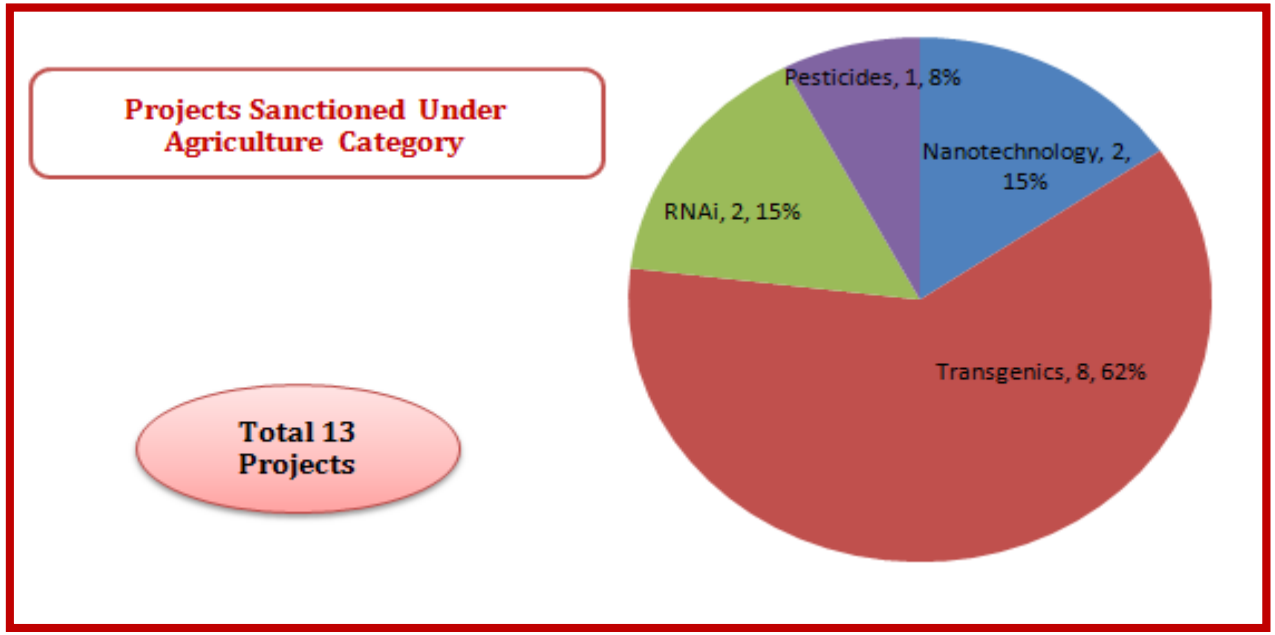
Total Proposals Received: 551

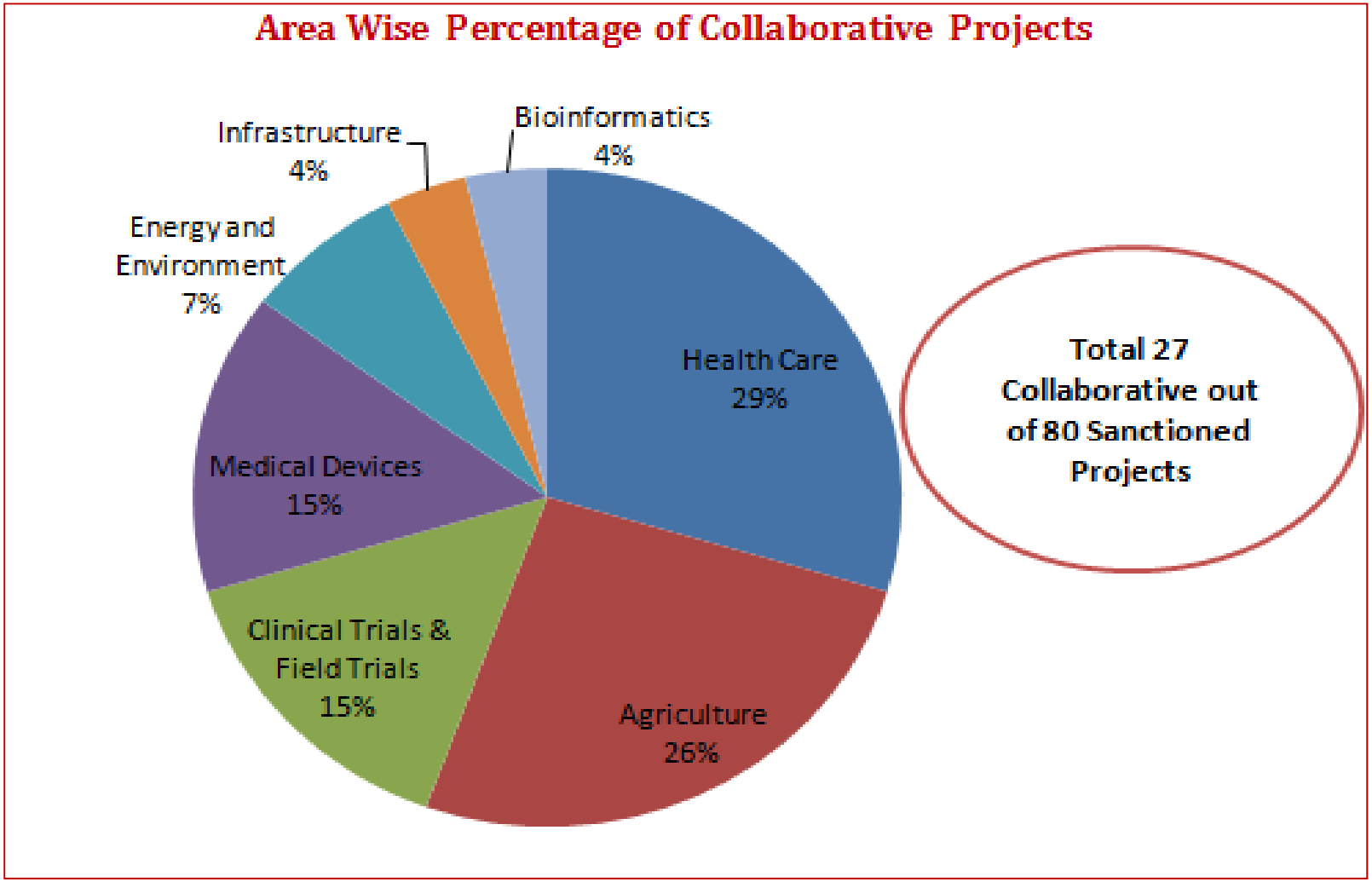


Area Wise Sanction of Projects Under BIPP




Projects Sanctioned Under Health Care Category
Vaccines, 6, 22%
Biosimilars, 7, 26%
Diagnostics, 3, 11%
Therapeutics, 11, 41%
Total 27 Projects


Projects Sanctioned Under Agriculture Category
Pesticides, 1, 8%
Nanotechnology, 2, 15%
RNAi, 2, 15%
Transgenics, 8, 62%
Total 13 Projects


Area Wise Percentage of Collaborative Projects
Infrastructure 4%
Bioinformatics 4%
Energy and Environment 7%
Health Care 29%
Medical Devices 15%
Clinical Trials & Field Trials 15%
Agriculture 26%
Total 27 Collaborative out of 80 Sanctioned Projects

Key Elements of Effective Grant Writing

Play According To The Rules

- ✓ Read the Guidelines
- ✓ Understand the Guidelines
- ✓ Follow the Guidelines

Following the Guidelines

- Make sure that you are eligible
- Read the instructions carefully
- Respond to all sections
- Cover all the topics
- Keep all preliminary & support data ready
- Use headings that correspond to guidelines

Next Step After Reading the Guidelines

Developing the Proposal : Points to be addressed

- Problem addressed
  Aim of the proposal

Relevance and importance of the proposed project

Status – Review

Scientific strategy & approach

Objectives

Plan of work

Expertise & infrastructure

Time lines

Outcome / deleverables

Regulatory Issues

- Clear understanding and conformity with regulatory requirements

- Approval from regulatory authorities
  - ✓ rDNA work
  - ✓ Clinical trials/ Field trials

7/20/2012

Technology Ownership

- License to the Technology
  - ✓ License to the main technology if in-licensed
  - ✓ License to components required for practicing technology
  - ✓ Clarity on terms of license
    - Use, Produce, Sell
    - Territory
    - IP ownership on improvements/ modifications

Ownership of IP for Technology

- With applicant company and not with employees
- Clarity on IP sharing among collaborators

7/20/2012

THANK YOU !

BCIL

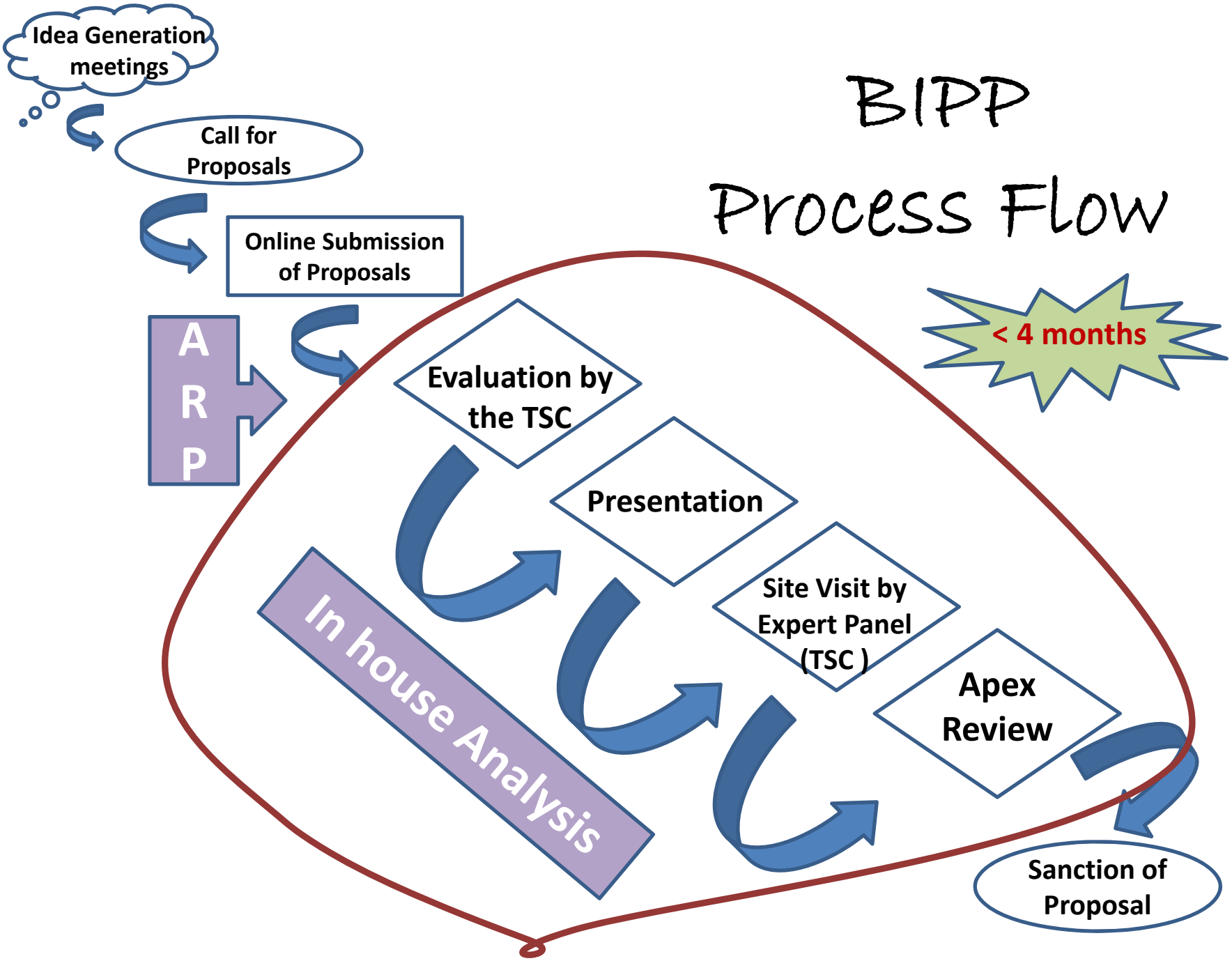
Mechanics of BIPP

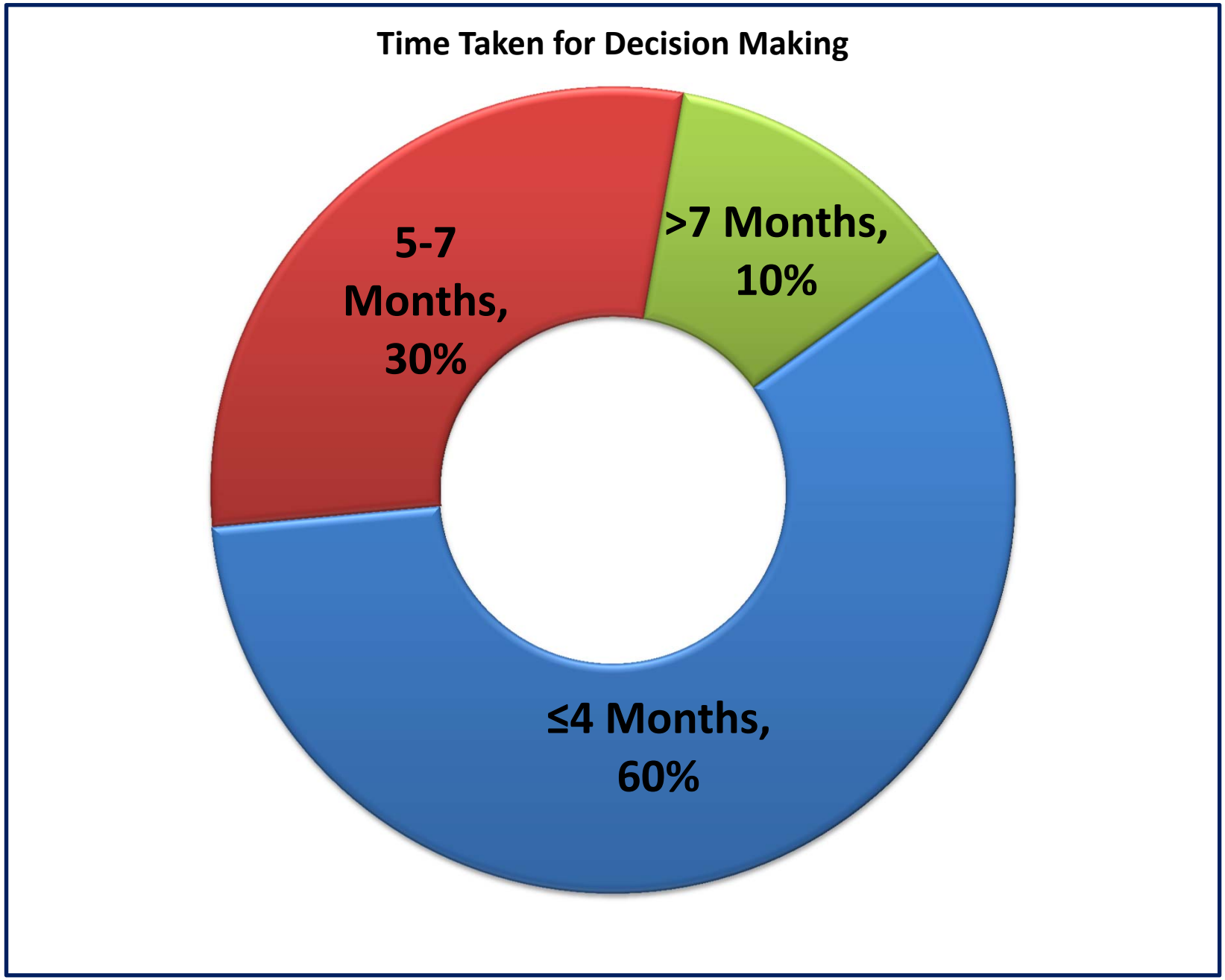
Ms. Shilpy Kochhar

Deputy Manager

Biotech Consortium India Limited (BCIL)

BIPP Process Flow




Time Taken for Decision Making
5-7 Months, 30%
>7 Months, 10%
≤4 Months, 60%

Expert Committee Meetings on priority areas

In house discussions

Discussions sessions chaired by Secretary, DBT

Idea Generation Meetings

Priority Agri Areas

H1N1 vaccine develop-ment

Secondary Agriculture

Biosimilars

Genesis of Special Calls

Antivirals

Affordable Health Care Technologies & Products

Call for Proposals

Regular Calls

thrice a year

- February
- June
- October

Special Calls

need based

21 Batches processed till date

10-Regular

11-Special

Regular Call is Currently Open Till 31st July, 2012

Duration of Call: 30 - 45 days

Information about an active call

- *Published in all national dailies*
- *Biotech magazines*
- *Can be accessed at any point of time from DBT/BIRAC /BCIL websites*

Submission of Proposals

Online only

www.birapdbt.nic.in

Register your company with BIRAP

- **Requires only minimum details**
- **No upper limit to the number of users with one company**

Choose the Relevant Call

- **In case of multiple active calls, relevant call needs to be chosen**
- **Begin proposal submission by filling in the *Basic Information Page.***

Final Submit

- **Submit all the Forms *(some forms follow a hierarchy and need to be submitted in a sequential manner only)***
- **Be careful about the information provided *(in particular for the milestones and financial data)***

Eligibility Issues

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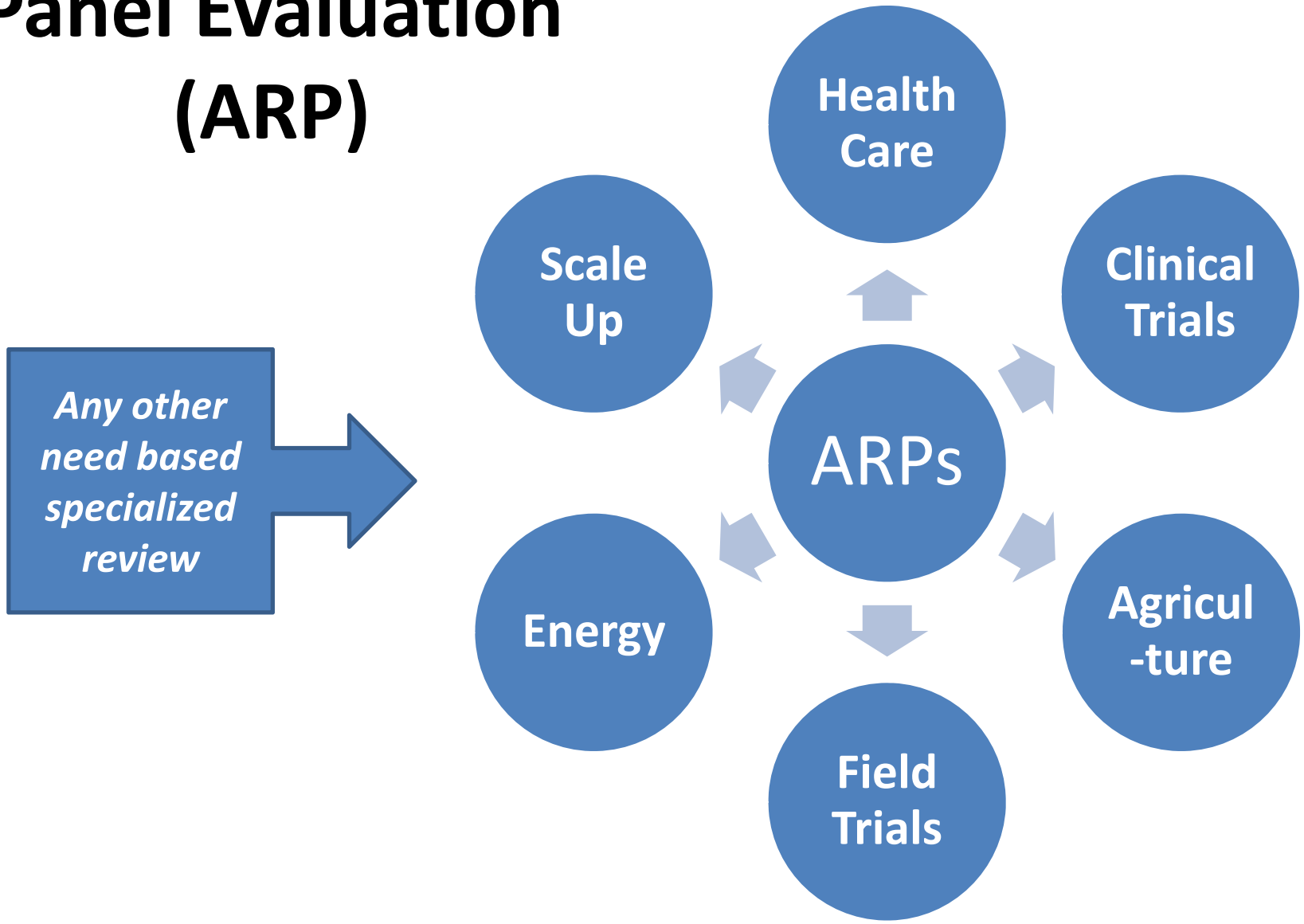
Submission of necessary documents is the key.

Area Review Panel Evaluation (ARP)

- *ARP evaluation is completely online*
- *First level of filtering based on scientific merit*



In house Expertise

- **Technical:**
  - A pool of scientists who prepare in-depth analysis reports/ SWOT Analysis for proposals

- **IP Issues:**
  - BIRAP-BCIL IP cell examines each and every proposal to identify the potential hiccups in the path of research/ commercialization

Due care of regulatory issues is taken and no project is sanctioned till regulatory requirements are met with

Technical Screening Committee (TSC)

TSC: Decision Making Body

TSC Review covers the following:

- Final decision on ARP Evaluation
- Review of Presentation by shortlisted ones
- Consideration of site visit reports
- Review of clarifications (as and when required)

TSC comprises eminent scientists from academic institutes and universities across the country

Site Visit:
Critical due diligence of the facts and figures

Technical

- Team of subject specific experts in the area
- Examination of facilities, manpower, budget, timelines, expertise…….

Financial

- An audit of the financial status of the company by a Chartered Accountant
- Examination of the key aspects: Liquidity, Profitability, Debts, Assets……..

Apex Committee:
Constitution and Review

- Final approving authority which recommends processing of a proposal for sanction by the DBT
- High level expert committee chaired by the Secretary, DBT
- Comprises members from different Ministries
- Consideration of Proposals recommended by TSC after exhaustive review process

Sanction and related processing

- Acceptance of Offer
- Finance Approval

Sanction Order Issuance

- Necessary Resolutions to be passed by the Board
- Signing by all parties

Agree-ment Signing

- No Lien Account
- Collateral in favor of DBT

Release of Install-ment

Standard templates can be downloaded from BIRAP website

Schedule for Release of Installments

Milestone based:

- 1st — 30% (Signing of Agreement)
- 2nd — 20%
- 3rd — 20%
- 4th — 20%
- 5th — 10% (Completion of the Project)

Monitoring of Sanctioned Projects

PMC Constitution

Submission of MCR by the Company
(including detailed technical report, financial documents, Statement of Expenditure)

Examination of Technical Report by the PMC and Financial Docs (incl. Bank statements, invoices etc.) by Financial Experts

In case of delays, interim report is obtained from company, examined by the PMC and extension order issued

Clarifications on the queries raised by PMC Members/FE

Release of Installment due upon satisfactory report from the PMC and FE

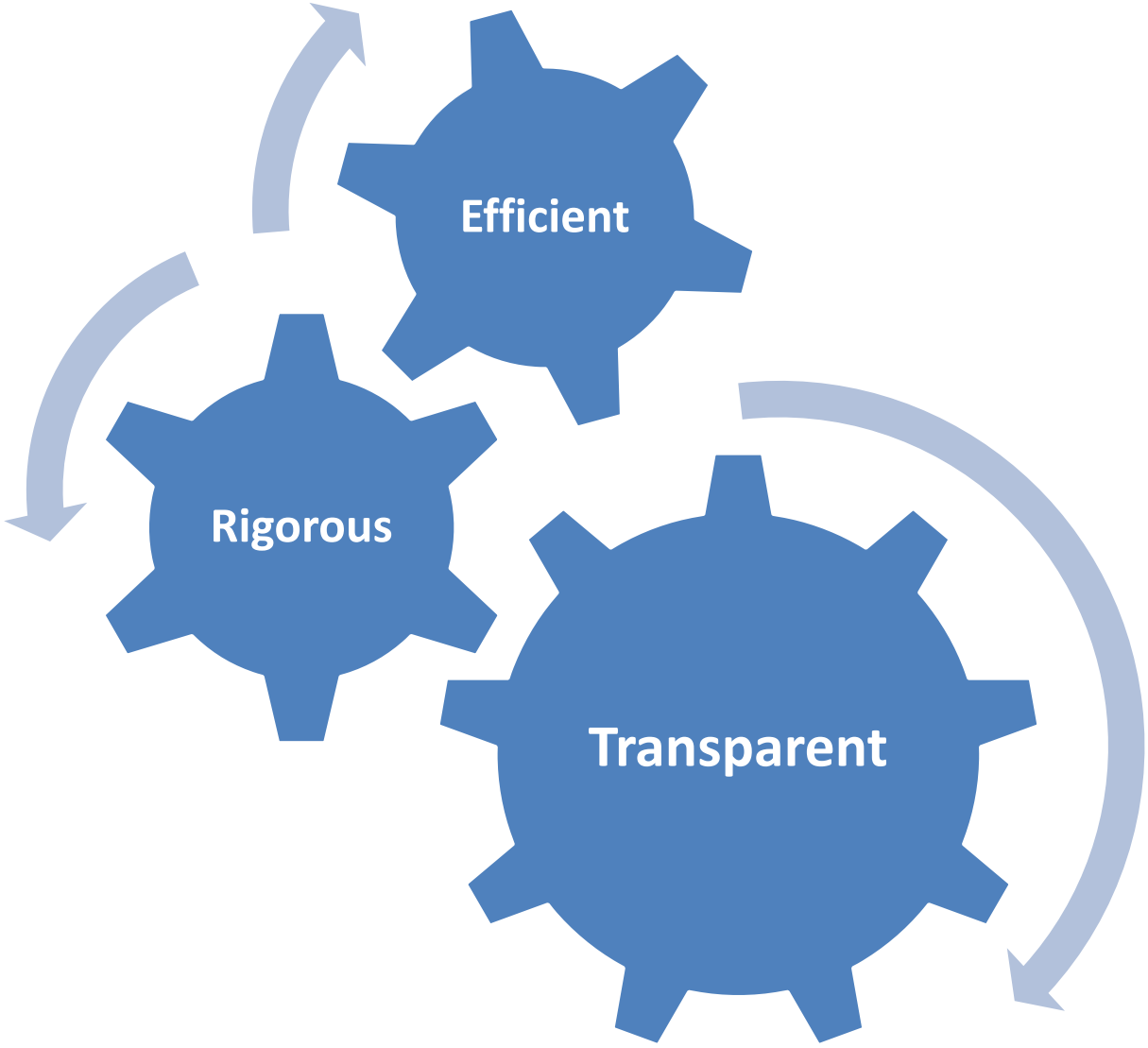
In case of short term projects, at least one site visit is ensured.

Site Visit prior to 3rd and Final Installment

Presentation before TSC sometime between 3rd and Final installment

PMC members are also assigned the role of mentors, wherever felt necessary

To Conclude: BIPP is



THANK YOU

QUERIES, IF ANY ?????

DBT/BIRAP : experience

Some simple rules to get the grant:

Have a strategy

Definite Objective

Measureable Deliverables

Avoid complexity in presentation

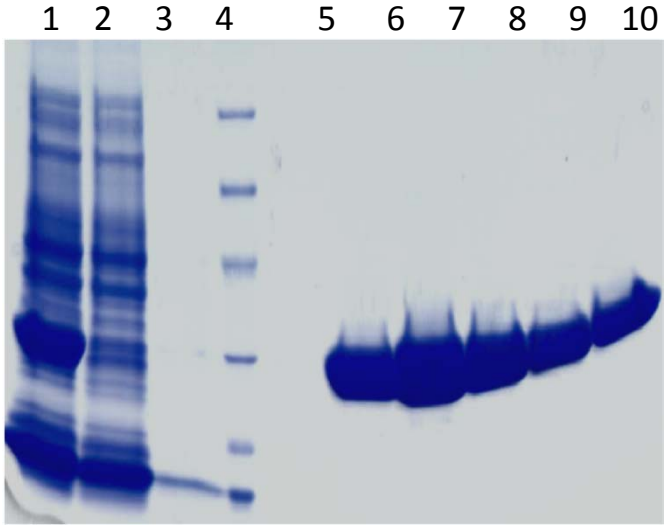
If process is complex give a proof that you are capable to handle it

Show that you have already started the project and at least 10-20 % is done.

Do not overstate the claims

KETOREDUCTASES - WHOLE CELL BIOTRANSFORMATION FOR CHIRAL CHEMISTRY

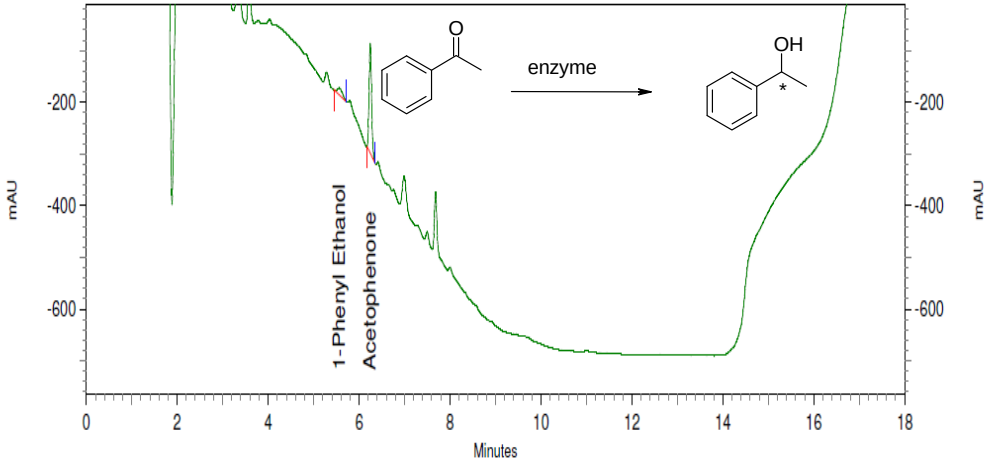
Purification of His-tagged FabG on Talon resin



1: Lysate
2: Flow through
3: Wash
4: Marker
5: Elution 1
6: Elution 2
7: Elution 3
8: Elution 4
9: Elution 5
10: Elution 6

Codon opitmized *fabG* was synthesized and cloned into pET21d
The protein was characterized by MS, purified and activity was measured

Preliminary results

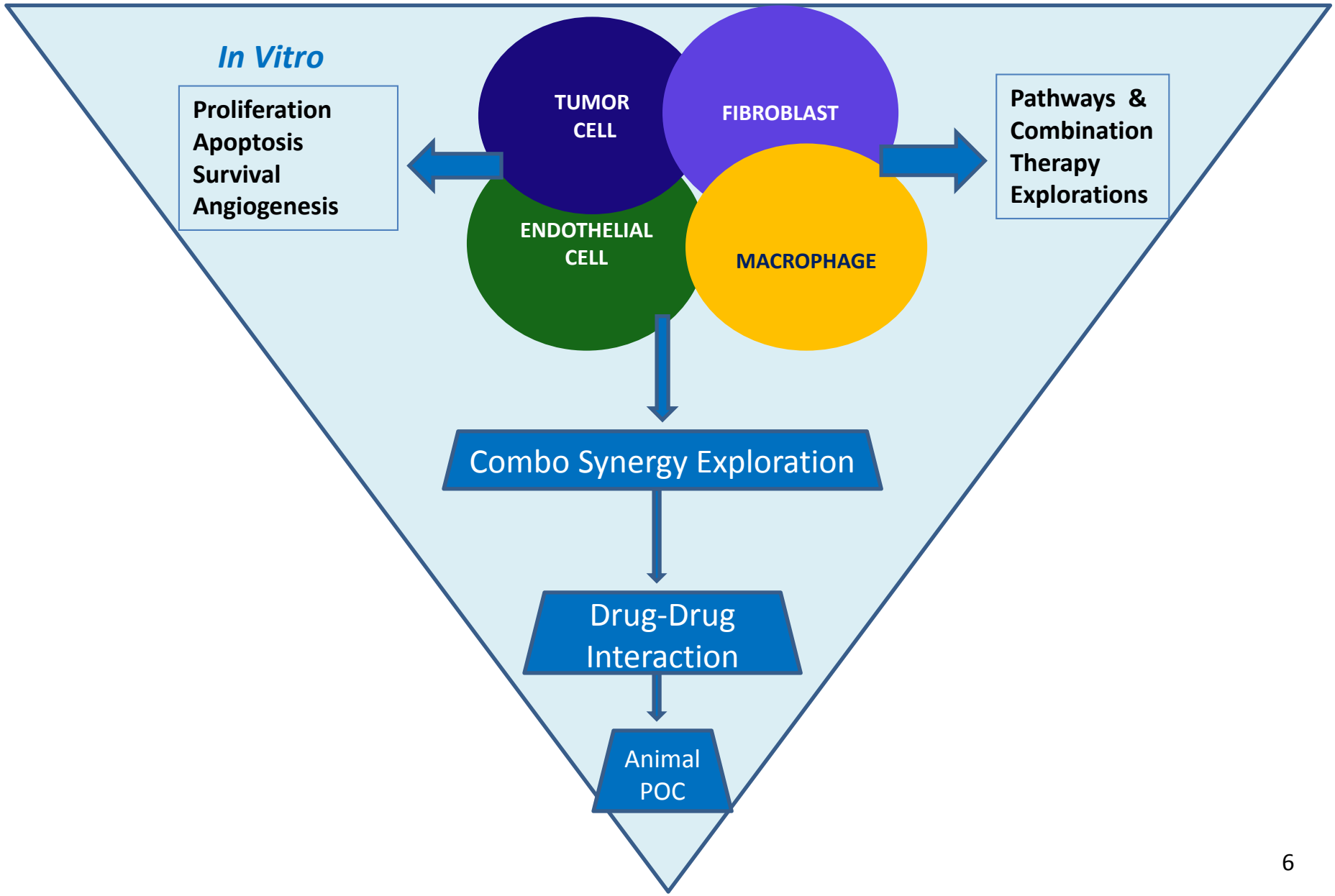


VWD: Signal A,
205 nm Results

Pk #	Ret. Time	Area	Area %	Name
1	5.567	1813624	11.754	-Phenyl Ethanol
2	6.247	13616145	88.246	Acetophenone
Totals		15429769	100.000	

Substrate	% conversion to chiral alcohol
Acetophenone	11%
4-chloroacetophenone	5%

In silico Driven Approach to Design NSCLC



Current Status:

- Completed stand alone Tumor Cell
  - Enhanced with pathways in NSCLC- EML-ALK4, c-KIT
- Completed other Cell types
  - Endothelial, Fibroblast, Macrophage
- Integration of Tumor Cell with Endothelial Cell is being tested
- MOA of 50 drugs have been characterized in the drug library
  - Includes drugs that have been implicated in Oncology and those that have never ever before been used in Oncology
- Scoping for combinational synergy evaluation SW begun

Strategy means nothing until it is executed.

How to write an effective grant proposal?

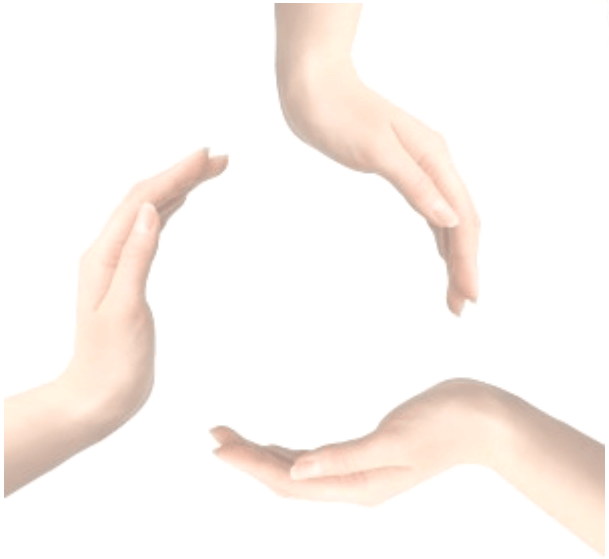
P. Balasubramanian
Centre for Plant Molecular Biology
Tamil Nadu Agricultural University
Coimbatore 641 003

Grantseeking is a 'multimillions-a-year' business

- Grantmakers give away money because of their concern about social problems, injustices, or inequities.
- Grantseekers that are successful have correctly perceived the sponsor's view of the world and incorporate that view in their grant proposal.

Major elements

- Component of innovation – be clear about it
- Novelty
- Comprehensive but realistic budget and its components
- Confidentiality

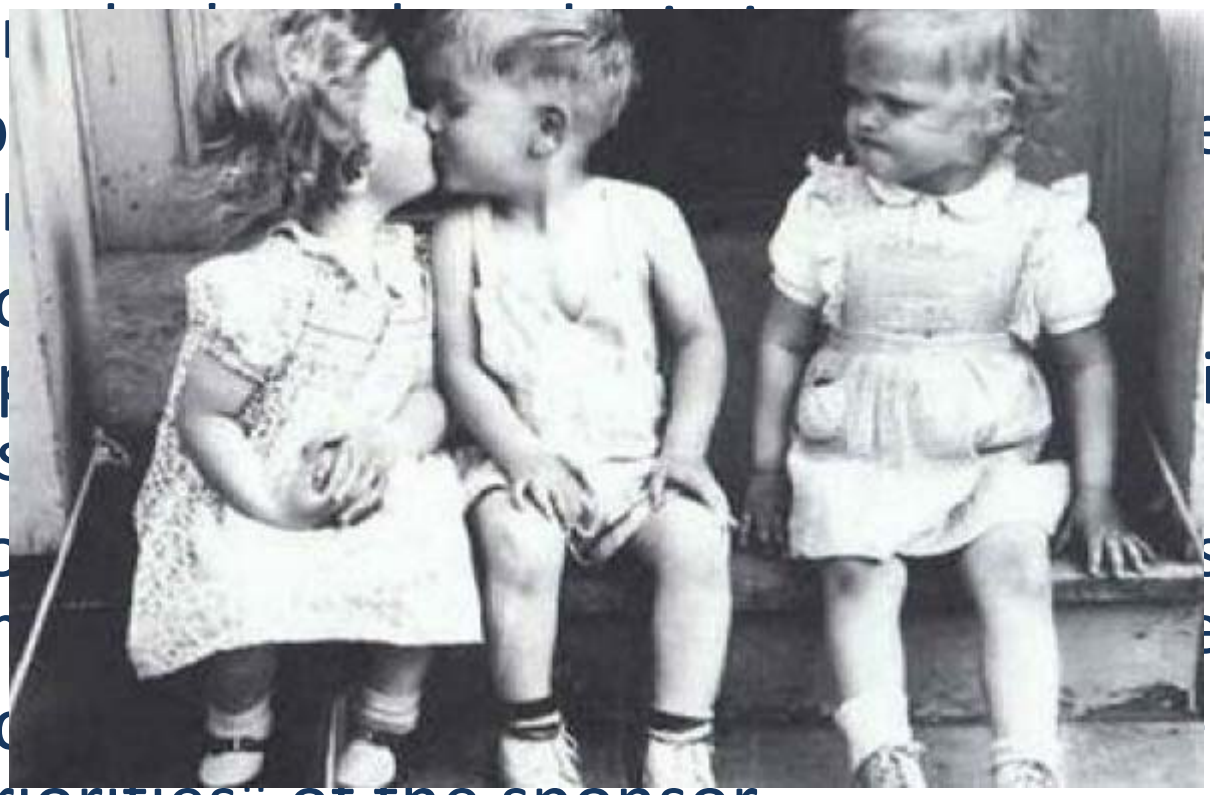


Precise elements in a successful proposal

- Level of innovation
- Novelty
- National/societal importance
- Level of Risk
- Potential for commercialization

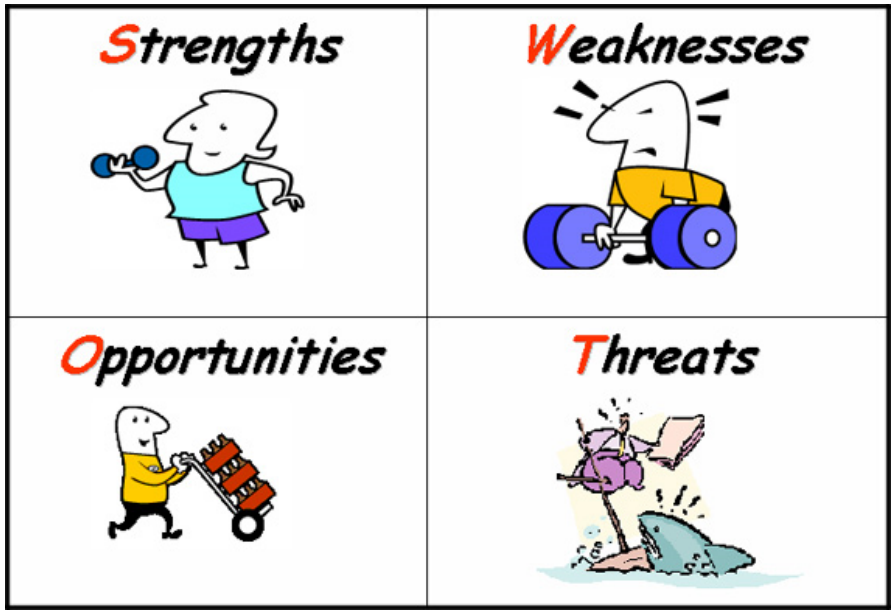
Possible causes of rejection of a grant proposal

- Dwelling on your own need for funding Vs the grantı
- Not p e grantı
  - Spc ir imp mis
  - Pro s the sar er.
  - Suc ct the "priorities" of the sponsor.



Before you write the proposal …….

- Is there a problem or need of significant magnitude that you propose to solve?
- Does your agency have the means and the imagination to solve the problem or meet the need?



The Plan of a Proposal

- Who is my audience?
- What do I want my audience to get from my proposal?
- How can I make sure my audience understands what I want them to know?
  - You must put yourself in the shoes of your audience.

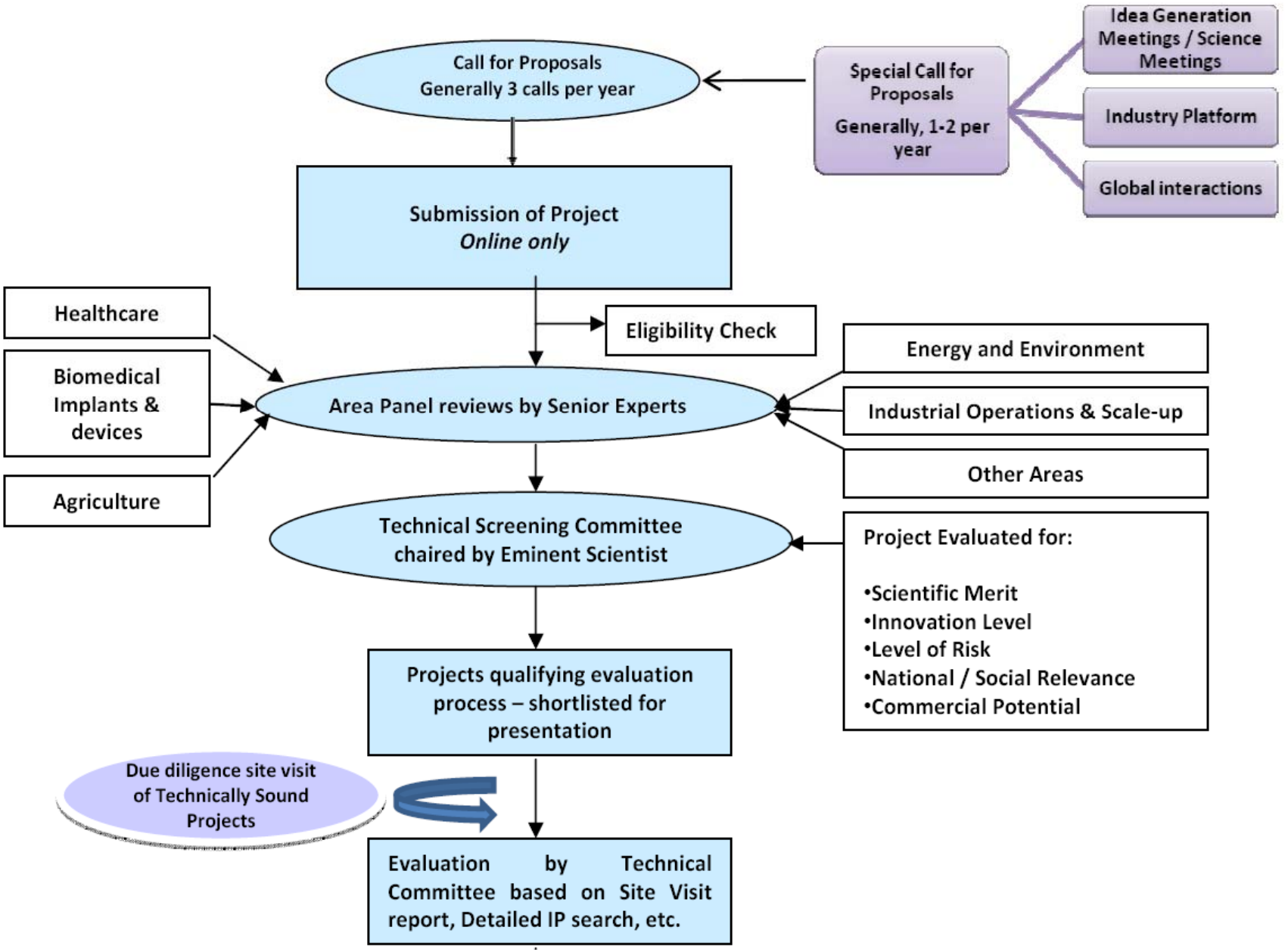
The Style of a Proposal

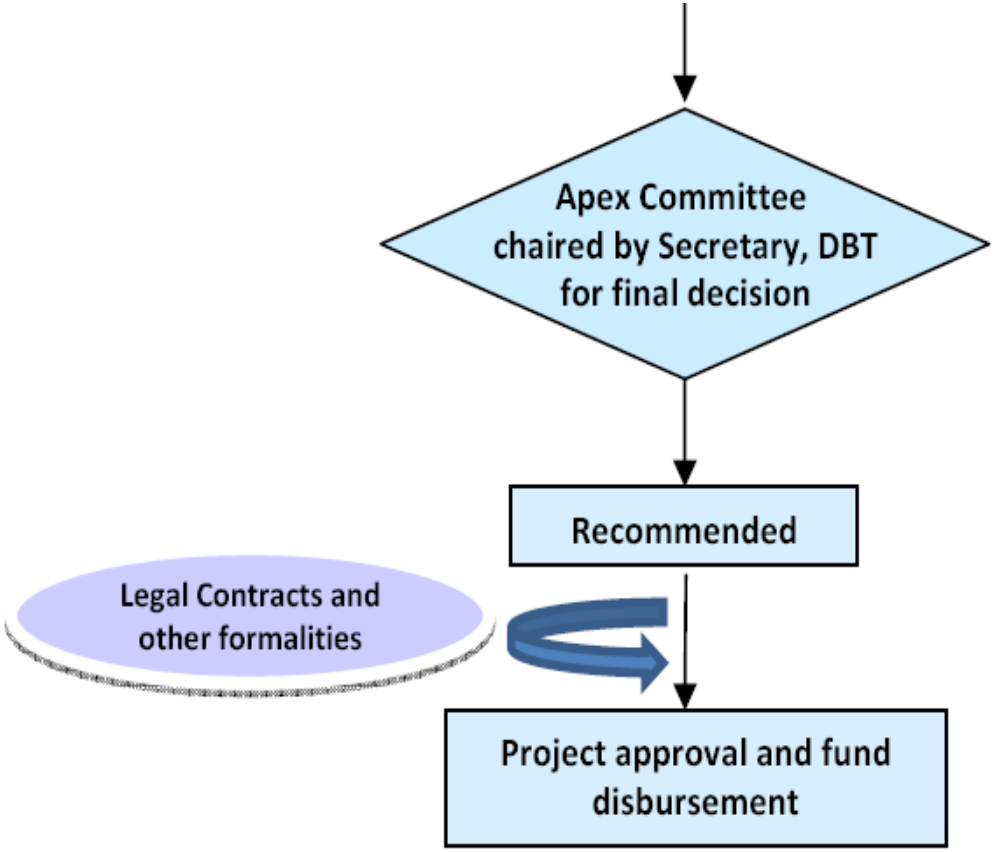
- The basic writing style of a proposal is the same for any type of technical writing. For proposals to be effective try to follow these tips:
  - State the purpose clearly at the beginning of the proposal.
  - State the background information the reader will need to understand your proposal.
  - Use language that everyone can understand.
  - Use short sentences that are clear and to the point.
  - Make sure that your ideas are not hidden between unnecessary words.
  - Make sure that the reader has all the important information needed for the final decision.

Common Mistakes in Proposal Writing

- Failure to provide the proper context to frame the research question.
- Failure to delimit the boundary conditions for your research.
- Failure to cite landmark studies.
- Failure to accurately present the theoretical and empirical contributions by other researchers.
- Failure to stay focused on the research question.
- Failure to develop a coherent and persuasive argument for the proposed research.
- Too much detail on minor issues, but not enough detail on major issues.
- Too much rambling — going "all over the map" without a clear sense of direction. (The best proposals move forward with ease and grace like a seamless river.)
- Too many citation lapses and incorrect references.
- Too long or too short.
- Sloppy writing.

BIPP – Operational Mechanism





Process of Evaluation / Decision Making takes 4-5 months. Decision is conveyed at each stage.

BIPP - Categories of Programmes

- **Category I – Areas with major social relevance but having uncertainty**
- **Category II – High risk discovery innovation research**
- **Category III – Evaluation and validation of already existing products of high national importance**
- **Category IV – Shared cost major facilities**

Broad Parameters for Evaluation

Category I&II

A.	**Significance / Scientific Merit**	/15
i	National importance/societal relevance of the problem being addressed by the present proposal	
ii	Contribution to advancement in the existing scientific knowledge	
iii	Level of advancement of technology	
B.	**Approach and Methodology**	/20
i	Is the conceptual framework, design, methodology, and analysis adequately developed, well-integrated, well-reasoned, and appropriate to the aims of the project?	
ii	Is the research plan, research objective and proposed scheduled clearly presented and realistic?	
iii	Does the applicant acknowledge potential problem areas and consider alternative strategies?	
iv	The proposal aims at: a. Discovery Linked Innovation b. Establishing proof-of-concept c. Validation of existing R&D hypothesis	
v	Level of Risk* * High scores are allotted for high risk projects	

C.	**Innovativeness**	/15
i	Level of innovation	
ii	Does the project generate novel concept, approach, methodology, tools, or technologies	
iii	Does the project challenge existing paradigms?	
iv	Does it address an innovative hypothesis or critical barrier to progress in the field?	
D.	**Intellectual Property**	/20
i	Relevance of the background IP for the proposed project	
ii	Possibility of generating foreground IP	
iii	Does the applicant have freedom to operate in the proposed area?	
iv	Does the applicant acknowledge potential restrictions towards freedom to operate?	

E. Commercial Potential/ Societal Relevance /10

i. Importance * of the unmet national need:

*Considerations include

- Relevance to human /animal needs
- Addresses issues of mortality /morbidity etc. where mortality ranks > morbidity.

ii. Level of Commercial potential

F. Investigators credentials /10

i. Is the work proposed appropriate to the experience level and training of the PI(s) and other researchers?

- No

ii. Do the PI (s) and investigative team bring complementary and integrated expertise to the project, if applicable?

G. Adequacy of Research Infrastructure /10

i. Are the research facilities available for the proposed work adequate

ii. Extent to which high end equipments proposed to be used are already existing in the company

iii. Extent of support available from other ongoing similar projects/scheme?

CASE STUDY OF An AGRICULTURE RELATED PROPOSAL- Category I and II

- To present the erroneous vs appropriate way of writing a proposal using a dummy proposal

- To individually deal with the specific elements of grant writing

- To discuss certain lacunae and approaches to address them

TITLE of PROPOSAL

- The project title should be short, concise, and preferably refer to a certain key project result or the leading project activity. Project titles that are too long or too general fail to give the reader an effective snapshot of what is inside.
- It should be explanatory and define the essence of the Project
- Example:

Multi technological interventions to develop various biotic stress tolerant vegetable hybrids for Indian & International markets" - Title is diffused

"RNAi , MAS and Transgenic approaches to develop insect-pest, diseases & viruses tolerant vegetable hybrids for Indian & International markets" – Title is more specific

It is clear from the title that specific molecular biology techniques are used for raising a strong vegetable product with multiple fold resistance against biotic stress.

Project Abstract

The project abstract should present a concise summary of the project. It should be no longer than a page and include:

- the need for the project and whom it will serve
- a brief description of the project
- its goals and objectives
- the amount of funding that is being sought
- the expected output and also the success indicators

The abstract should be the last section you write.

Preliminary work done

- Some scientific data should be added. Should have experiments which have be been done before to support the concept

In one proposal use of only single insect resistance gene was presented. It was not supported by literature or experimental proof .

Proposal lacked simple data like gene details, cloning vector, promoter which was used for over expression .

The company background Information consisted of relevant references, in good pier reviewed journals.

Strong experimental data existed for individual events like use of GL (ginger lectin) gene, RNAi-mediated resistance, use of inbred lines to tackle the problem and use of MAS. They were combined together to develop new vegetable hybrids with increased yield and quality

NOVELTY

➢ In Agri products novelty may be presented by newness of application of a pre-existing concept.

✗ Use of transgenic approach by incorporating a single gene of a pest resistance to raise a biotic stress tolerant vegetable.

Old strategy. The single gene strategy may not work as it may lead to breaking of resistance in the field .

✓ Combining traits for virus tolerance in vegetable by exploiting host and viral genomes. RNAi-mediated resistance to ToLCV and GBNV along with the naturally occurring host plant resistance for Fusarium, TMV, Veriticillium and nematodes (originating from rich vegetable gene pool) and; genetically engineered sucking pest tolerance is a novel strategy.

Novel strategy. This novel combination of traits & technologies would enhance productivity of vegetable significantly

Inventive Step

➢ Concept to tackle an unmet need was present. Efforts towards making it more plausible and of more practical value.

Incorporation of only single insect resistance gene into a crop would later lead to :

Breaking down of resistance of the hybrid when exposed to field conditions.

Incorporation of GL (ginger lectin) gene and RNAi-mediated resistance to various viruses into elite vegetable inbreds carrying MAS bred resistance to fungi and and nematodes is an inventive step.

Procedure would convert the existing hybrids to multiple insect & disease resistant versions of high yielding vegetable hybrids with significant saving of valuable time.

National Importance and Relevance

- The proposal should provide some justification of the product or even the idea behind it in terms of market value and national importance and unmeet need

Importance of Single gene trans genic product

India being an agricultural country would not require a product which may not provide a long field life.

Multiple stress Resistant product (biotic)

The development of virus tolerant, insect and disease resistant vegetable to increase productivity, help Indian farmers to increase their income through superior yield & lower pesticide costs , Will have positive environmental impact by eliminating use of pesticides & insecticides

Objective and Timelines

- They broadly define the scheme or work plan of the proposal in terms of experiments which will be the part of the proposal. Timelines (months) should not be over ambitious and give a realistic time period of completion of Task.
- Example:

Use of several molecular biology techniques for generation and analysis of insect pest resistant transgenics.

This is an oversimplifications of objective which should have been split into several distinct sub topics each defining a separate individual step towards a final goal. For eg :

a. MAS based pyramiding of multiple host plant resistant genes (0-12) months

b. Vector construction and genetic transformation of the vegetable with x,y,z biotic stress resistant genes. (6-24) months – shows //ll activity

c. Stacking of RNAi mediated resistance to a, b, c viruses (12-36) months

MILESTONES

- Milestones should be SMART

  Specific, Measurable, Achievable, Realistic, Timely

The milestones should be well defined and not diffused

Should not be made diffused by making tasks like Procurement of material, Staff appointment, Setting of lab space a part of the milestone.

Representative Milestones of the particular objective should define a quantiable part of that objective

a. The T2 and T3 generation seedlings will be analysed for genome anlysis and selected plants will be selfed

b. Vector construction and genetic transformation of the vegetable with x,y,z biotic stress resistant genes.

c. Trait evaluation of each gene contruct

Work Plan – Transgenic Development

- Generation of Transgenics: one gene vs. two genes
- Number of events: identification of the best event
- Level of phenotyping
- The crossing programme for gene stacking/pyramiding
- Bio-safety testing

Marker Assisted Breeding

- How many genes?
- All with validated markers?
- Crossing programme? Is it MABB?
- Foreground and background selection? Generation?
- Populations size? Cost?
- Integrating phenotyping with genotyping?

OTHER CRUCIAL PARAMETRES

BUDGET : Should not be over projected, nor under project. The strong site visit team makes a realistic analysis of the cost challenges

IP : The companies are encouraged to do their own FTO (freedom to operate search) as it would give them a fair idea of the competition in terms of technology and product

Technical Team : Should carefully explain the expertise of its In- house technical team. Their tasks should be well defined and correlated to the project

General Lacunae

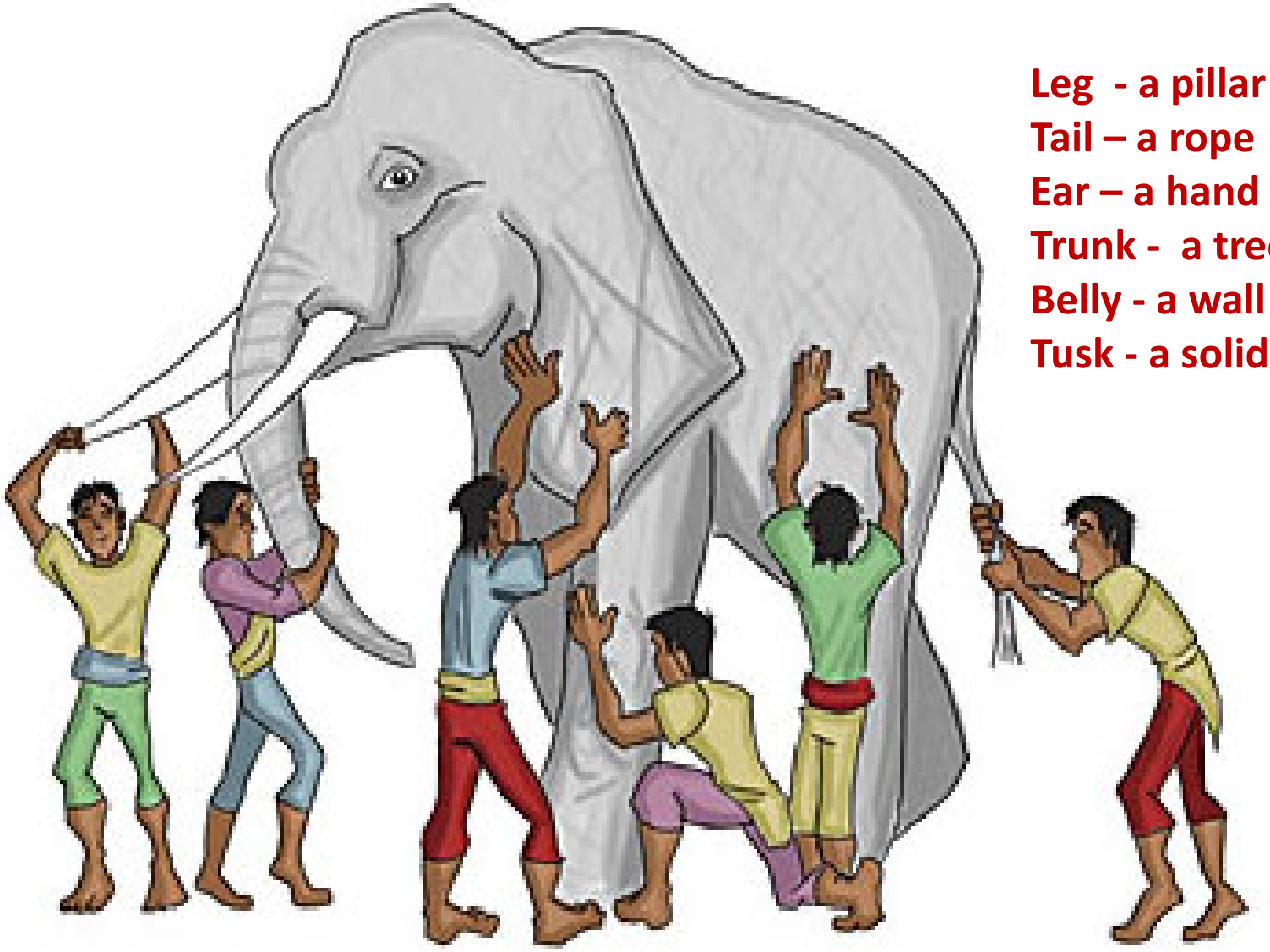
- In agriculture related projects, sometimes absolute innovation is not practical. The proposal should highlight its innovation in terms of application of a preexisting concept, technology or improved product quality

- Sometimes a good market research of the proposed product is entirely missing. The product should show its relevance in terms of filling up a major gap in the market.

- With the presence of only limited traits to be manipulated in terms of biotic and a biotic stress transgenic, care should be taken to establish a clear FTO

- It is extremely important to know the regulatory implications before planning a proposal of product destined for market release.

Project – Identifying an Elephant



Leg - a pillar
Tail – a rope
Ear – a hand fan
Trunk - a tree branch
Belly - a wall
Tusk - a solid pipe

Sources of Reference

- http://www.civicus.org/new/media/Writing%20a%20funding%20proposal.pdf
- http://nonprofit.about.com/od/foundationfundinggrants/tp/grantproposalhub.htm
- http://research.microsoft.com/en-us/um/people/simonpj/papers/Proposal.html
- http://www.cpcwnc.org/Toolbox/writinggrants.html
- http://www.einstein.yu.edu/ogs/Guide/Writing.htm
- http://facpub.stjohns.edu/~roigm/plagiarism/

BIRAC Effective Grant Writing Workshop: Kolkata, July 17, 2012

R. Mukhopadhyaya, Ph.D.
Formerly,
Principal Investigator: Virology,
ACTREC, Tata Memorial Centre,
Kharghar,
Navi Mumbai.

Cell *136, March 20, 2009*
Leading Edge Analysis

The Indian government is launching a series of new initiatives to boost public-private research partnerships and to jump start science-driven economic growth.

….initiatives include a 2 year $6.5 million pilot program called the Biotechnology Industry Research & Development Assistance Program (BIRAP), launched in September 2008. DBT set up BIRAP to manage its industry R&D programs and to provide strategic support including intellectual property management, technology transfer, regulatory advice, and clinical and field trial support (for agricultural and medical biotechnology).

After completion of the 2 year pilot study, BIRAP will become an independent not for-profit council called BIRAC that will manage 30% of the DBT budget set aside for public-private partnerships.

BIRAC promotes high risk, transformational technology/process development. No incremental development is supported under this program.

This scheme do not support pure basic research

Indicative priority areas for consideration

(A) Agriculture Technologies
(B) Public Health Technologies
(C) Energy /Environment

Some salient aspects of a grant proposal that a reviewer will focus

1. **What Does The Present Proposal Aim At?**

Establishing proof-of-concept , Discovery linked innovation, validation of existing R&D hypothesis? **What are the compelling reasons**

2. Is this Proposal Based on IP owned by The Company/Collaborator/Licensed From Abroad; competence of the company Possibility of generating foreground IP, Freedom To Operate-a solid convincing team expertise and infrastructure

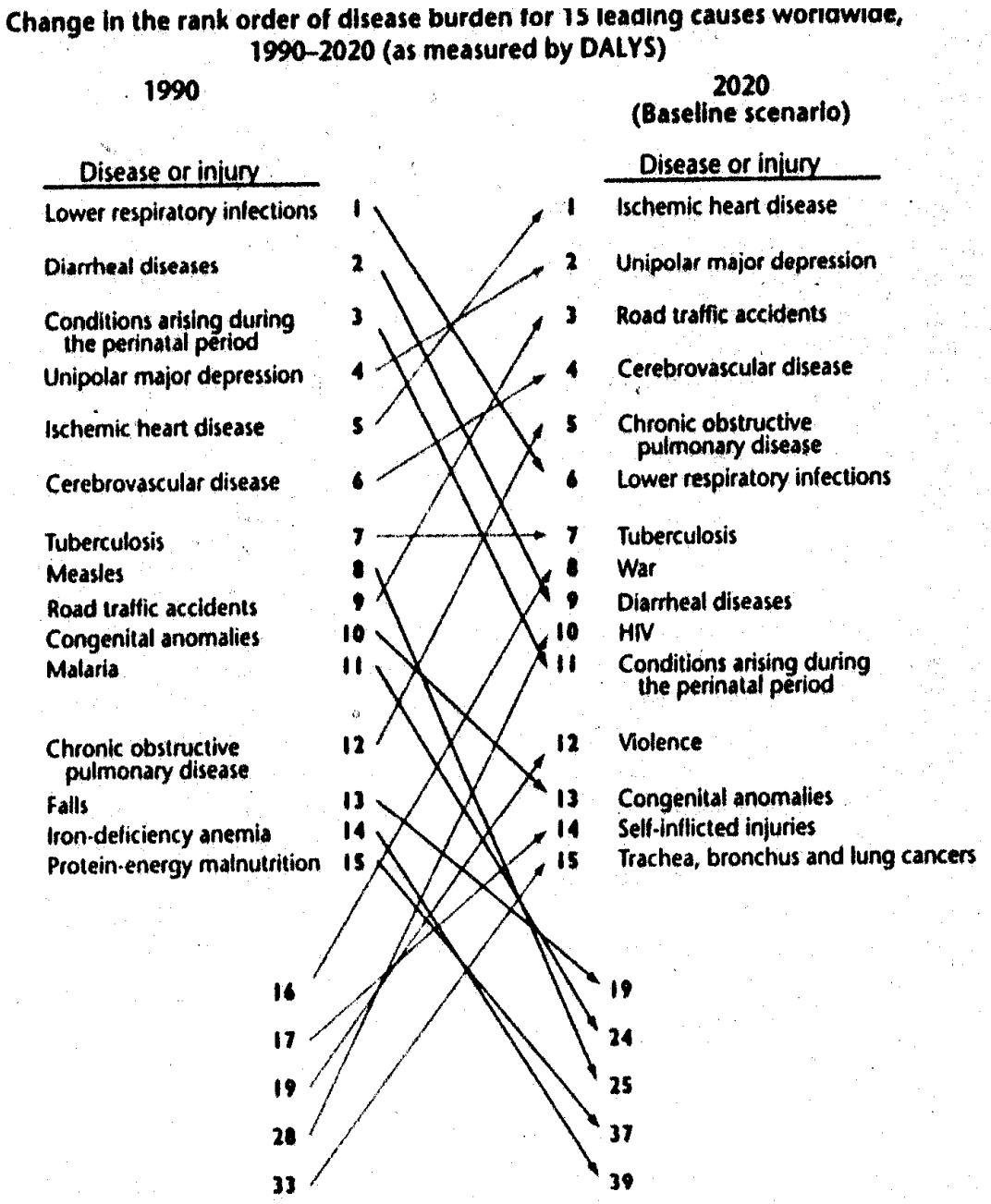
3. Anticipated Outcome/Deliverables The outputs of a project are what you expect to be in place at the conclusion of the project.

Potential for commercialization in the areas of human and animal health, diagnostics, bio-markers, immunobiologicals/vaccines and various industrial products like antibiotics, industrial enzymes, Vitamins etc.

Novel devices for simpler diagnosis-better if operable under technologically challenged semi-urban/rural set up, multiple disease diagnosis combo system, desired bio-product separation

While we may capitalize on our strength in bio generics, innovation is needed for development of new products and processes.

There is a need to create a critical mass of small/medium business units that have the potential to drive the innovation and grow further.



Nat Med (1998) 4:1241-43.

Indian scenario

Problems

TB-drug resistant
Malaria
Dengue
Chikungunya
Transzoonotic influenza: H5N1 from poultry & H1N1 from swine
Diabetes-Juvenile
Heart diseases-sedentary life style/ food habit & mental tension associated
Diarrheal diseases
Respiratory disorders-COPD
Cancer

Scope

Simple point of care diagnostic systems/ devices for health parameter monitoring;
Cost effective combo diagnostic for multi infections;
Non-invasive diagnostics;
Biomarkers for prognosis/disease burden monitoring
Affordable drugs for infectious diseases;
Vaccine candidates.

Broad Outline on Developing a Proposal

- Start with an original idea not patented with Freedom To Operate

- Carry out proper literature search to strengthen originality of your idea-read between the lines of prior art literature in details

- Provide specific technical expertise of members of the team

- Ensure some preliminary work is done on this idea, with robust data

- Devise a crisp plan with clarity along with other members of the company or collaborators-show job resonsibilities clearly

- Set objectives and milestones that are achievable

- Work on a realistic & appropriate budget for the proposal

What are the aspects to take care for a biotech process proposal

An unique approach has First-mover advantage

An indigenous development of existing item(s) that do not interfere with IP has to be priced lower enough to take over market with dominant foreign players

The approach even if unique has to be easily adaptable and should be of high/significant demand enough to be of commercial interest

Make sure that the end point is of distinct values of robust nature-no ambiguity

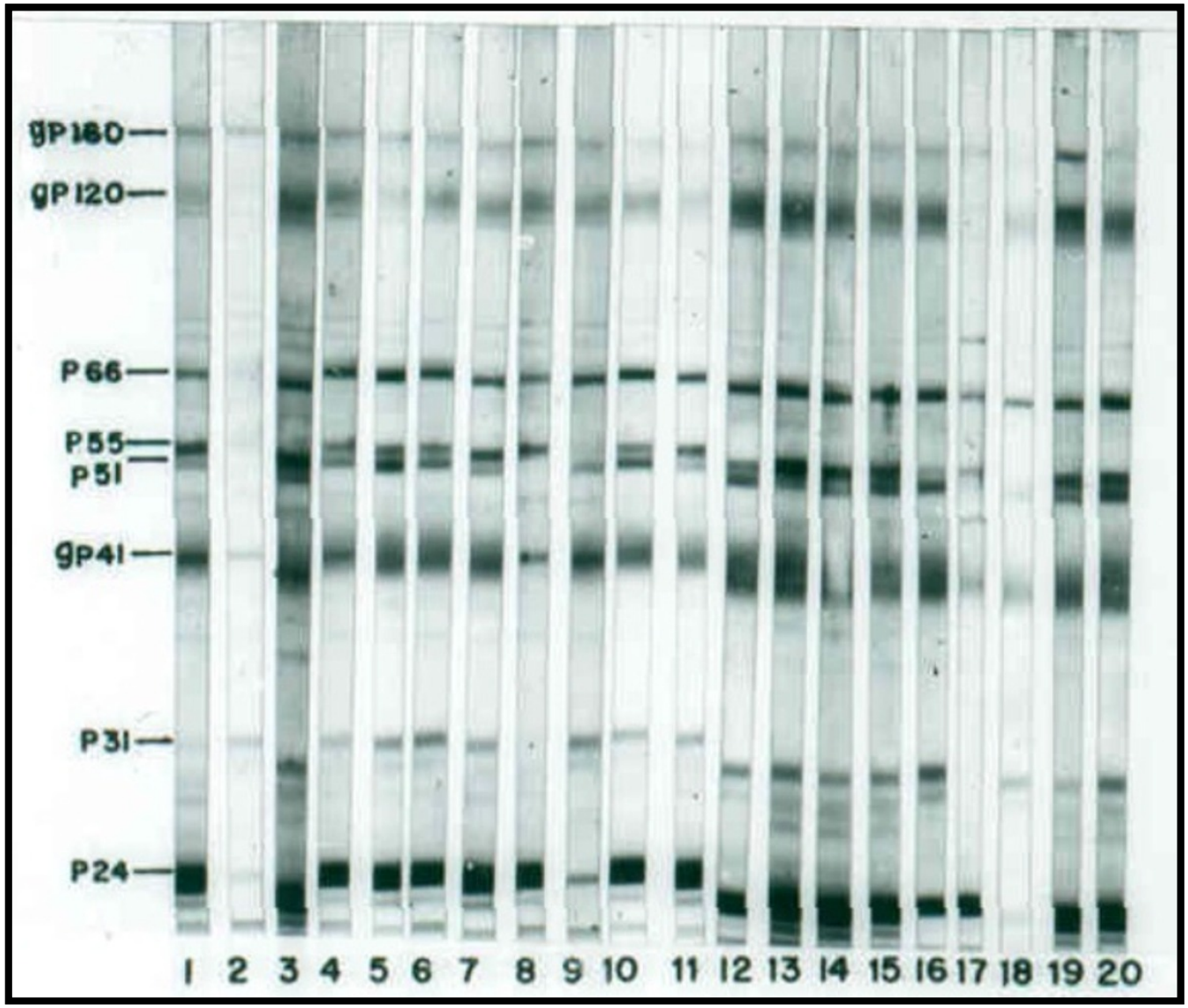
Any system, a device or an assay or a drug, has to be independently validated,

If the development in concern is from a research set up it needs a total reshaping for commercial viability-that awareness and needful steps are to be expressed explicitly in the plan of work, often these take long unforeseen time.

An example from experience: development of an indigenous HIV serodiagnostic Western Blot Using Indian HIV isolate

Licensing a research lab finding to a commercial set up-a case study

HIV-1 WB Profiles



Laboratory to kit production - unperceived problems.

- Manpower training
- Manpower retaining
- Apprehensions to handle HIV culture
- Information on long-term reagent stabilization
- Transportation of biological reagents
- Component economics

Licencee: J Mitra & Co. Ltd., Okhla, New Delhi

Translating a research lab process/product to a commercially acceptable format has several hurdles unperceived by the research lab personnel-be aware that such concerns are addressed specifically.

Failure of promises in biotech-an example

Another blow for inhaled protein therapeutics

Nature reviews | **drug discovery, volume 7 | March 2008**

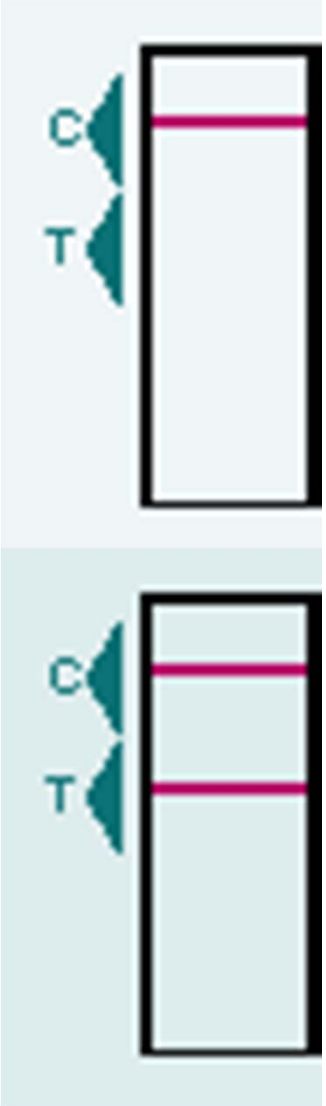
Novo Nordisk discontinued the development of its fast-acting inhaled insulin product AERx iDMS, which was in Phase III development. Just 3 months before, Pfizer withdrew Exubera, the first approved inhaled human insulin powder and lung delivery device.

"The instrument was bulky and not easy to use. ……., the patient had to go in for periodical lung function tests." Those inconveniences negated its big advantage: reducing the burden of injections.

Efforts are on for buccal delivery with mist inhaler, reagents such as calcitonin, morphine, heparin

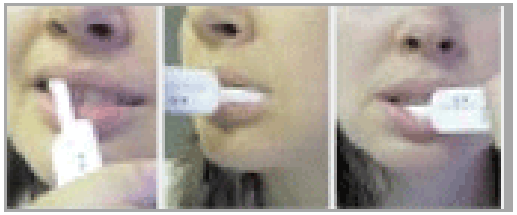
Issues for acceptability: Reproducibility, cost, ease of use over existing systems-these aspects should be taken in concern.

Example: Original Idea-Innovation-commercial application



Orasure is a non-invasive, quick, accurate way to test for HIV-1 antibodies without blood, needles.

Non-reactive result
Only control area show line
No line in test area



Reactive result

Control & test lines present; may not be of similar intensities

Oral mucosal transudate has high concentrations of IgG; saliva has practically none. Oral mucosal transudate comes from the tissues of the cheek and gum; saliva comes from the salivary glands.

Even a simple innovation can be highlighted and can become the stronghold of an application

PROPOSAL SUMMARY

Essence Of The Proposal Highlighting The Following

Novelty Does the project generate novel concept? From the existing scientific knowledge / inventions develop a product What is new in your project?

Inventive Step Is it planned to develop a new approach / process to exploit the existing scientific knowledge?

Scope Of Industrial Application What is the scope for industrial development?

National Importance/ Social Relevance Importance of the unmet national need; Relevance to humans / animal needs / Addresses issues of mortality / morbidity etc.; will there be economic benefits to the society?

Market Potential Demand supply gap / Edge over competitors / Cost effectiveness / Improved specifications

Risk Factors What are the potential risks/bottlenecks – both scientific and commercial, and alternative strategies/approaches in case of roadblocks

An ideal grant proposal profile

A novel method of producing high level of EPO in mammalian cells using virally transduced EPO transgene and knock down of cellular elastase.

Significance & Scientific merit: Novelity of the approach: virally transduced cell line as opposed to transiently transfected and selected cell line-advantages over the existing system; production level achieved is best so far.

Commercial Potential/Societal Relevance The demand of EPO is very high globally; more than 10 companies manufacturing EPO in India. EPO is an accepted therapeutic agent for management of anemia due to chronic renal failure and several other underlying causes; reasons of expected lower production cost.

Innovativeness: Viral transduction method, it eliminates antibiotic selection of clone for ever, the cell line is further metabolically engineered by viral transduction mediated knock down of elastase, which otherwise will reduce EPO production.

Approach & methodology: Details of obtaining/amplifying and cloning the gene, sequencing, sub-cloning in viral vector, transduction in desired mammalian cells, expression of the protein and characterization with immunoblotting, metabolic engineering of the cell line, limiting dilution to obtain the highest producer cell clone, adaptation of the high yield clone in SFM, purification of the EPO, quantification at per cell per day basis, comparison with reported yield so far at lab scale level, in vitro bioassay, in vivo bioassay following approved method. Pit falls-back up clone preservation.

IPR status: Patent filed; priority date if available

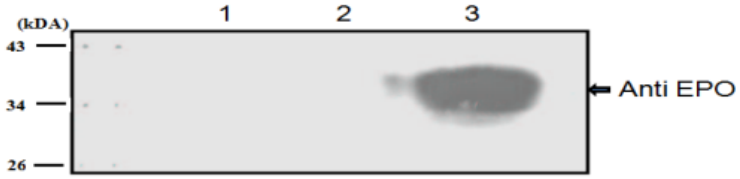
Company manpower: Scientists with Mol Biol/Protein Chem/down stream processing background, technicians with long term expertise in fermentation and down stream processing/ protein purification; earlier product development track record/contract research experience if any in related field.

Company infrastructure: Existing facility component listing, small scale fermentation infrastructure, if available; infrastructure for ongoing work that can be used for proposed project.

Budgeting: Consumables and infrastructure for up-scaling production with better media formulation and arrangements for improved cell metabolism to obtain higher yield; manpower hiring-loan amount requirement from BIRAC and matching contribution from company with request for a grant component.

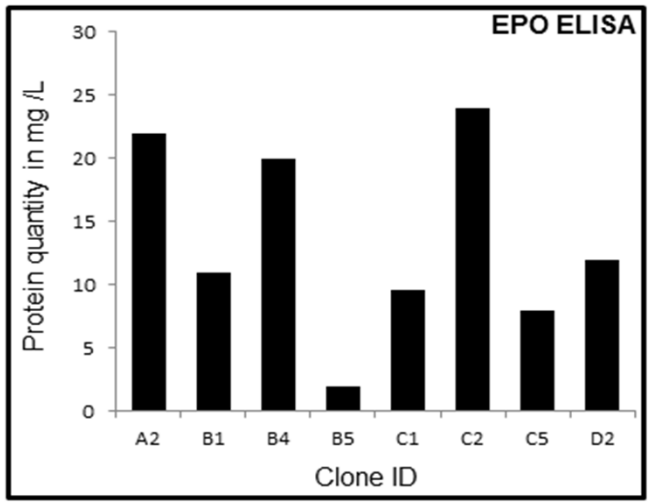
Deduced AA sequence of your clone

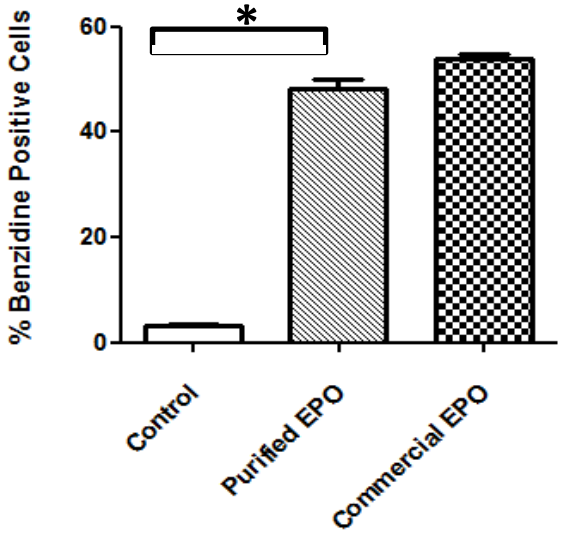
M G V H E C P A W L W L L L S L L S L P L G L P V L G A P P R L I C D S R V L E R Y L L E A K E A
E N I T T G C A E H C S L N E N I T V P D T K V N F Y A W K R **M** E V G Q Q A V E V W Q G L A L L
S E A V L R G Q A L L V N S S Q P W E P L Q L H V D K A V S G L R S L T T L L R A L G A Q K E A I
S P P D A A S A A P L R T I T A D T F R K L F R V Y S N F L R G K L K L Y T G E A C R T G D R **Stop**



Immunoreactive rhEPO detected in media of transfected HEK-293 cells.

Lane 1: complete medium; lane 2: untransfected HEK-293 culture supernatant; lane 3: Culture supernatant from cells transfected with plasmid encoding hEPO.





NOVELTY (Prior art search report to be enclosed)

The process provides simplification of culture monitoring and source stability

- ✓ The **novelty of the project** is to produce very high level EPO using a cell line with viral vector mediated EPO gene integration and metabolic engineering.

The process indicates further scope of production improvements by subsequent viral vector mediated metabolic engineering

- ✓ The **novel part of technology** is to use the vector mediated gene manipulation towards higher EPO production

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Should clearly state how the core content of the proposal can address the existing gap

Approach & methodology

“SHARP“& “QUANTIFIABLE”

- ✖ Design
- ✖ Feasibility
- ✖ Optimization
- ✖ Validation

- ✓ Upscaling with simultaneous betterment of metabolic conditions to achieve low volume high density cell culture with increasing EPO yield
- ✓ Batch to batch consistency in EPO yield with sustained bioactivity.

Clearly state the strategy with probable outputs

PRELIMINARY WORK DONE

(BACKGROUND INFORMATION)

The company has submitted lab scale data of EPO production showing the production level not reported so far. Bioassay of the product shows its appropriate bioactivity.

- Detailed preliminary background data showing working hypothesis should be provided.
- Even for discovery projects some scientific basis or some experimental data should be provided
- Collaborator's and Company's role in the proposal should be clearly stated
- Wherever possible, proof of concept data in the form of tables, pictures and graphs should be submitted

MILESTONES WITH TIME LINES

MILESTONES – “SMART”, “ACHIEVABLE”, “REALISTIC”

- Development of prototype assays
- Pilot lot manufacturing
- Submission Of Report

ESTIMATED TIME PERIOD SHOULD BE RELEVANT TO MILESTONE

Should be monitorable, time bound and specific

BUDGET supported with proper quotes

Equipment: should be as per the need of the proposal

- High end equipment specific to the proposal

Manpower: salaries should be as per Govt. standards

Consumables: should be asked only for the proposed work

Outsourcing: should be minimized to extent possible

Travel and contingency: should be properly justified

Should not be highly inflated or underestimated

Offer a moderate, realistic budget within which you can deliver the promised outputs in the promised time, and thereby contribute to some stated desirable impact.

Common lacunae in grant applications

- Lack of originality/ Innovation or Uniqueness
- Unconvincing case of commercial potential / societal impact
- Poorly written with vague descriptions
- Insufficient technical details & preliminary data
- Lack of competent manpower overall
- Unrealistic timelines or objectives
- Unconvincing infrastructure
- Unclear about potential pitfalls or risks or solutions
- Unfamiliar with relevant published data / IP restrictions
- Noncompliance with regulatory requirements

What should be taken care while drafting the proposal

Significance & Scientific merit: Level of advancement is sought

Innovativeness

Commercial Potential / Societal Relevance with pertinent background information/statistics/an in depth market survey/feedback from clinicians or health care workers

Approach & methodology: Clarity of methods with reasonable amount of details (with key references), awareness about potential problems & alternative strategies for bypassing those pitfalls.

Investigators & team credentials: **Manpower quality is the most important denominator for any success** write up should reflect through knowledge of the team.

Adequacy of Research Infrastructure; IPR aspects; Correct financial disclosure

Budget

A good grant application will have no redundancy, good logical approach to the proposal with a crisp methodology, robust preliminary data backed up by a very competent team with required minimal infrastructure and good business ethics.