



सत्यमेव जयते

GOVERNMENT OF INDIA
MINISTRY OF SCIENCE AND TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY
BIOTECHNOLOGY INDUSTRY RESEARCH ASSISTANCE PROGRAM



Organized workshops on

HOW TO WRITE AN EFFECTIVE GRANT PROPOSAL
SECOND SERIES-2011

in association with



ASSOCIATION OF BIOTECHNOLOGY LED ENTERPRISES

BIOTECH CONSORTIUM INDIA LIMITED

Managed by



SATHGURU MANAGEMENT CONSULTANTS PVT LTD

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BANGALORE



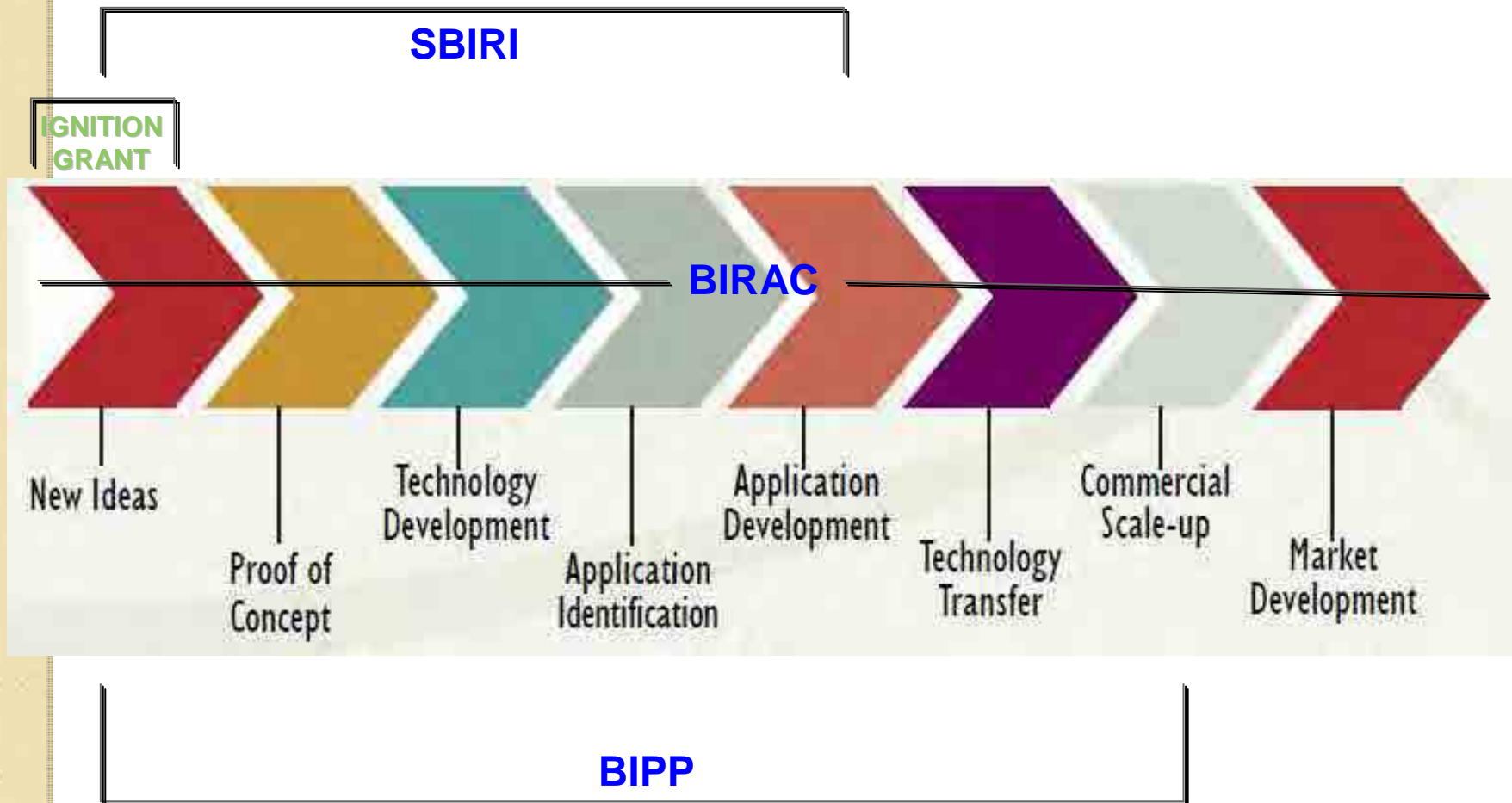
BIPP: An Overview & Key Elements of An Effective Grant

**Dr. Purnima Sharma
Managing Director
Biotech Consortium India Limited
New Delhi**

Innovation Funding

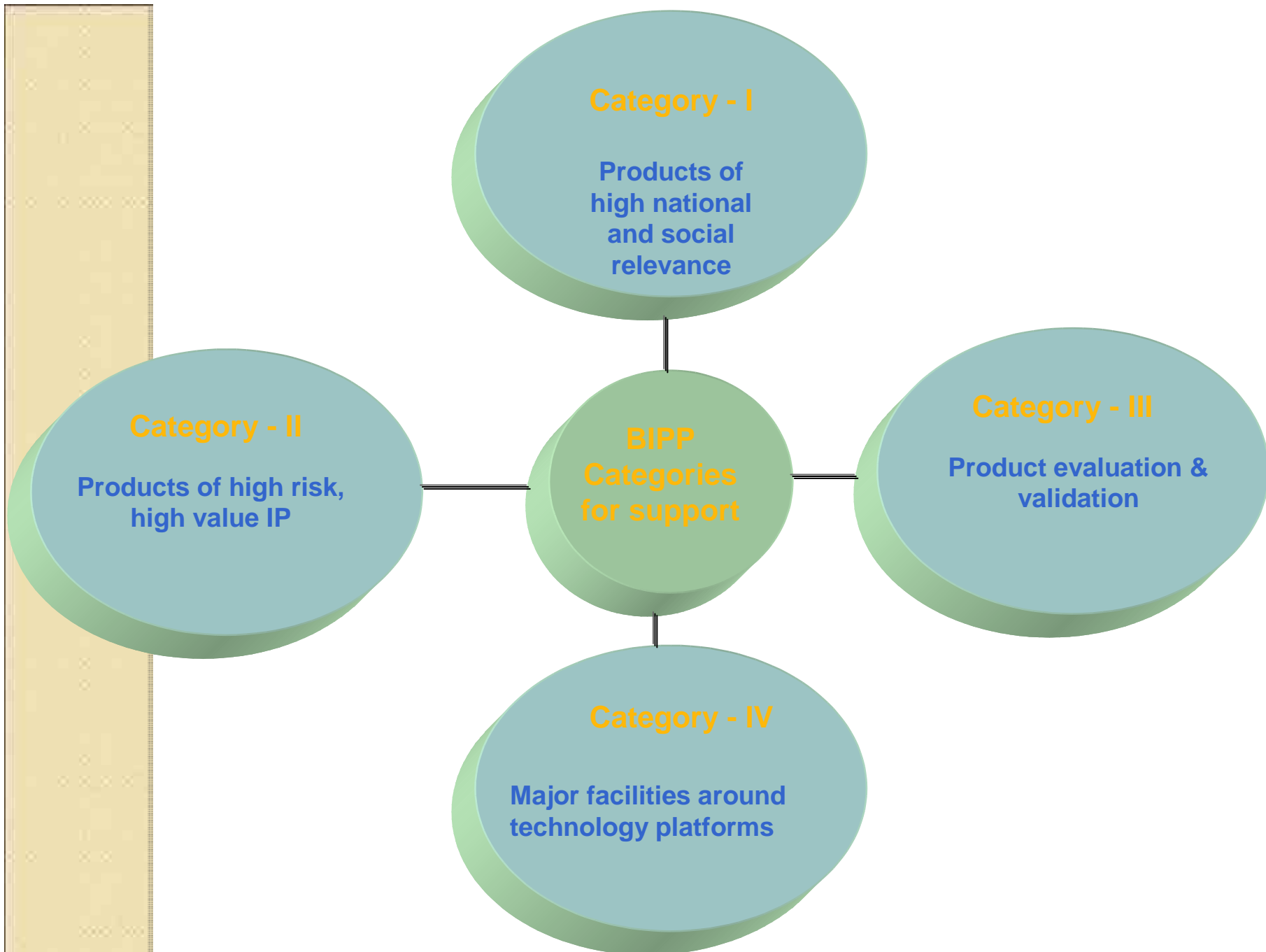
- Small Business Innovation Research Initiative
- Biotechnology Industry Partnership Programme
- **Ignition Grant**

Support across value chain



BIPP: Key Features

- For large, medium and small scale industry.
- Support for discovery, innovation or technology to products.
- An Advanced Technology Scheme to make India globally competitive.
- Major rather than incremental innovation preferred.
- Varying models of grants, loans or grant / loan available.



More than 500 projects received so far and approx. 50 Agreements executed

Guidelines

- **IP rights belong to industry**
- **Varying models of grants, loans or grant / loan**
- **Extent of support ranges between 30-50%**
- **Loan**
 - upto Rs. 10.00 crore – 2% interest;
 - above Rs. 10.00 crore – 3 % interest
- **Royalty**
 - 5% of net sales for 5 years or
 - twice the amount of grant

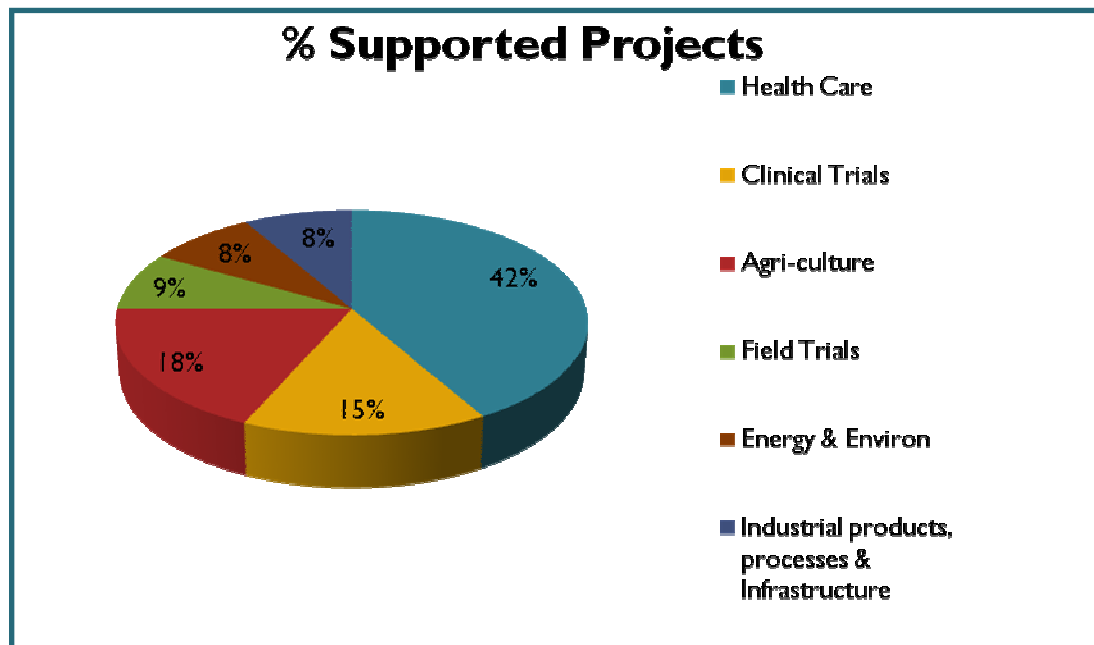
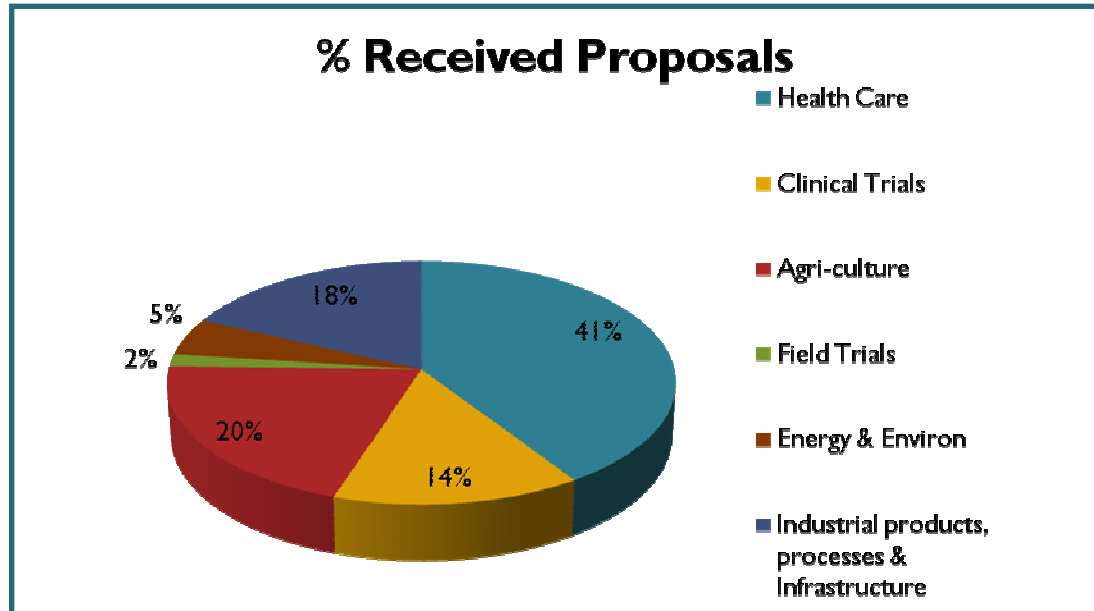
Broad Parameters For Evaluation

- Significance / Scientific Merit
- Approach and Methodology
- Innovativeness
- Intellectual Property
- Commercial Potential/ Societal Relevance
- Investigators credentials
- Adequacy of Research Infrastructure/ Environment

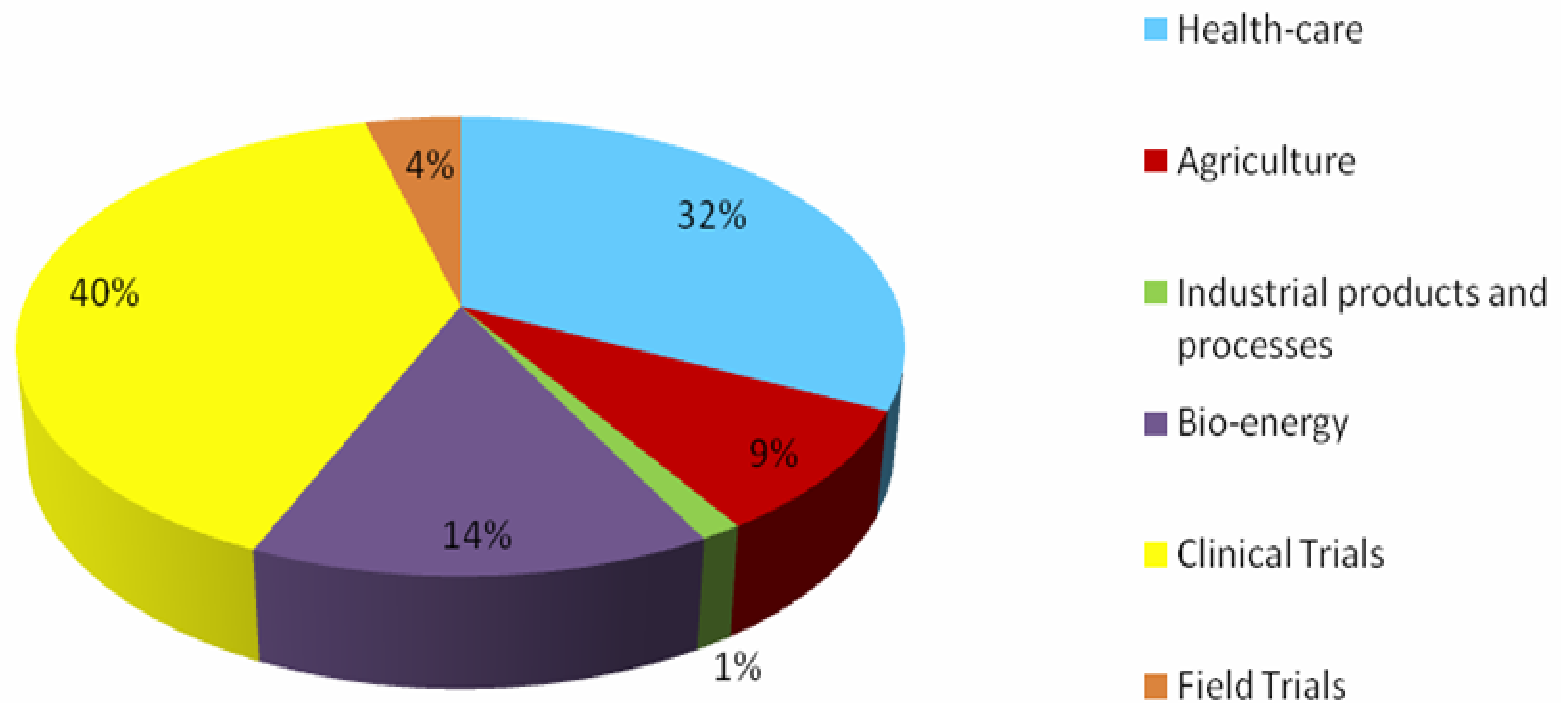
Biotechnology Industry Partnership Programme (BIPP)

- **Scheme Launched: November 2008**
- **First Call Launched: December 2008**
- **Total Rounds of Proposals processed: 14**
 - *7 regular and 7 special calls*
- **Process completely automated: 6th Batch onwards (Feb 2010)**
- **Total Proposals Received: 450**
- **Approved Projects: 60**
- **Agreements Executed: 60**
- **Beneficiary Companies: 51**

Area wise distribution of Received & Supported Proposals



Area wise distribution of BIPP Projects' funds



Biotechnology Industry Partnership Program (BIPP) Projects Supported - An insight :

- **Development**

- HPV vaccine
- H1N1 vaccine
- Porcine Pulmonary Xenograft as a Conduit in Cardiovascular Surgery
- Point of Care - Handheld PCR for infectious disease
- Biotic and Abiotic stress resistant Rice, Cotton, Onion, Brinjal
- Self glucogenic Pearl Millet for Bio-ethanol products
- A process for Enhanced Ethanol Yield from Molasses Fermentation
- Biological Hydrogen and Butanol Production



- Phase – II and Phase – III trials of Novel Molecules
 - Diabetes associated heart failure and cardiovascular (CV) risk factors defined by Metabolic Syndrome (MS).
 - Oral insulin for type 2 diabetes
 - Rota virus Candidate vaccine
 - Inactivated JE vaccine

- Field Trial of
 - Maize expressing synthetic cry genes genetically
 - Genetically engineered *Brassica* for heterosis breeding and yield improvement.

- Pilot Plant and Infrastructure
 - 10 ton Lignocellulosic biomass processing plant to produce about 3000 Litre ethanol
 - cGMP compliant Bioprocess Facility for large – scale production of Microbial antigens and Monoclonal antibodies
 - Facility for high end structural and functional characterization of protein therapeutics and peptides



Writing a Proposal

Writing a Proposal is like Winning a Game



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



7/14/2011

Developing a Proposal : An Overview

- ✓ Have an original idea/product/process not published or patented with Freedom To Operate
- ✓ Ensure some preliminary work is done regarding this Idea
- ✓ If required find expert academic partner(s)
- ✓ Devise a plan with clarity who will do what
- ✓ Decide the IP ownership and benefit sharing
- ✓ Set objectives and milestones that are achievable
- ✓ Decide a realistic & appropriate budget for the proposal
- ✓ Ensure adequate infrastructure to execute the same

7/14/2011

The Title

- The Title is Important
- It should convey what the project is about
- It facilitates in assigning review groups

Technical Details

- ✓ Rationale
- ✓ Significance of the Proposal
- ✓ Intellectual Property Status

Intellectual Property

- ✓ Background IP
(*Information needed to implement the project or needed for using the new generated IP in project*)
- ✓ Possibility of generating foreground IP
- ✓ Freedom To Operate
- ✓ Potential restrictions in FTO
- ✓ Strategies to address restrictions or risks

Commercial / Societal Relevance

Importance of the unmet national need

- ✓ Relevance to humans / animal needs
- ✓ Addresses issues of mortality / morbidity etc

Commercial potential

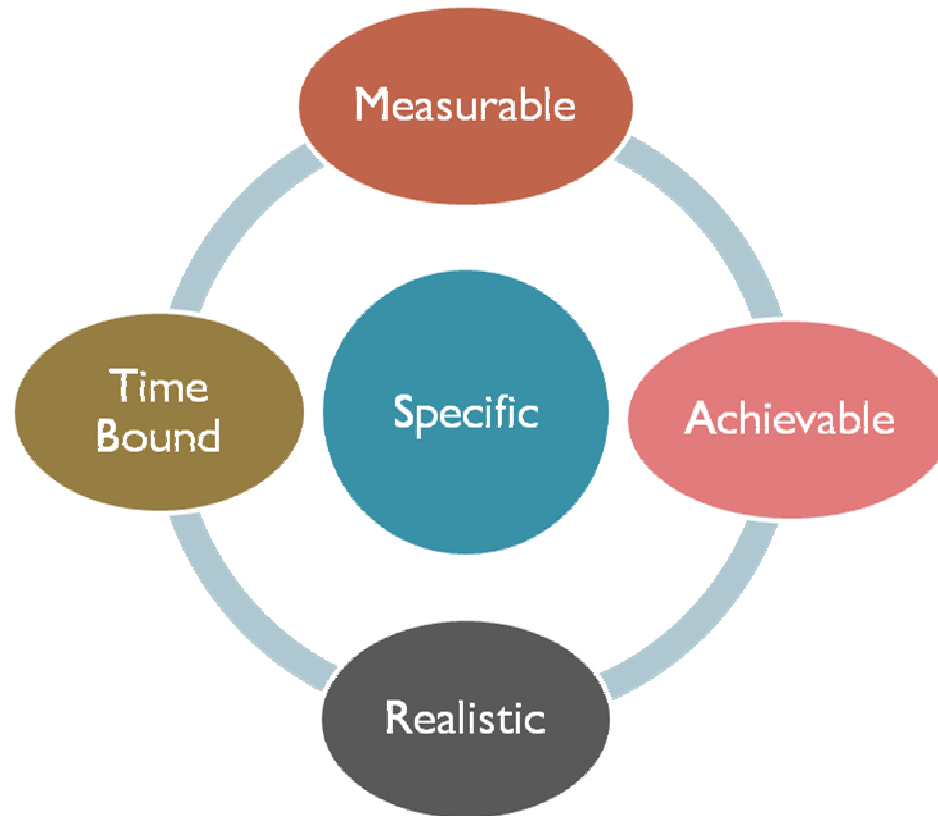
- ✓ Demand supply gap
- ✓ Edge over competitors
- ✓ Cost effectiveness
- ✓ Improved specifications

Research Team & Infrastructure

Should have:

- ✓ Relevant experience & expertise
- ✓ Patents / published articles related to the proposal
- ✓ Collaborations in complimentary areas
- ✓ Adequate infrastructure to execute the project

SMART Objectives



Scientific Merit and Innovativeness is the Key

Innovative

Patentability

- ✓ Technology not in public domain, including own technology
- ✓ Prior Art Search for Novelty Assessment

Possibility of owning IP in the identified territory

Commercial Potential

□ Freedom-to-Operate

- ✓ Other blocking patents/ Potential restrictions
- ✓ Strategies to address restrictions or risks

□ Market Potential

- ✓ Demand supply gap
- ✓ Edge over competitors
 - Cost effectiveness
 - Improved specifications

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

Regulatory Issues

- ❑ Clear understanding and conformity with regulatory requirements

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

Approach & Methodology

Should be

- ✓ Adequately developed
- ✓ Well-Integrated
- ✓ Well-reasoned
- ✓ Appropriate to the aims of the project
- ✓ Realistic research plan with specific milestones
- ✓ Clarity on regulatory pathway
- ✓ Potential Problems and alternative strategies

Preliminary Results

Should

- Justify capability in pursuing the Idea
- Be legible
- Raw data should be enclosed
- Not have any messy blots / data / tables

Experimental Design

Should :

- Be relevant to objectives
- Include details of experiments
- Have appropriate controls
- Be manageable in stipulated time
- Not be too ambitious
- Have alternative strategies
- Have validation strategy

Work Plan

Should

- Have a clear depiction of duration and sequence of key activities
- Indicators for progress of each activity
- Role of collaborators in each activity
- Gantt Chart or Bar Chart or a Diagram is a good choice to show the work plan

Milestones, Outputs and Deliverables



Budget

Should

- Be realistic and justifiable for the proposed work.
- Clear depiction of all sources of promoters contribution
- Not be over/under budgeted
- Use same unit throughout the proposal
- Mention clearly Recurring and Non Recurring

Supporting Data

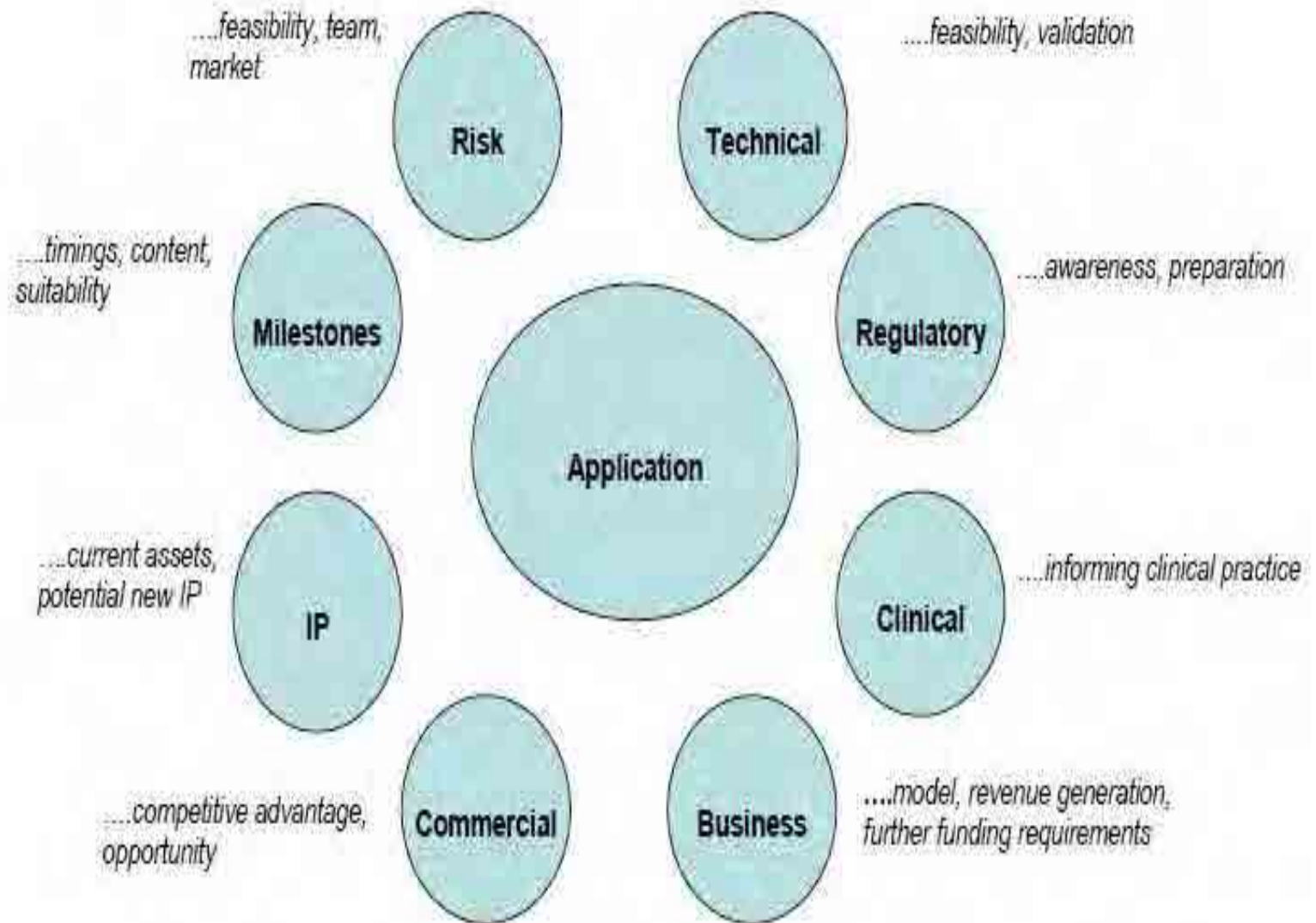
Should Have

- Collaborators details & relevant documents like
(NDA/ MoU/ MTA/ License Agreements etc)
- Resumes of PI's & Scientific Team
- Patents Status (FTO reports / Prior art search)
- Financial Statements of the company

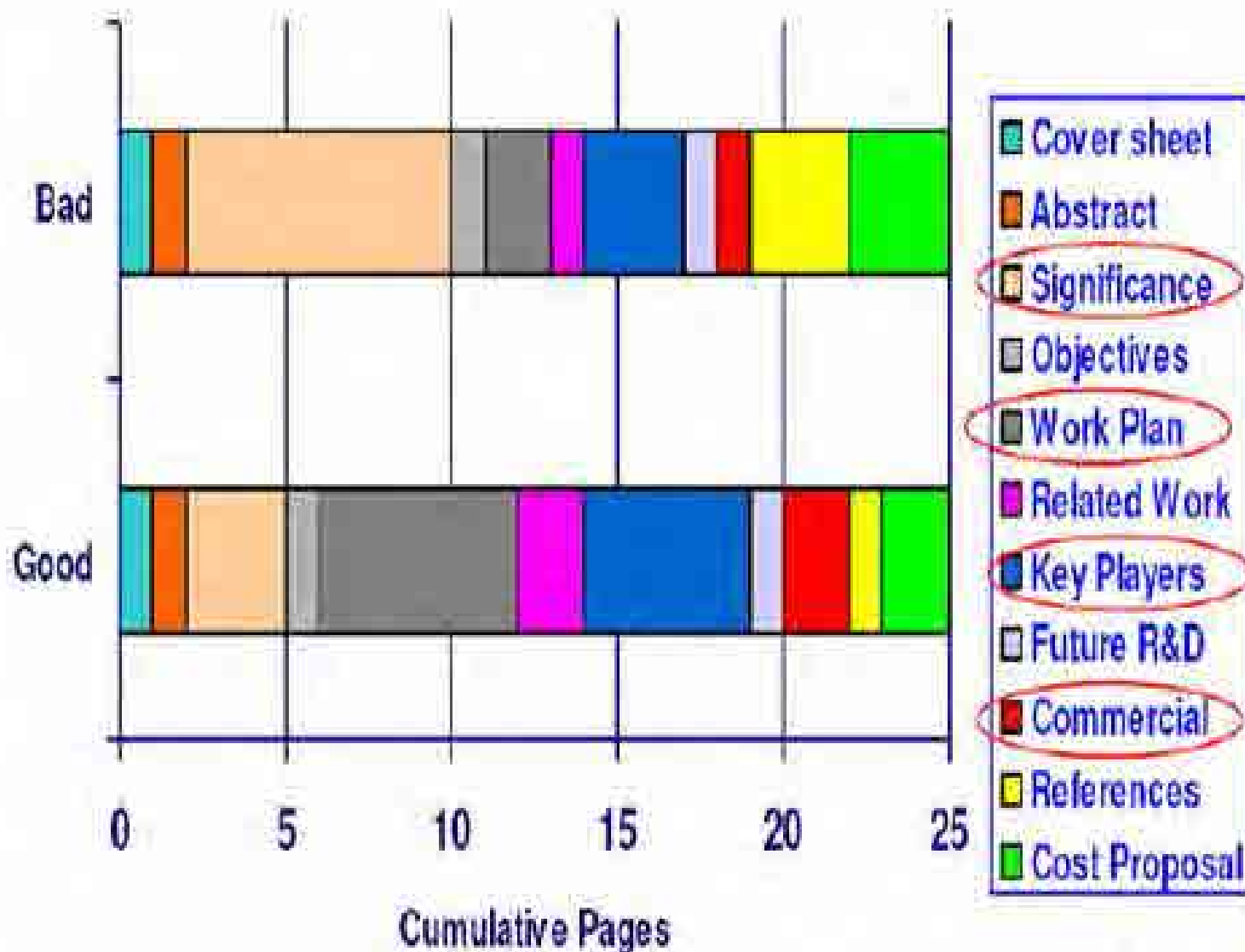
Summary

- ✓ Anticipated outcomes / Deliverables
- ✓ Novelty / Innovative step / Industrial applicability
- ✓ Project Team
- ✓ Experience / Expertise / Leads available
- ✓ Work done so far
- ✓ IP details
- ✓ Budget Details

Key Issues to be Addressed



Good Vs Bad Proposal



Potential Causes for Rejection

- ✓ Poorly written
- ✓ No evidence of Innovation or Uniqueness
- ✓ Insufficient technical details
- ✓ No originality in Idea
- ✓ Unclear about potential pitfalls or risks or solutions
- ✓ Lack of credible PI or team
- ✓ Unrealistic timelines or objectives
- ✓ Unconvincing case of commercial potential / societal impact
- ✓ Unfamiliar with relevant published data

THANK YOU !





Department of Biotechnology
Ministry of Science and Technology

HOW TO WRITE AN EFFECTIVE GRANT PROPOSAL



Biotech
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BIRAP

The Biotechnology Industry
Research Assistance Program

Incubating. Discovering. Innovating



WRITING A GRANT PROPOSAL – A PROJECT

- The word *project* comes from the Latin word *projectum* and the Latin verb *proicere*, "to throw something forwards" which in turn comes from *pro-*, which denotes something that precedes the action of the next part of the word in time and *iacere*, "to throw". The word "project" thus actually originally meant "something that comes before anything else happens".
- When the English language initially adopted the word, it referred to a plan of something, not to the act of actually carrying this plan out.



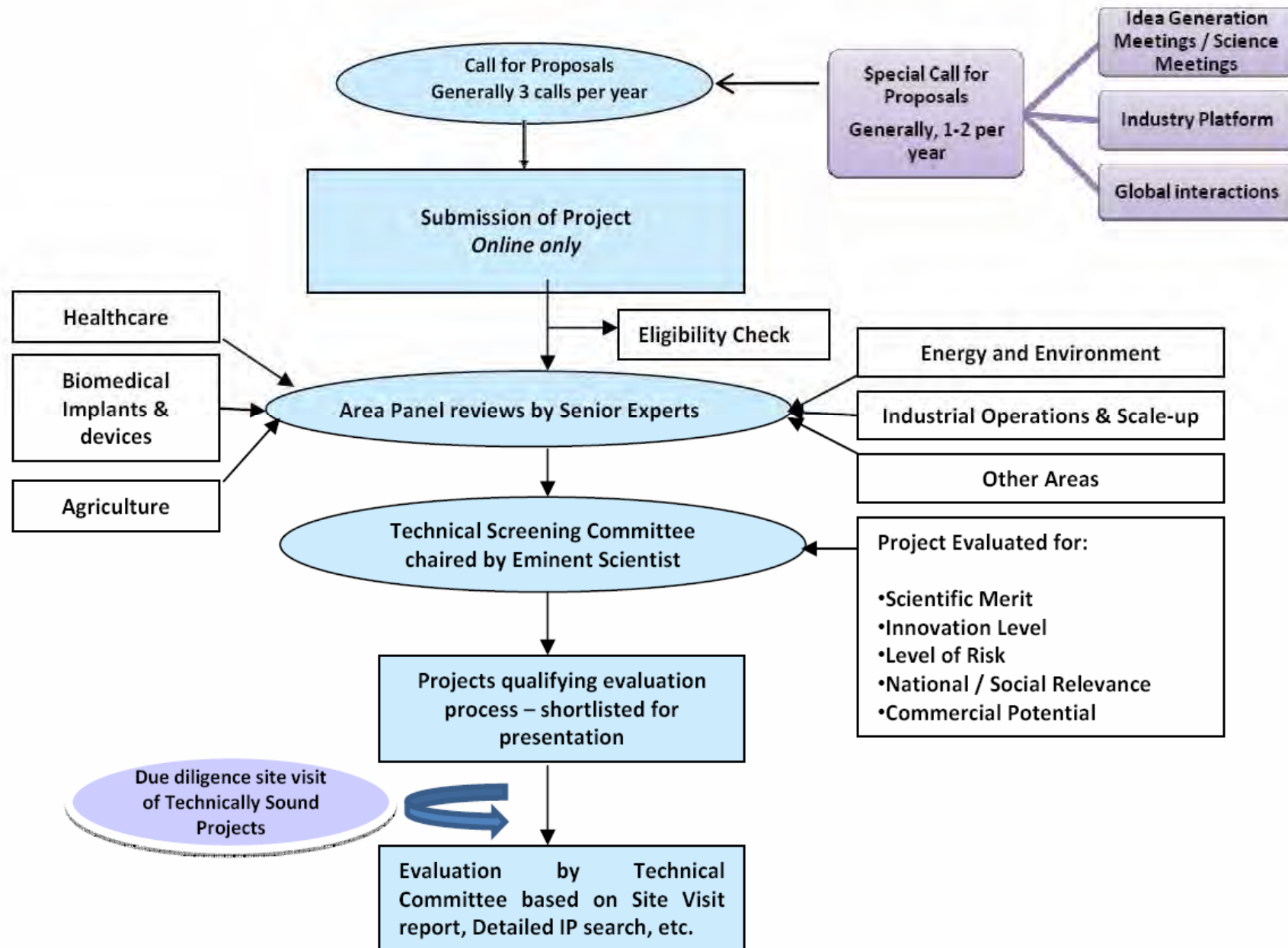
Project – Crossing a Tunnel

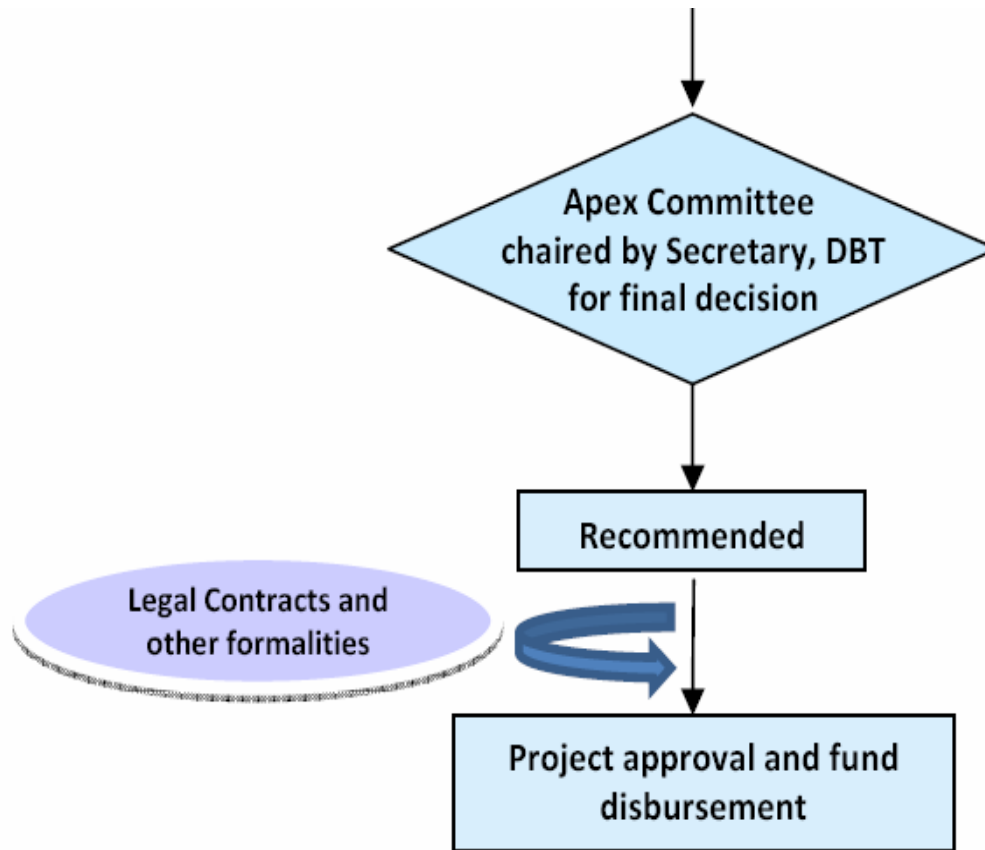


TUNNEL



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?

o 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

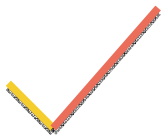


TITLE of PROPOSAL

- 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

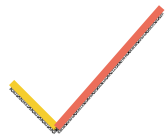
➤ Some scientific data should be added. Should have experiments which have been done before to support the concept



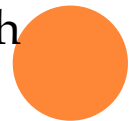
In one proposal use of only single insect resistance gene was presented. It was not supported by literature or experimental proof.

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 peer 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



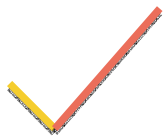
NOVELTY

➤ 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

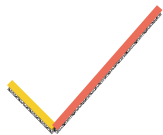
➤ Concept to tackle an unmet need was present. Efforts towards making it more plausible and of more practical value.

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 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

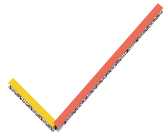
➤ The proposal should provide some justification of the product or even the idea behind it in terms of market value and national importance and unmet need

Importance of Single gene transgenic 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.

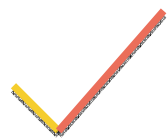
➤ Example:



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

This is an oversimplification 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



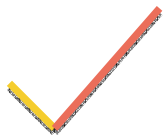
MILESTONES

- Milestones should be **SMART**
Specific, **M**easurable, **A**chievable, **R**ealistic, **T**imely

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 quantifiable part of that objective

a. The T2 and T3 generation seedlings will be analysed for genome analysis 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 construct



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

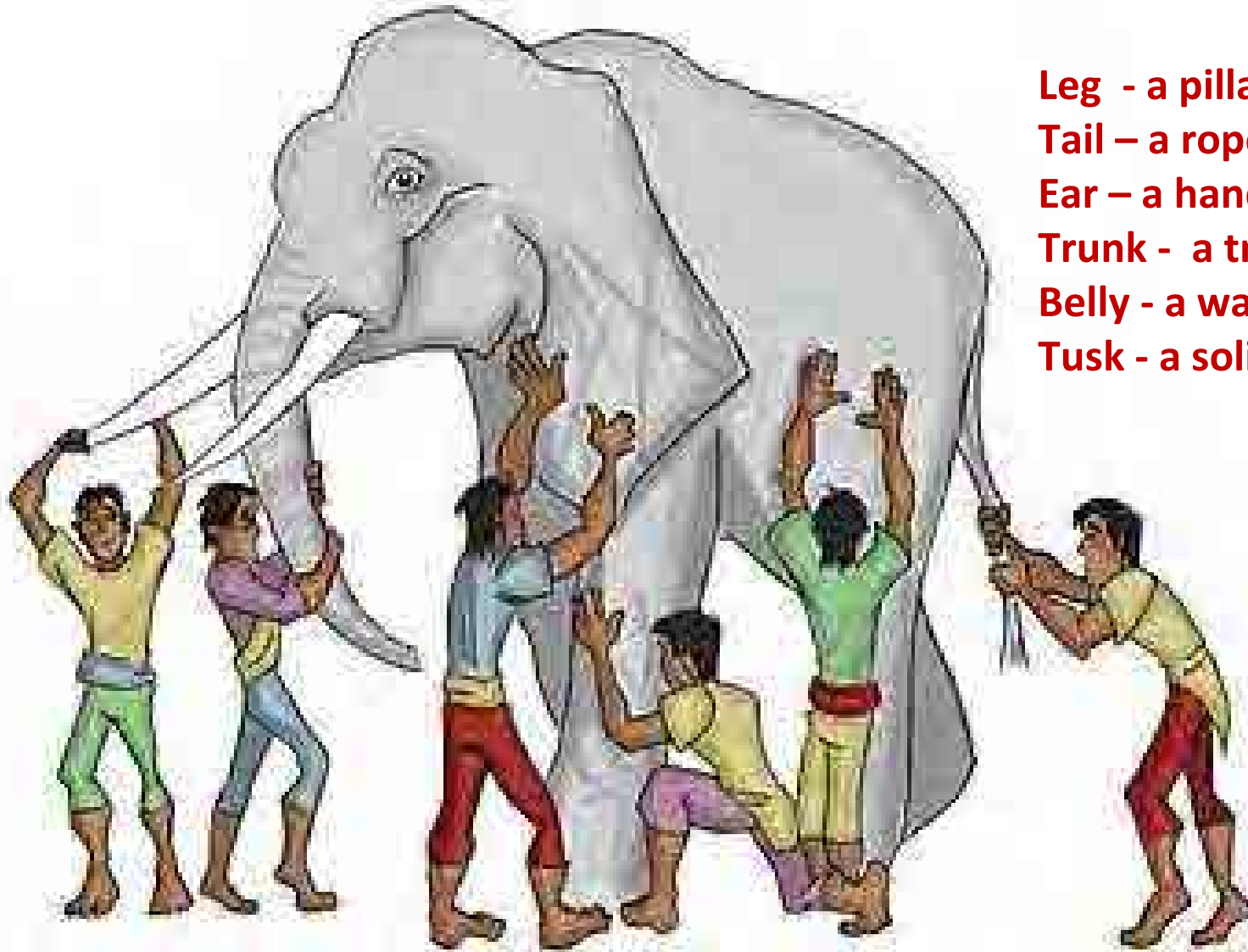


General Lacunae

- 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**





Department of Biotechnology
Ministry of Science and Technology

HOW TO WRITE AN EFFECTIVE GRANT PROPOSAL



Biotech
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BIRAP

The Biotechnology Industry
Research Assistance Program

Incubating. Discovering. Innovating

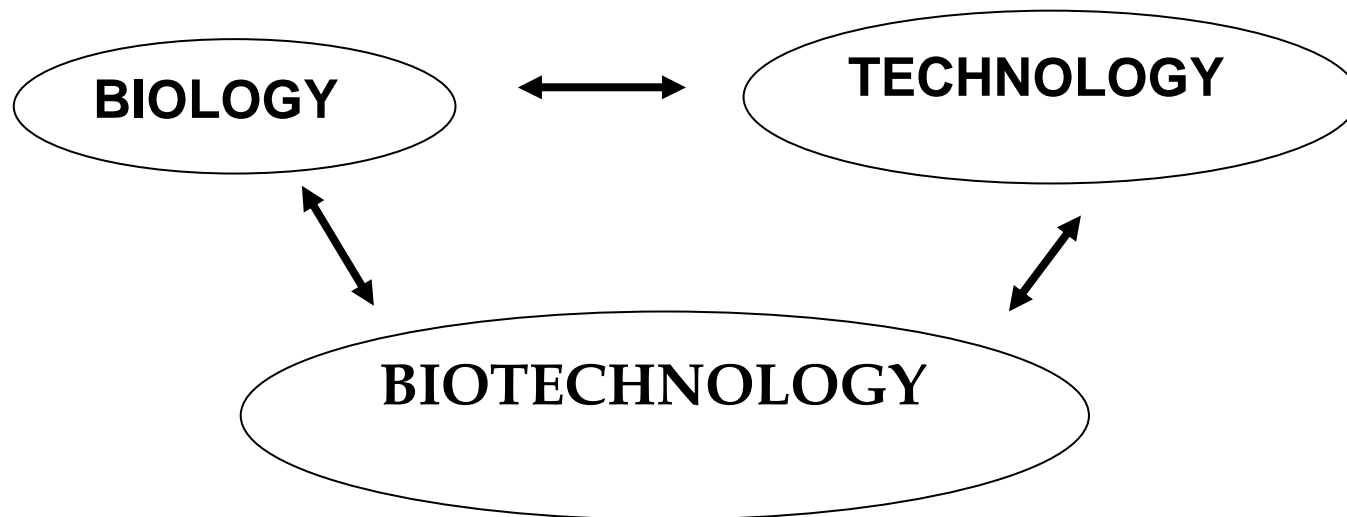


Sathguru
Catalysing Success

BIOTECHNOLOGY

Technological exploitation and control of biological processes

VII International Biotechnology Symposium
1984 - New Delhi.



Industrial Biotechnology

Application of chemical engineering principles to biology, for cost effective production of biologicals

Microbe, fungus, yeast, viruses DNA, RNA, enzymes, plant cell, Animal cell, insect cells, hybridoma, transgenics, tissues

Substrate



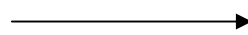
Product

19th Century



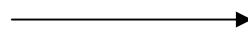
Fermentation

20th Century



Biochemical Engg.

21st Century



**Biomolecular
Engineering**

Application of Microorganisms for Production of Useful Compounds

1. Whole Microbial cells (food, vaccines)
2. Primary Metabolites (acids, alcohol)
3. Secondary Metabolites (antibiotics)
4. Biotransformation (enzymatic, steroid)
5. Exploitation of Metabolism
 - microbial leaching , waste treatment
6. Recombinant Proteins
 - heterologous therapeutic protein
 - gene delivery vectors/DNA vaccine

Estimates of species diversity in nature

Group of Organisms	Estimated species	Accessible (known) Species (as % of total)
Animals (mammals, birds, fishes)	3.5×10^4	>90
Arthropods/ Invertebrates	$10^6 - 10^7$	10
Nematodes	5×10^5	3
Higher plants	2.7×10^5	>90
Algae	$10^4 - 10^5$	[70]
Bryophytes	2.5×10^4	70
Fungi	1.5×10^6	[5]
Bacteria	$10^4 - 10^5$	[1-10%]
Archaea	$10^5 - 10^6$	[0.1-1%]
Viruses	$10^5 - 10^6$	[4]

Important Model Bio-Processes

1. Penicillin from *P. chrysogenum*
2. Conversion of Glucose to HFCS
3. Insulin from recombinant *E.coli*
4. Shikonin from *Lithospermum erythrorizon*
5. Hepatitis B surface antigen from Yeast
6. EPO/ HuMab from CHO/NSO cell lines
7. PHB from *Alcaligenus/ E. coli* ?

History of Penicillin Production

Year	Penicillin Yield (g/l)	Cost (\$/Kg)
Discovery	0.001-0.02	15,000
1941	0.06	↓
1971	18	↓
1991	30	↓
1998	60	35
2000	>60	20
2002	70	15
2006	~ 100	10
2010	--100	25

Biology has four types of Molecules

- ▶ **Proteins**
- ▶ **Nucleic Acids**
- ▶ **Carbohydrates**
- ▶ **Lipids**

It is difficult to get potent compounds against the last three types of molecule with high specificity and toxicity.

Thus proteins are ideal for both for targets to develop new drugs and drug itself.

Proteins can have multiple uses

1. Therapeutics (hormones, interferon)
2. Enzymes [catalyst]
high value product, value addition
3. Diagnostic tool
4. Vaccine
5. Biomarker
6. Monoclonal antibody
7. Transgenic systems

A MODEL HEALTHCARE PROPOSAL

CASE STUDY – DIAGNOSTIC AREA

An ABC company has submitted a proposal under BIPP to develop novel (X Antigen and Antibody) immunoassay format using flash type chemiluminescence and magnetic particles as matrix for HPV

Information on Biosimilar and Vaccines

AREAS COVERED

1. Title of Proposal
2. Novelty/Inventive step
3. Preliminary work done/Proof of concept
4. National importance
5. Objectives
6. Milestones with timelines
7. Budget
8. General lacunae in Proposals
9. Evaluation process
10. After the project is sanctioned

TITLE OF PROPOSAL

- ✓ To develop novel immunoassay format using flash type chemiluminescence and magnetic particles as matrix for HPV.
- ✓ Development of immunoassay based diagnostic kits for HPV using magnetic particles.

- ✗ An ABC company proposal to develop novel immunoassay format
- ✗ Diagnostic kits for detection of Human Papiloma Virus

- ✗ Immunodiagnostic kit using magnetic particles

Title should be appropriate with clear expression of concept

Sham went to market to buy a black horse

1. **Sham** went to market to buy a black horse
2. Sham went to **market** to buy a black horse
3. Sham went to market to **buy** a black horse
4. Sham went to market to buy a **black** horse
5. Sham went to market to buy a black **horse**

Innovation in Diagnostics

Areas :

1. Novel markers for the disease/serotypes
2. Ways and means to produce and characterize the marker
3. Improvement in detection (specificity)
4. Reducing noise or enhancing signal
5. Stability of the assay (accuracy and precision)
6. Automation and miniaturization
7. Networking/information processing

NOVELTY (PRIOR ART SEARCH REPORT TO BE ENCLOSED)

The assay reduces the window period of detection

- ✓ The novelty of the project is to design a universal assay methodology amenable for automation in clinical settings for HPV

The assay can be automated for high throughput screening

- ✓ The novel part of technology is to use universal assay protocol and universal core reagents to detect different analytes using specific antibodies/antigens in an automated setting.

Should clearly state how the core element of proposal can address the existing gap in the market

INVENTIVE STEP

Innovation is the combinatory manner and specific binding of XYZ magnetic particle, reporter and linkers

- ✓ The inventive step is to utilize the XYZ particles as matrix, chemiluminescent reporter molecule and A and B as the linkers in developing universal reagents, harmonized assay protocols in different assay formats such as competitive, indirect, sandwich. The assays will utilize flash type chemiluminescence for faster turnaround time and higher throughput

Innovative process or product should be set apart from the usual approach

PRELIMINARY WORK DONE (BACKGROUND INFORMATION)

The company has submitted PoC data of antigen/antibody binding with XYZ coated magnetic particle. The complex then forms the matrix-tracer complex which binds to the analyte

- 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.

NATIONAL IMPORTANCE AND RELEVANCE

Various studies have established that oncogenic Human Papilloma Virus (HPV) is associated with almost all cases of cervical cancer. Simultaneously, outside Africa, India has the highest number of people living with Human Immunodeficiency Virus (HIV) that is known to increase the chance of acquiring and persistence of oncogenic HPV in them. The high incidence of mortality and morbidity rate (HPV 16 & 18 in women with cervical cancer in India - 76.7%) in India shows a grim picture due to lack of high throughput automated immunoassay systems and reagents. There is no indigenous technology available for performing the assays in an automated manner. This endeavour will make this technology available to the masses. The indigenous development will reduce the dependence on expensive foreign suppliers and allow public institutions to provide more healthcare support for the same amount of money.

Describe the ways through which the present proposal can deal with unmet needs of the society

OBJECTIVES

Objectives should be “SHARP” & “QUANTIFIABLE”

- ✗ Design
 - ✗ Feasibility
 - ✗ Optimization
 - ✗ Validation
-
- ✓ Development of XYZ labelled magnetic particles as a universal matrix for different assay formats for different analytes.
 - ✓ Flash type chemiluminescence reporting for enhanced sensitivity and improved signal to noise ratio.

Clearly state the strategy with probable outputs

MILESTONES WITH TIMELINES

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

- Initial risk report with alternatives to the strategy/approach
 - The binding between XYZ particle, reporter and linkers will not work
 - Automation of assay will not produce high specificity and sensitivity
- 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

Timelines

Year 1

Year 2

		Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	
Objective 1	1A	→									
	1B	→									
	1C	→									
Objective 2	2A	→									
	2B					→					
	2C		→								
	2D				→						

Innovation in Biosimilar Product (Insulin)

1. Different expression system
(*E.coli* / *Lactobacillus* / yeast / CHO / fungus)
2. Different version of *insulin*
(*normal/ long acting/first acting/peg-insulin*)
3. Novel way of purification and refolding
4. Novel way of delivering insulin
(oral/mucosal/single dose)

Noble prizes have been awarded four times on different aspects of insulin

Recombinant Insulin

Insulin Requirement

500 mg/person/year (type I Diabetes)

World Diabetic population and requirement

1987 - 30 million

1995 - 135 millions

2025 - 300 million

Indian Diabetic Population and Requirement

2000 - 30 million

2010 - 70 million

2025 - 100 million

Assume 10 % Type I Diabetic

Requirement for India is 5 Ton

Development of Vaccine

1. Complex molecules
2. Given to healthy people
3. Have long term effect
4. Novel vaccines are more challenging
(Rota and HPV vaccine)

Steps in Vaccine Development

1. Proof of concept (antigen+ adjuvant +delivery)
2. Expression system (stable and reproducible batch)
3. Process development for preclinical evaluation
4. Facility for clinical supply
5. Manufacturing facility
6. Supply chain with stability analysis
7. Assay developments
8. Clinical trial (assay for protection)
9. Regulatory frame work
10. Marketing/Pharmacovigilance

Buckland BC, *Nature Medicine*, 11, S16 (2005)

GENERAL LACUNAE IN PROPOSAL

- Without Team competence and prior experience of the area proposal submitted.
- No Proof of Concept data submitted.
- Without completion of requisite data and regulatory clearances the next stage proposal submitted.
- Clinical Trial project submitted in R&D category form.
- Specific structure/class of the molecule, genes expressing specific proteins are not revealed.
- Deliverables are not realistic and relevant to objective.

Evaluation Process

Areas	Marks
1. Scientific Merit	15
2. Methodology	15
3. Innovativeness	15
4. Intellectual property	20
5. Commercial potential	15
6. Investigator credential	10
7. Adequacy of infrastructure	10
<hr/>	
Total Marks	100

After getting the project

1. Execution and Accountability

- *stick to time lines*
- *PMC and technical evaluation*
- *Expenditure from your own*
- *Regulatory concern if any*
- *Loan return*

2. Going to higher level of innovation

- *Developments of advanced version of the technology*
- *Diversification (leads from side reaction)*
- *Scaling up the operation/internationalization*
- *Translate techniques to technology*
- *Demonstrate effectiveness*

If you want to go fast : move alone

If you want to go far : move together

[BCIL/BIRAP]



Domains of Biotechnology

Industrial Biotechnology

Production of biologicals (proteins, antibiotics, solvents, amino acids, vaccines)

Agricultural Biotechnology

(Plant biotechnology, food biotechnology, transgenic plant, secondary agriculture)

Animal Biotechnology

(Cell culture, aquaculture, embryo biotechnology, transgenic animal , toxicology)

Medical Biotechnology

(Immunology, gene therapy, transplantation, tissue engineering)

Environmental Biotechnology

(waste treatment, solid waste disposal, effluent treatment)

Vaccine Targets

1. Vaccine

analytical characterization

(size, dose, safety)

functionality of antibody

Immunological assay used as surrogate for protection

passive immunity/memory response ?

2. Expression system

Quality of antigen

Stability of expression system

Master bank/seed lot

Scalability

3. Process development

Process is also the product

Vaccine provides a cost effective way of health care treatment for Infectious disease

Best examples: Small pox eradication

Investment

Two Decades: US\$ 25 millions/year (Expenses)

Total of US\$ 500 millions

Results

Live saved 40 Millions /two decades

US\$ 275 million /year on quarantine and treatment

Total saving US\$ 6500 millions

Hepatitis B Surface Antigen (HBsAg)

- Need three injections (0, 1 and 6 month)
- Recombinant Yeast process (1986)
- 1st recombinant vaccine

Year	Yield	Cost/dose	
		USA	Indian
1986	200 mg/L	US \$ 12	-----
1995	1000mg/L	US\$ 12	(Rs.450)
		US\$ 10	(Rs. 300)
1998	1000 mg/L	US \$ 10	(Rs. 150)
2000	-----	US\$ 5	(Rs 50)
2002	-----	US \$5	(Rs 25)
2005	2000 mg/L?	US \$ 5 ?	(Rs 10)

Recombinant Vaccine Manufacturing

1. Fermentation Process Development

Fed-batch fermentation/perfusion culture

E. coli : 5-10 g/L, Yeast : 500-1000 mg/L

CHO/NSO : 1-4 g/L

Bacterial vaccine 10^9 / ml (> 50 OD₆₀₀ culture)

2. Purification

Around 30-50 % recovery, avoid tag

look for soluble aggregates

3. Formulation and stability

Adsorption/ new adjuvants/excipients/delivery

Recombinant Hormones

Insulin and its (analogs) growth hormone, follicle stimulating hormone, salmon calcitonin.

Blood products

Albumin, thrombolytics, fibrinolytics, and clotting factors (Factor VII, Factor IX, Tissue plasminogen activator, recombinant hirudin)

Cytokines and growth factors

Interferons, interleukins and colony stimulating factors (Interferon, α , β and γ , erythropoietin, Interlukin-2, GM-CSF, GCSF)

Monoclonal antibodies and related products

Mouse, chimeric or humanized; whole molecule or fragment; single chain or bispecific; and conjugated (rituximab, herceptin, infliximab, bevacizumab)

Recombinant Vaccines

Recombinant protein or peptides, DNA plasmid and anti-idiotypic (HBsAg vaccine, HPV vaccine)

Recombinant Enzymes

(Pulomozyme, Aldurazyme, Myozyme and Urate Oxidase)

Miscellaneous products

Bone morphogenic protein, conjugate antibody, pegylated recombinant proteins, antagonist

Penicillin

4 Amino acids → US \$ 25/Kg

Insulin

51 Amino acids → US \$ 300/Kg

Assume Insulin is 100 times more complex than Penicillin

Cost of production should be US \$ 30/g

Hepatitis B

227 Amino acids → US \$ 1300/Kg

Assume HBsAg is 1000 times complex than Penicillin

Cost of production should be US \$ 1000/g

That is US \$ 1/mg = US\$ 0.02/dose (20µg)

Rs 1.00/20 µg (one single dose)



Meeting your strategic goals – BIPP is your gateway

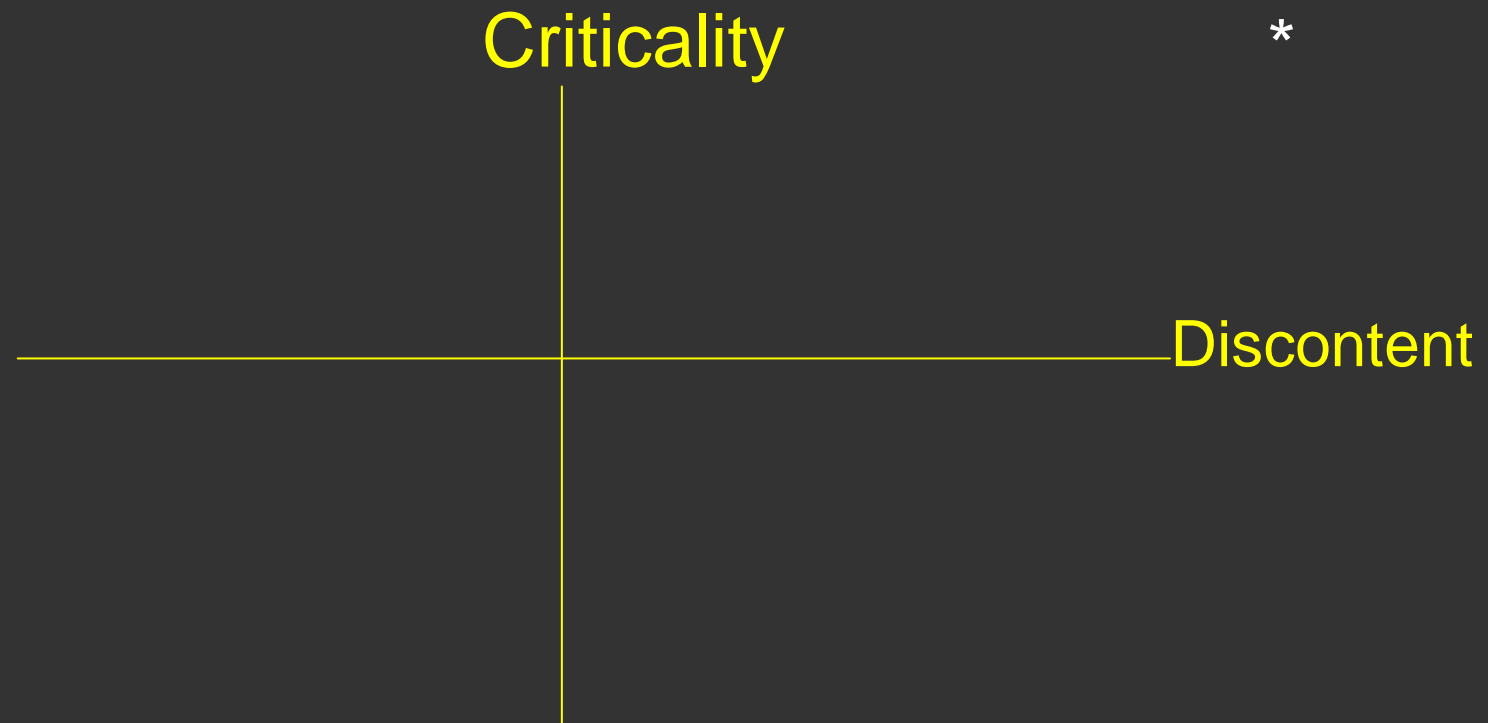
Sathguru Management Consultants
Hyderabad, India



Discussion focus

- Drivers for your strategic leadership.
- Conceiving and structuring your winning plan.
- Expressing your winning plan.
- Ensuring compliances.

Strategic planning for technology leadership – Understanding critical gap.



Innovation priorities are determined by sensing
criticality of the discontent.



Key innovation triggers?

- By interaction – customers who use our product and those who do not.
- Questioning conventional wisdom.
- Knack of sensing the obvious.
- By perceiving a serviceable value to an existing knowledge.
- Anthropologist approach – Deep examination of context through participant observation.
- Observe customer's pain points – Customers often times tell you what they aspire and not the problem they have or the solution that will fulfill their aspiration. Most market surveys do not tell that either.

Innovation sustainability

- Clearly, the goal of innovation is continued relevance – building features that continues to retain attention.
- Innovation should address next level of solution and more attractive economic proposition.
- Articulate your innovation trigger clearly, concisely and confidently.

Strategic planning process

- Product development strategies
- Reaching the market
- IP and technology management policies

The product development effort can be in different phases

- Core Research phase (Science validation).
- Product development phase
- Product validation phase
- “Go to market” phase.

Research phase (FOCUS ON GOOD SCIENCE, WELL DEFINED HYPOTHESIS) – Stage 1

- Prior research experience and focus on research quality.
- Weeding out essentially equivalent efforts carried out by others.
- Relatively uncertain time frame – far more academic and established entity dominance.

**OUTPUT: PATENT/TRADE SECRET/COPY RIGHT/KNOW-HOW –
PROTECTION OF RESEARCH RESULTS.**

**OUTCOME: EXPLORING APPLICATION OF RESEARCH
RESULTS.**

Choose between in-house development vs. licensing

- Identification of biological material.
- In-house development of trait gene Vs. In-licensing of the trait gene.
- Making choice of other biological materials – Promoter, selectable marker etc.
- In-licensing of other biological materials.
- Selection of the right parent material for trait development and selection of right germplasm for trait integration.

Technology access issues

**Every gene or strain of value is protected by patent
– Restriction on access to basic biological
materials – Perceived as opportunity by some
and hurdle by others**

**Are there similarities in other sectors? How
do they handle this?**

Research Tools: Problems



- Many research tools are costly to develop and have significant competitive value to the firms that own them.
- Biological innovation requires access to multiple technologies and materials
- Case by case negotiations for permission to use research tools and materials create significant administrative burdens that delay research.
- Many agreements are limited to use for "research purposes" and exclude use for "commercial purposes," sometimes without defining those terms

Material Transfer - Research



- **The MTA dictates how the materials, and the results from using the materials can be used, along with other significant terms, conditions and obligations**
- **In some cases, MTA may provide that the material may be used for research purposes only, or that the material may not be transferred to another person without the owner's consent.**
- **If the provider of research materials will not make them available except on stringent conditions, look for alternative sources for technology access.**

Judicious ways in co-developing / accessing platform technologies.



- Technologies that can address CROSS FUNCTIONAL AND CROSS PRODUCT APPLICATIONS.
- Technologies that can address PRODUCT needs across the GLOBAL regions.
- Technologies that can be integrated with other technologies/traits/remedies.

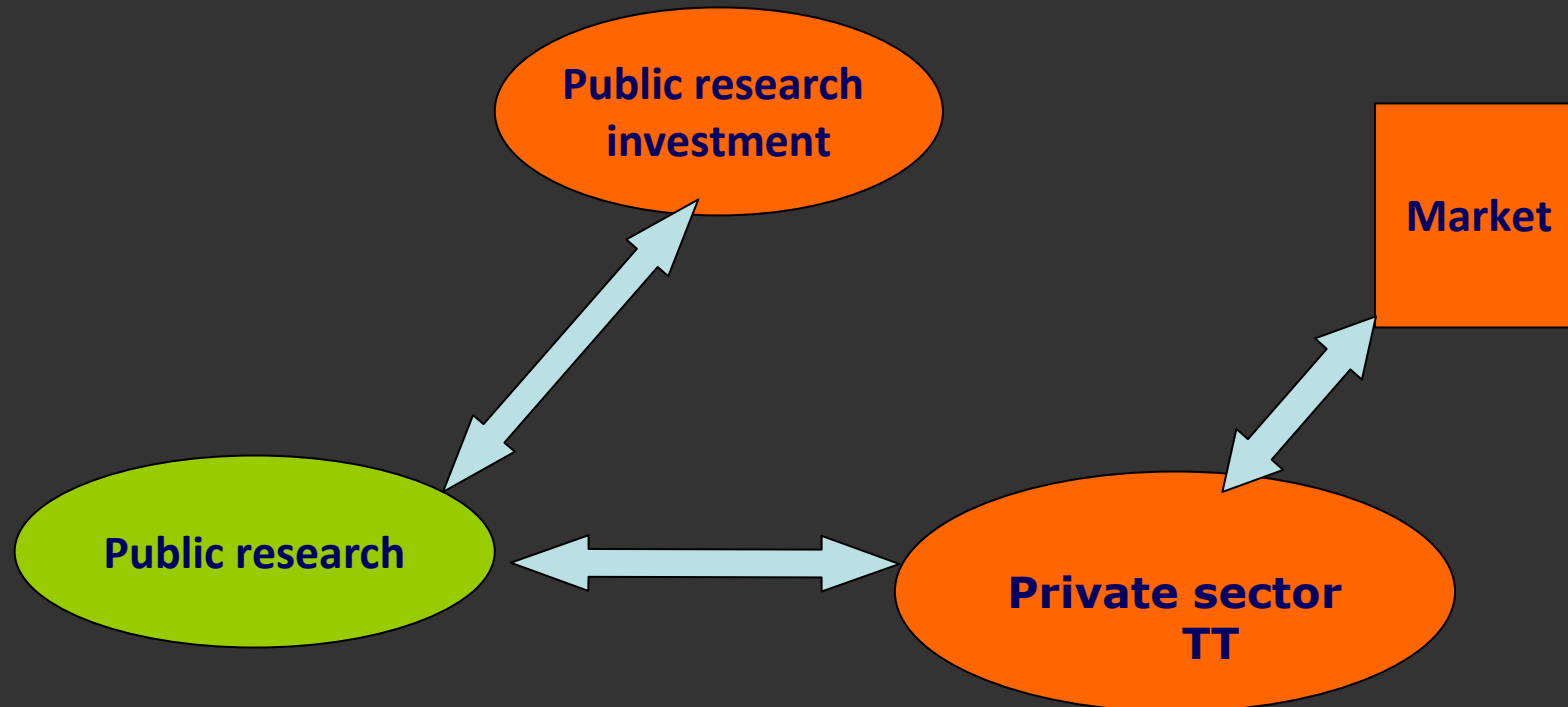
**YOU CAN'T ACCESS BROADER MARKETS WITHOUT PLATFORM
TECHNOLOGIES**

COLLABORATIVE RESEARCH

- Bridge the technology – market gap.
- Multi-partner role.
- Resource augmentation potential.
- Public – private research partnership.
- New orientation to Corporate Research ability and focus.

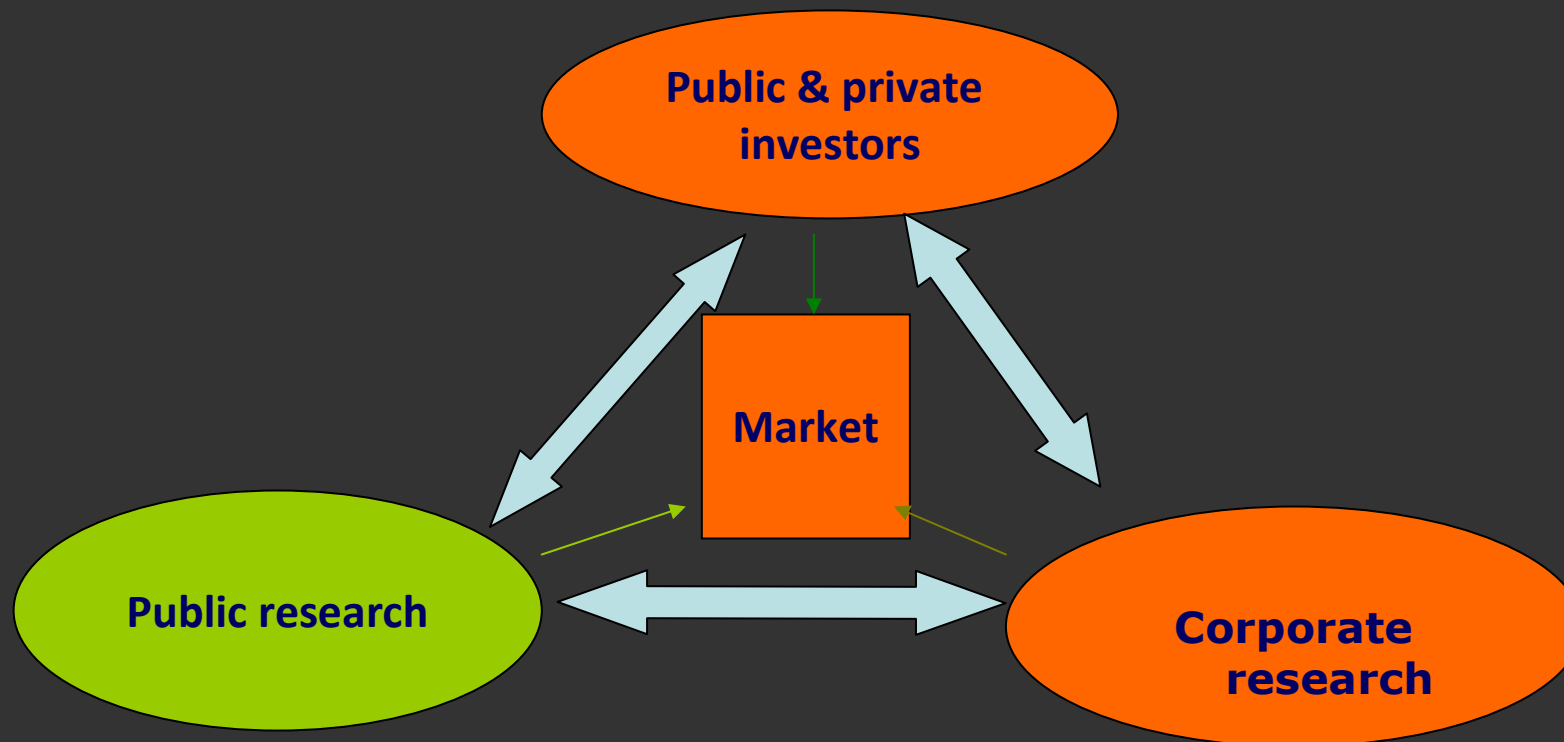
WHOLE FOCUS ON SPEED (Knowledge generation – access – markets)

Emerging relationships drive consolidation of research investments and research efforts – BIPP is a model in this direction.



Traditional development model

The new relationship model – converging investment and research efforts – BIPP is a model in this direction.



PRODUCT DEVELOPMENT PHASE – Stage 2

Goal: To develop product(s) / prototype(s) / chemical / molecular data etc, applying the Intellectual asset generated during stage 1.

- Convert research output into a set of product options, preliminary data (chemical, molecular) or develop a set of prototypes.
- Timeline: could be 12 months to 18 months.
- Innovation functionality is the key focus.
- Regulatory compliance issues begin to emerge.
- Mentoring on technology, regulations and IP could be of value.

PRODUCT DEVELOPMENT PHASE

- Technology and strategy integration.
- Strategy mentoring for product differentiation and value focus.
- **Output:** The chosen product/prototype, data, ready to be further validated through the regulatory process.
- **Outcome:** Structured product value creation, Licensing, JV, Spin-off, pre-market validation.
- **Agreement:** Nature of partnership for product validation, ownership pre-clearance, Intellectual Property protection and co-ownership (assignment).

PRODUCT VALIDATION PHASE – STAGE 3

Goal: To validate product/prototype/chemical/molecular data etc, applying multi various tests of validation (Scientific, markets and operational).

Combine Science and strategy all through the validation.

Output: A product that has been validated .

Outcome: **Licensing agreement, spin-off, Joint venture etc.. (exploring multiple paths to commercialization) Enterprise readiness to commence “Execution plan”.**



PRODUCT COMMERCIALIZATION – STAGE 4

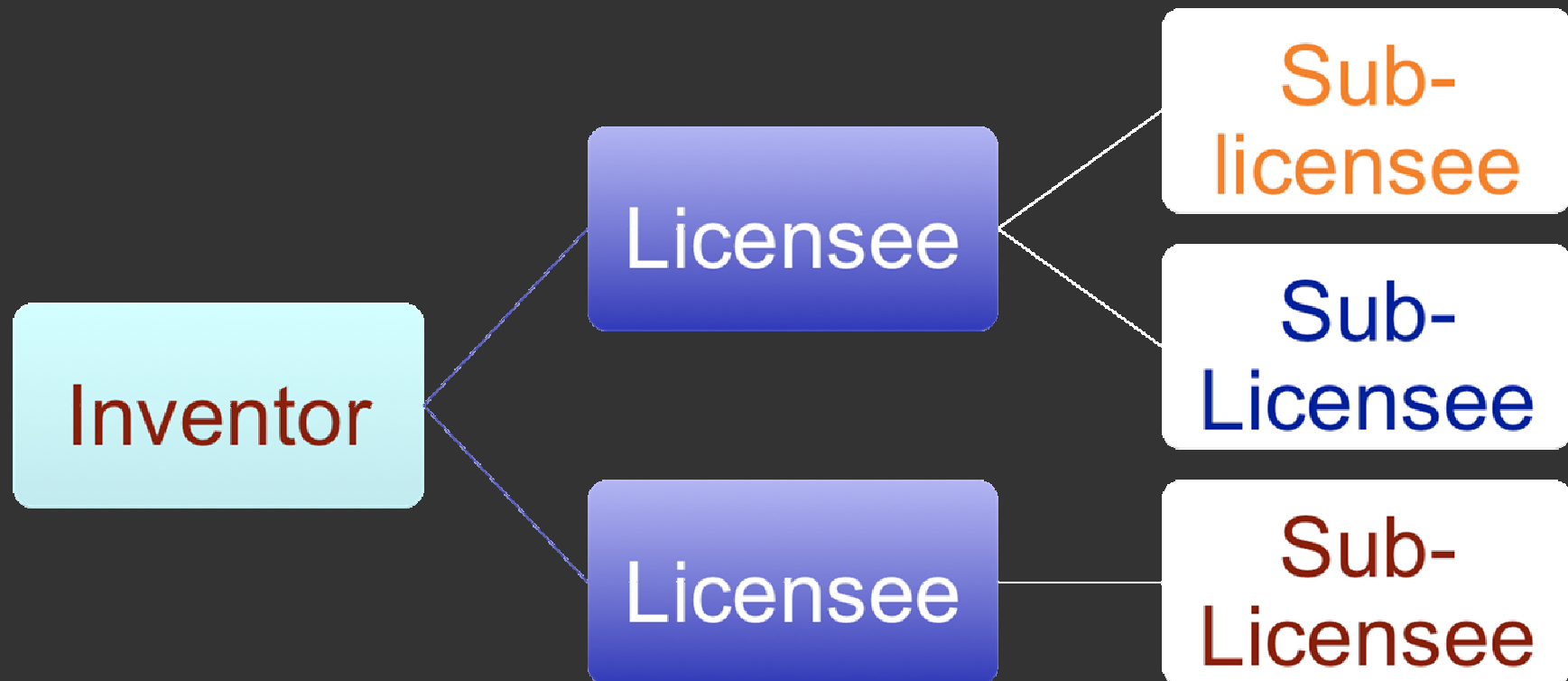
- AUGMENTING ORGANIZATIONAL CAPACITY (STAND ALONE OR IN PARTNERSHIP).
- CREATING AND MANAGING TECHNOLOGY PROVIDER – MANUFACTURER – MARKET BRAND OWNER RELATIONSHIPS.
- MANY TIMES A MULTI-PARTY CONVERGENCE.
- Focus on benefit sharing as ownership – revenue and profit vest in different bodies.
- Territorial factors, licensing and sub-licensing options.
- FOCUS ON SPEED TO MARKET AND TECHNOLOGY MANAGEMENT.

Stage 4 – Combine execution effectiveness and strategy



**THE INGREDIENTS WITH WHICH
ENTERPRISES CREATE GO-TO-
MARKET ACTION PLAN**

Technology reach to markets – You can't lose time



Do you know you have not missed the markets?



Licensing Models for commercialization

- Licensing - Exclusive vs Non-exclusive.
- Can be limited by
 - Field of use, to a field, such as a particular indication, and/or
 - territory.
- Out-license some applications of your technology to generate revenues while reserving other aspects to commercialize yourself.
- Bundle IP for value enhancement - build partnerships with academia and industry through packages

IP Commercialization Strategies



- Grant a broad field of use license with the right to retract fields in case licensee elects not to pursue it
- Grant a narrow field of use license and give the licensee the right of first refusal on other uses.
- Broad license means more control and benefit from the process through sublicensing, even if the licensee lacks the resources to concurrently develop all possible uses or markets for the technology.
 - perform a Freedom-to-Operate search to discover third-party IP that cover, or are close to covering, all or part of our technology.
 - can help us find a potential partner by identifying others working in similar technology.

Commercializing IP



- **Field-of-Use Licensing:**
 - Aim to grant the narrowest field of use required by the licensee
 - Retain the opportunity to exploit other potential licenses—either newly discovered uses for the technology or in the case where a single licensee may not have the resources to fully develop the technology.
 - Always beneficial to seek a higher upfront payment rather than high royalties, and the amount of payment can indicate your partner's commitment to the technology.



Types of Commercial Licenses

- **Commercial Evaluation Licenses** grant the right to make and use the technology for the purpose of evaluating its commercial potential.
- **Internal Commercial Use Licenses** grant the right to make and use the invention for the purpose of internal use by the licensee. No sales or distribution rights.
- **Full Commercial License** grant the right (non-exclusive or co- exclusive or exclusive) to make, use and sell the invention.
- **Biological Materials License** for inventions desired for commercial purposes but not claimed in a patent or patent application; typically non-exclusive.



So, you have a winning model, how do you articulate this?

Bring your winning strategy and execution plan in BIPP format.

- Articulate concisely the broader context of your innovation plan – Avoid long opening text and indicate in general terms what is known about your innovation idea. Begin with what is generally available and move quickly to what you aim to deliver?
- Title of the proposal (250 words) be as creative and concise as possible.



Keep in mind the intended audience for the proposal

- Reviewers
- Investment approval committee.
- Understand precisely the review criteria and the investment criteria.

Writing style

- Are the subsequent sections organized logically? Are the key points clearly presented? Do you find the text easy to read? Are you repetitive?
- Avoid plagiarism
- Follow the “KISS” principle

Adopt the **CASE** model

- **C**hallenge
- **A**lternative analysis
- **S**olution
- **E**xecution.

IP at all stages



**BEFORE
PROJECT**

- Proposal Preparation
- Defining background IP
- Negotiating Confidentiality

**DURING
PROJECT**

- Possibility of generating foreground IP
- Strategy for protection of foreground IP
- Access rights

**POST
PROJECT**

- Protection of foreground IP
- Dissemination of foreground IP

Addressing IP Issues in a Grant Proposal



- Need clarity on potential background IP in knowledge that we own, or which we have acquired from external sources.
- Acknowledge those IP where we do not have sufficient clarity about FTO
- With such a preliminary IP survey,
 - think about, negotiate and describe the necessary authorizations and conditions for the use of background IP both during and after the project.
 - articulate in great scientific detail at length, possible IP hurdles that we envisage in the project.

Addressing IP Issues in a Grant Proposal



- In case of a potential IP roadblock, assess the impact on the project.
- Ensure alternative pathways, and propose solutions in sufficient detail to allow reviewers to assess the project.
- articulate the strategy for the dissemination of project research results and IP (foreground IP)
 - across markets
 - across geographies

Addressing IP Issues in a Grant Proposal



- Identify access to research tools; to unique equipment and instrumentation; and to collaborations and partnerships.
- If an MTA has stringent provisions, please make the restrictions on its use very clear in the research proposal, and provide an explanation of how the project will achieve its goals despite the restriction.
- DO NOT submit a grant application until you have applied for patents on your intellectual property.

Reference materials enrich your proposal

- Citation references - Adopt Uniform model. (See detailed notes provided for APA, MLA and CMS styles)
- Validate the quality of your references – **Beware of web references prior to citing. Many times they vanish when the reviewers visit them.** Look at the Author background and/organization background. See how often is the site updated.
- Provide quality market references from well recognized database.

Distinguishing scholarly from non-scholarly periodicals (articles and papers):

- **Scholarly**
- **Substantive news or general interest**
- **Popular**
- **Sensational**

Some indicative databases

- Agricola
- Agriculture network information center (www.agnic.org)
- Mintel markets and sector information
- Standards and Poor surveys
- FAO Stat and USDA – NAL database.
- MANN library electronic resource (VIVO)
- PubMed, MDConsult, Ovid, [Web of Knowledge](#), eBooks on Ovid, eMecidine, UptoDate etc.

Research ethics and code of conduct

- Ethical compliances – Internal and external.
- Governance for research.
- Indicate compliance to national regulations and international guidelines.
- Adherence to lab safety.
- Responsible use and handling of Biological materials.

BUDGET

- Strictly follow cost classifications as per the norms for BIPP.
- CONCEPT OF COST SHARING



Innovative, emerging organizations excel in securing high quality grants.

- Demonstration of vibrant Science and technology talent.
- Nimble organizations – inexpensive research – respect for IP - global connectivity and other advantage factors.

Cost, Timeline and market access risks provide barriers for commercialization and influence the reviewers' perspectives as well.

Indicate Key barriers articulate Key strategies concisely.

- Predictability in cost
- Predictability in timeline
- Predictability in market access.



Estimate all critical cost components with active engagement of your finance professionals.

- Technology acquisition/bio material development cost.
- Product development cost.
- Regulatory validation costs.
- Product launch costs.
- Communication and outreach efforts.

Conclusion

- The competitive advantage you have conceived and built is dependent on how well you articulate this advantage.
- A winning idea needs a winner's approach in expression.
- Make your efforts to BIPP seriously to convert your efforts to market reality.



Conclusion

- If you do not have competitive advantage, BIPP can help you gain it.
- If you have competitive advantage, you are bound to lose it. **THE ONLY WAY TO RETAIN IT IS TO CONTINUOUSLY INNOVATE.** Secure BIPP support to retain your competitive advantage.

Mechanics of BIPP

Ms. Shilpy Kochhar

Assistant Manager

Biotech Consortium India Limited (BCIL)

Idea Generation meetings

Call for Proposals

Online Submission of Proposals

A
R
P

Evaluation by the TSC

Presentation

Site Visit by Expert Panel (TSC)

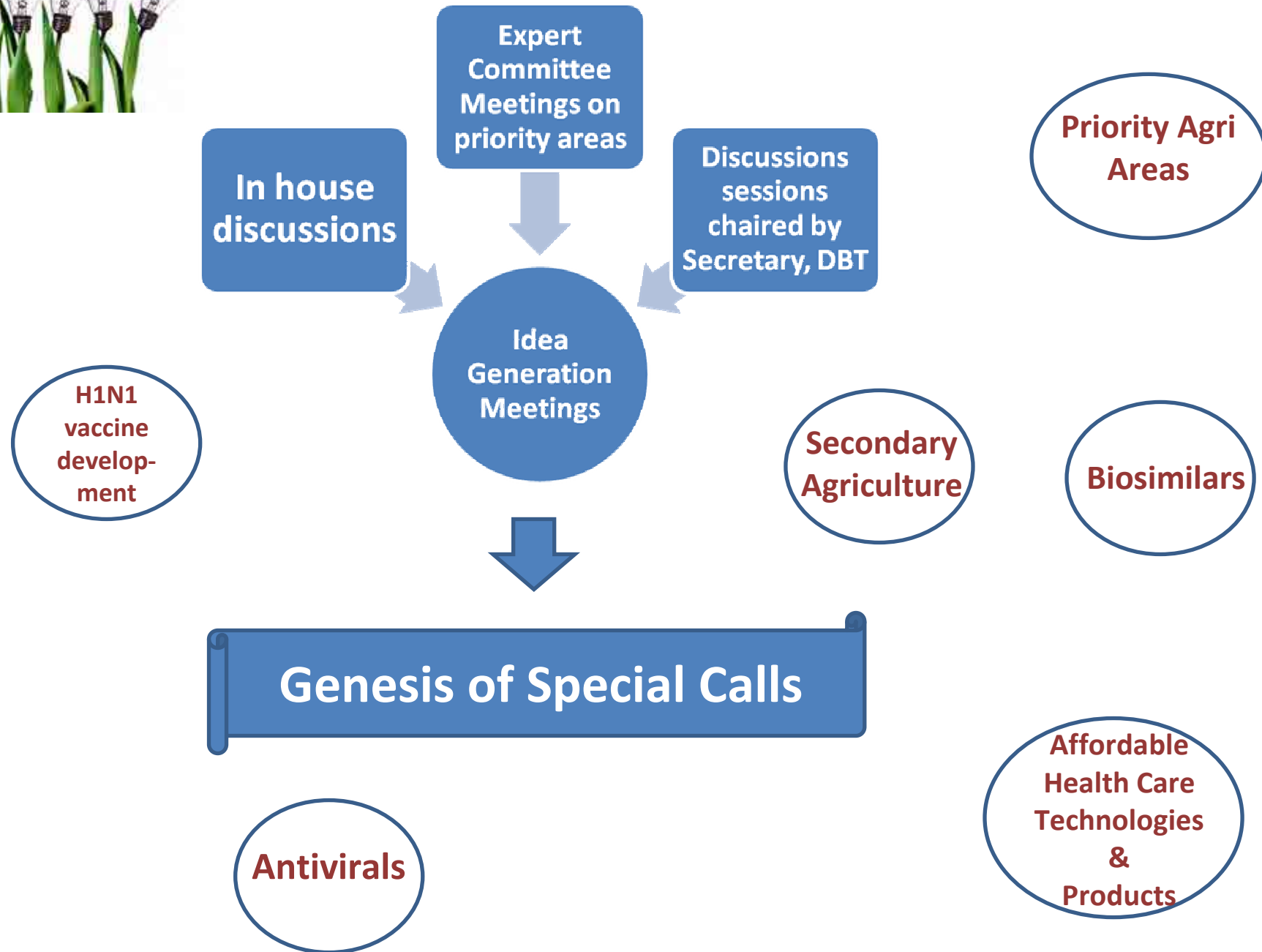
Apex Review

Sanction of Proposal

In house Analysis

< 4 months

BIPP Process Flow



Call for Proposals

Regular
Calls
*thrice a
year*

- February
- June
- October



Special
Calls
need
based

14 Batches
processed
till date
7-Regular
7-Special

2 calls: Currently Open
Till 01st August 2011

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/BIRAP /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



Primary Applicant

Eligible

- For Profit Company registered under **Indian Companies Act 1956**
- Minimum of **51%** shareholding with Indians and/or NRIs

Ineligibles

- 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

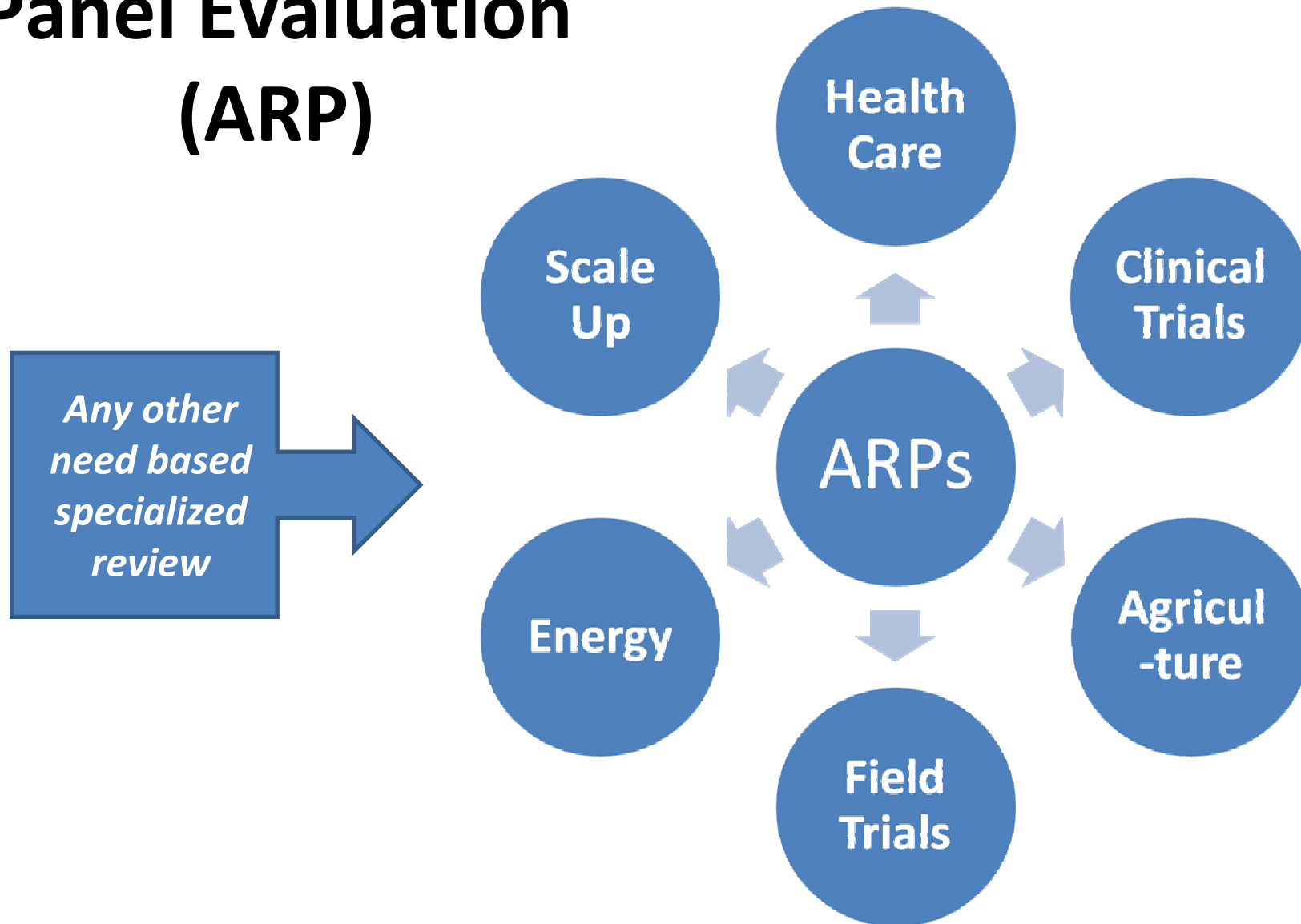
DSIR Requirements

- 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

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

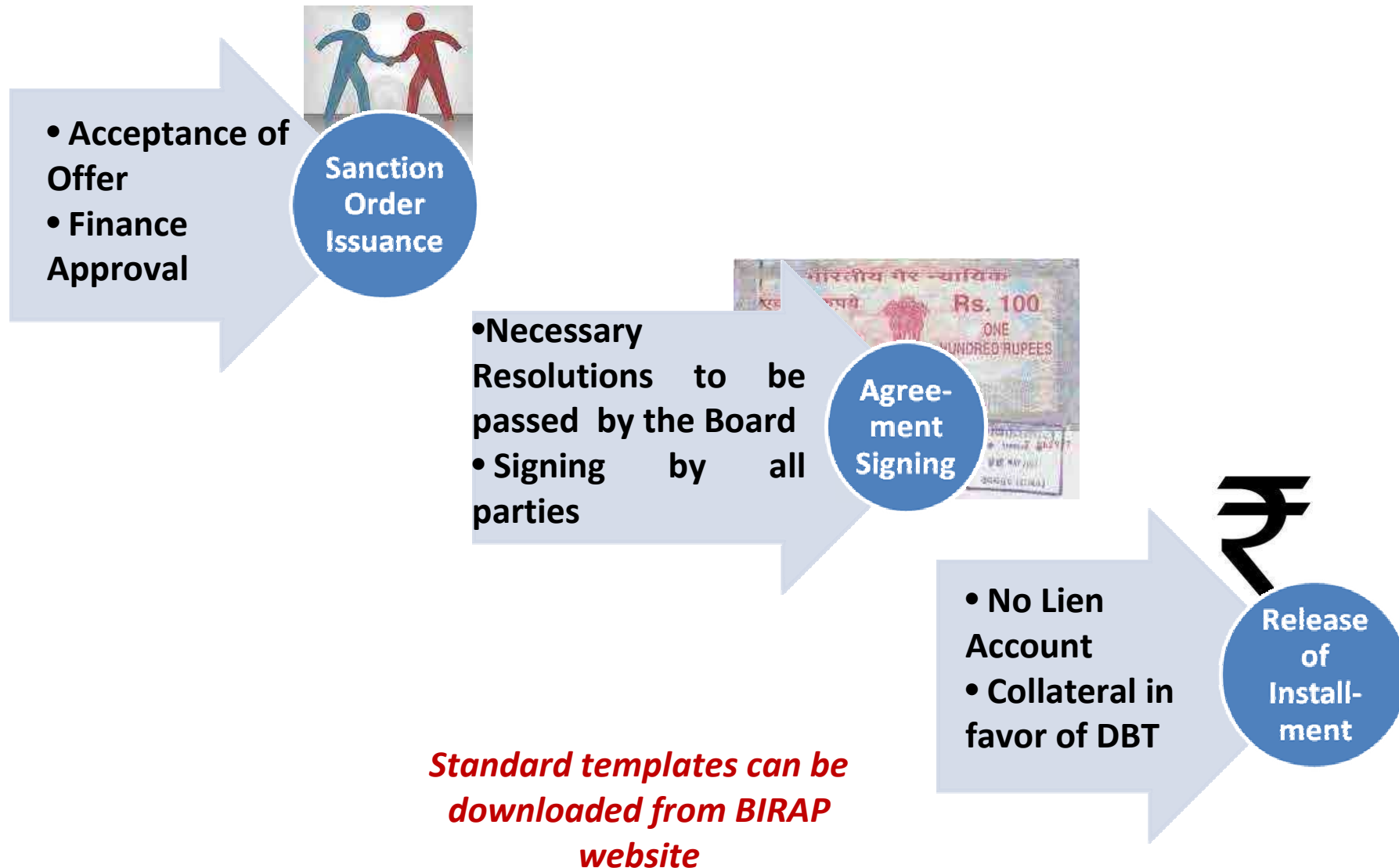
An audit of the financial status of the company by a Chartered Accountant

**Examination of the key aspects:
Liquidity, Profitability, Debts, Assets.....**

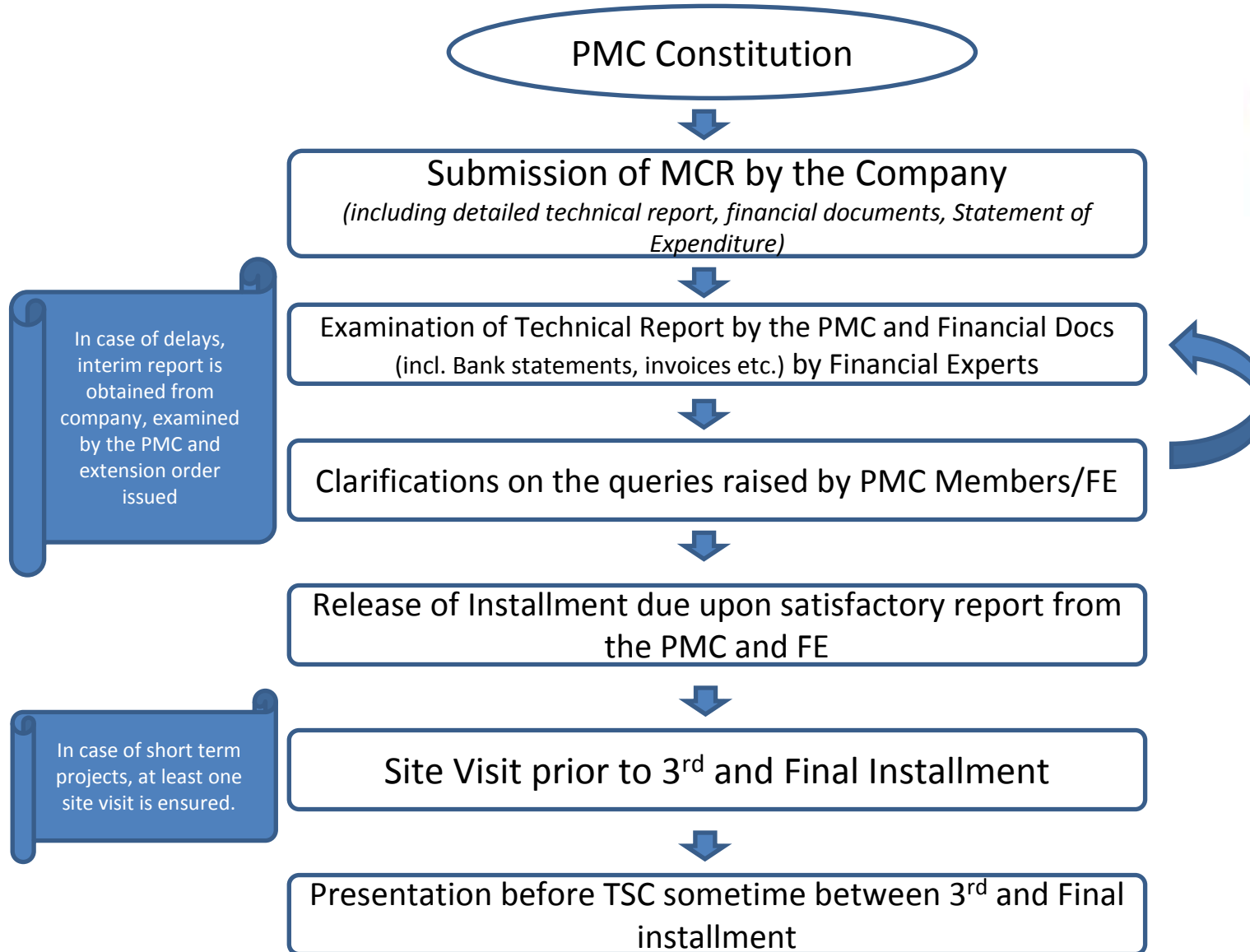
Apex Committee: Constitution and Review

- 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

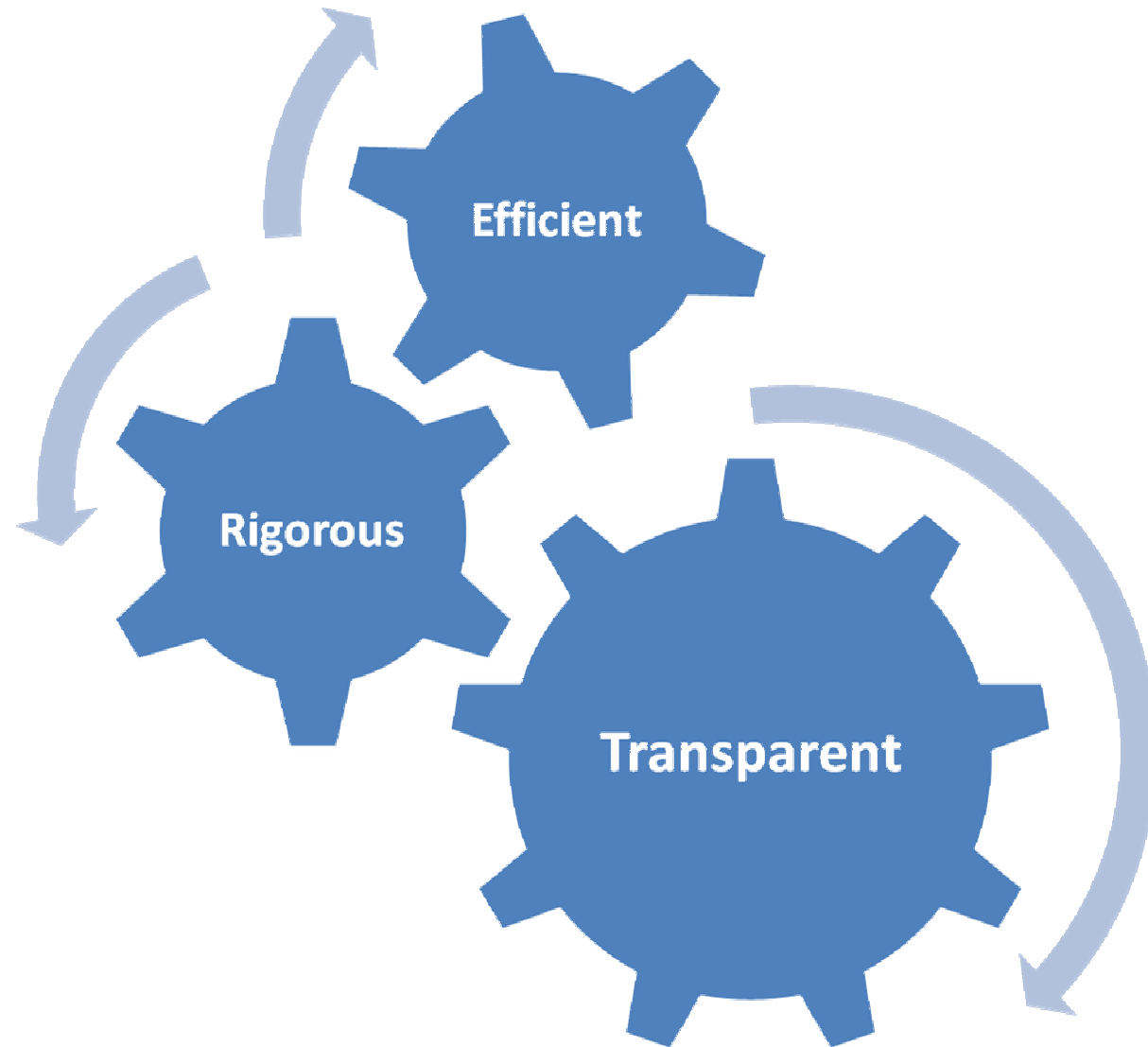


Monitoring of Sanctioned Projects



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

To Conclude: BIPP is



THANK YOU

QUERIES, IF ANY ??????