GOVERNMENT OF INDIA

MINISTRY OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF BIOTECHNOLOGY

BIOTECHNOLOGY INDUSTRY RESEARCH ASSISTANCE PROGRAM

BIRAP
The Biotechnology Industry Research Assistance Program

Organized workshops on

HOW TO WRITE AN EFFECTIVE GRANT PROPOSAL

SECOND SERIES-2011

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in association with

ABLE Association of Biotechnology Led Enterprises
The collective face of the Indian Biotech Industry

BCIL

ASSOCIATION OF BIOTECHNOLOGY LED ENTERPRISES **BIOTECH CONSORTIUM INDIA LIMITED**

Managed by

Sathguru

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DELHI | PUNE | BANGALORE

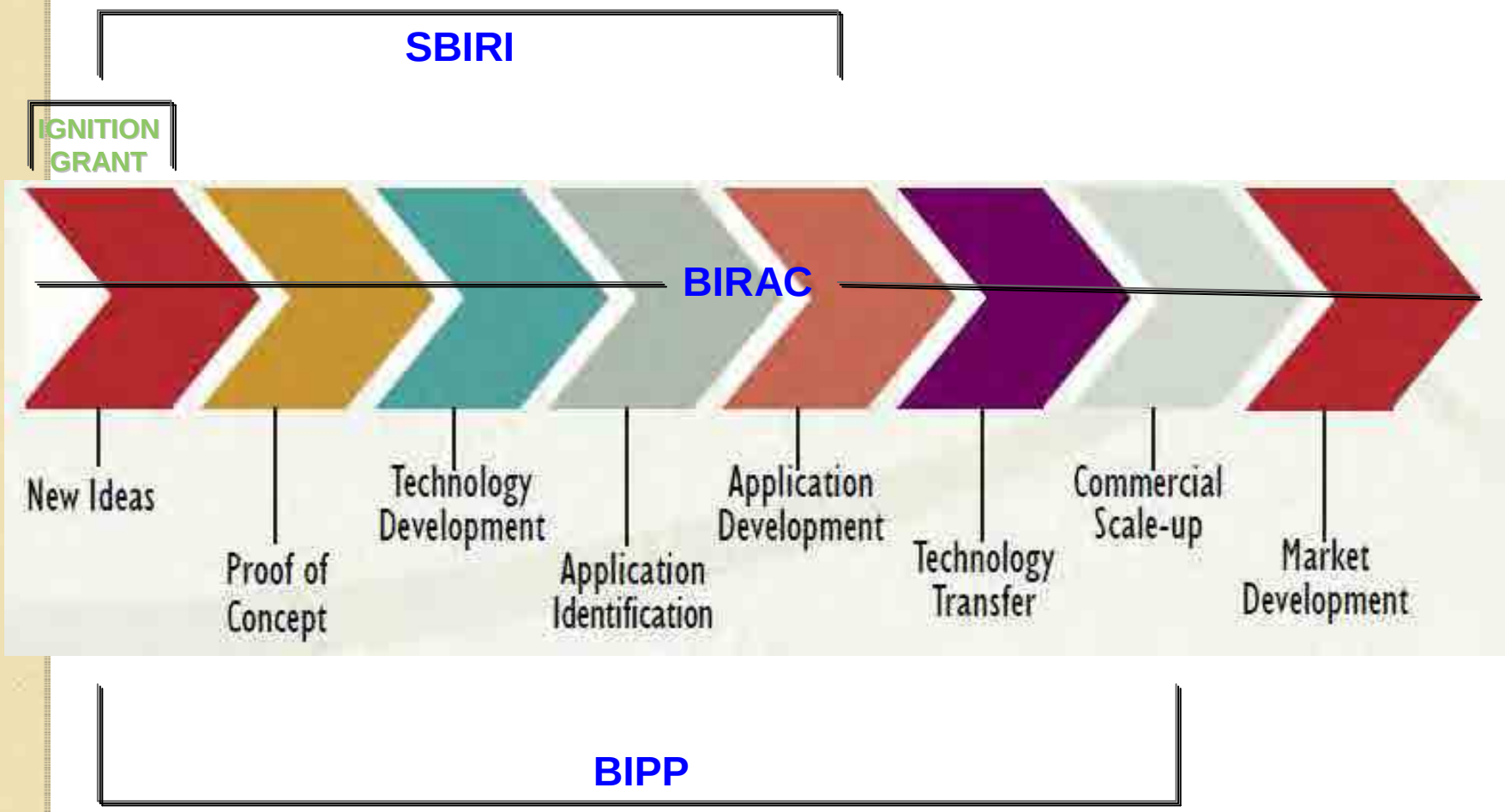
BIPP: An Overview
&
Key Elements of
An Effective Grant

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.

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

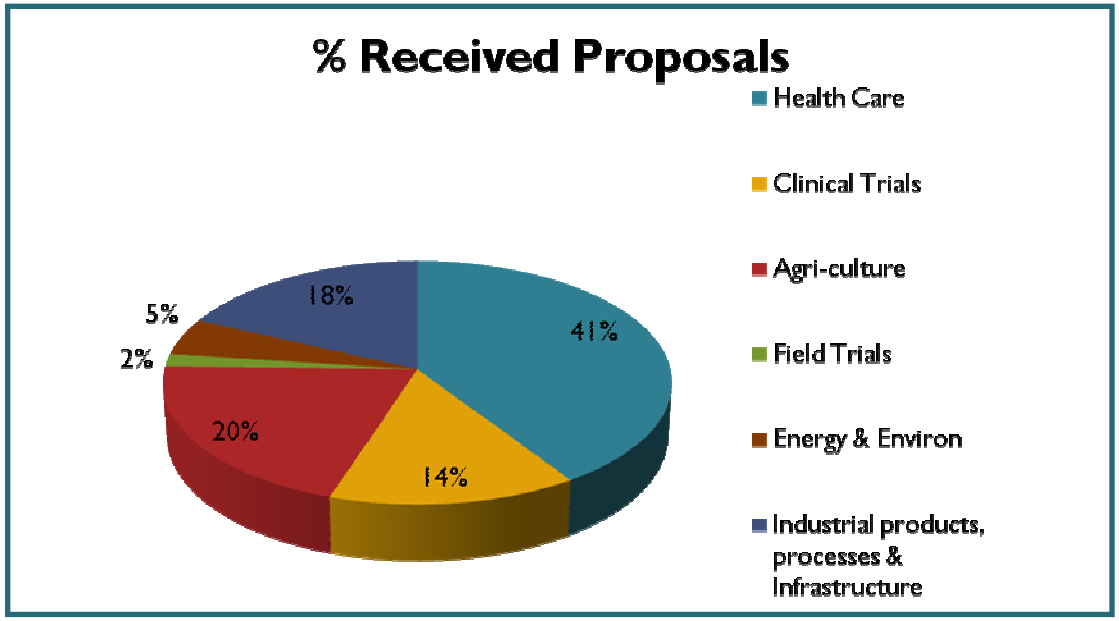
Broad Parameters For Evaluation

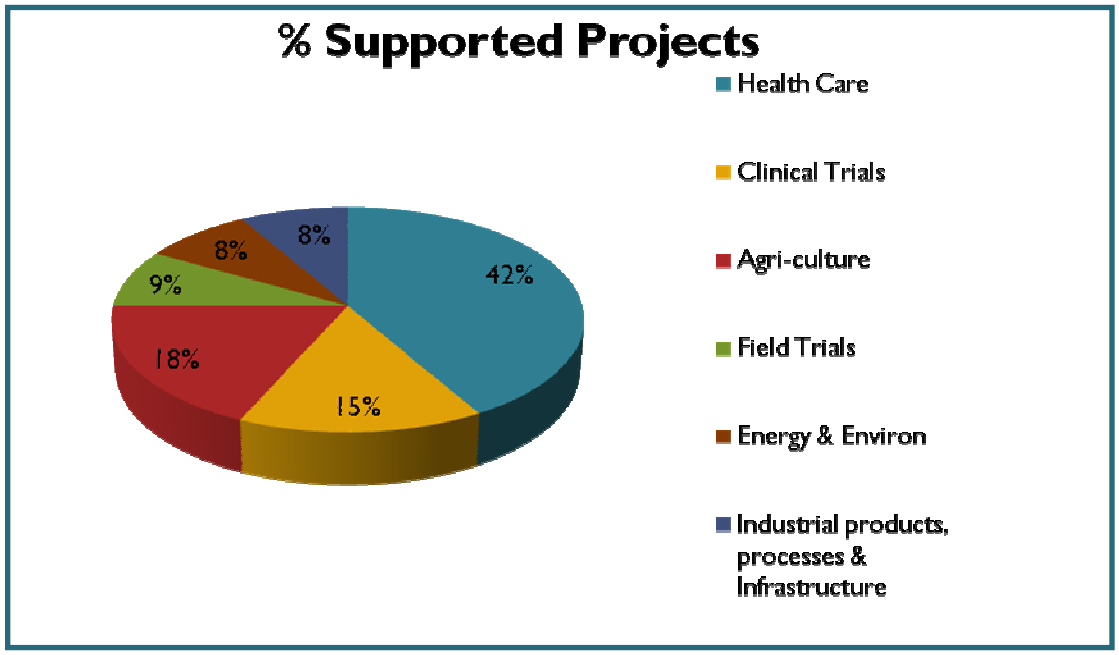
- Significance / Scientific Merit
- Approach and Methodology
- Innovativeness
- Intellectual Property
- Commercial Potential/ Societal Relevance
- Investigators credentials
- Adequacy of Research Infrastructure/ Environment

Biotechnology Industry Partnership Programme (BIPP)

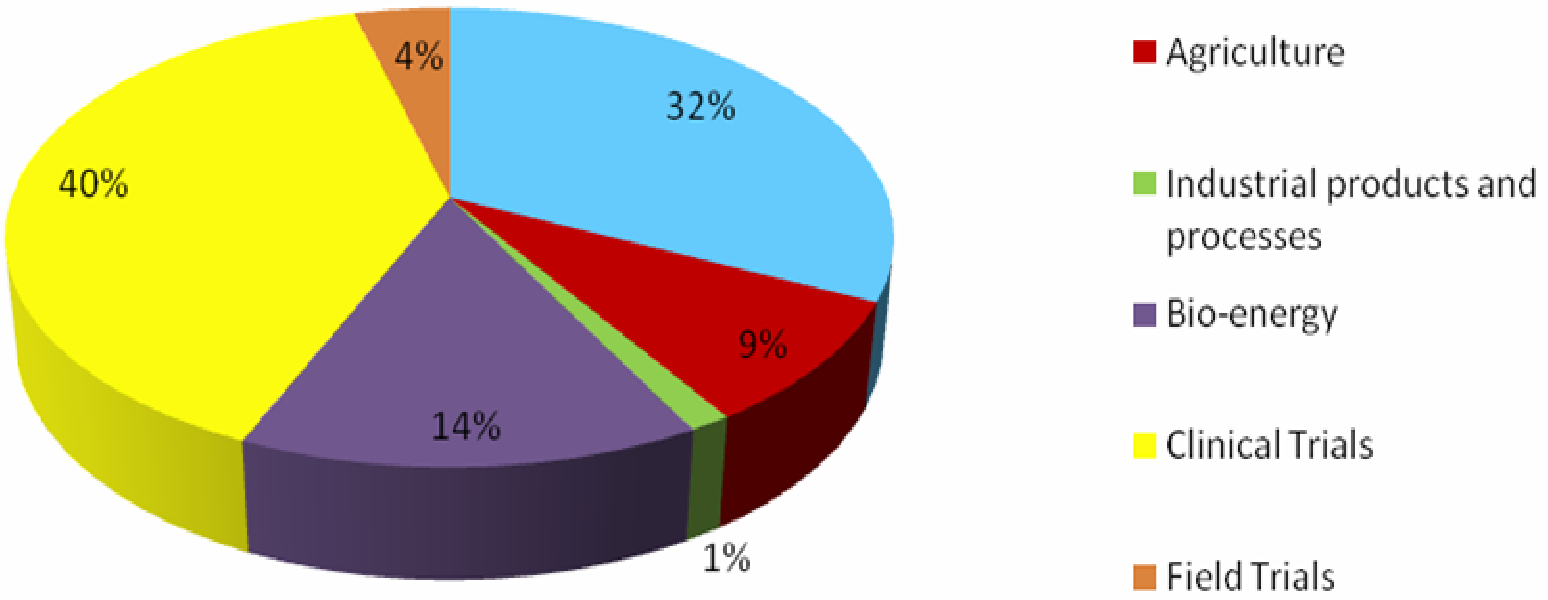
- **Scheme Launched: November 2008**
- **First Call Launched: December 2008**
- **Total Rounds of Proposals processed: 14**
  - ***7 regular and 7 special calls***
- ***Process completely automated: 6th Batch onwards*** *(Feb 2010)*
- ***Total Proposals Received: 450***
- ***Approved Projects: 60***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

BCIL

- 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

BCIL

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

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

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

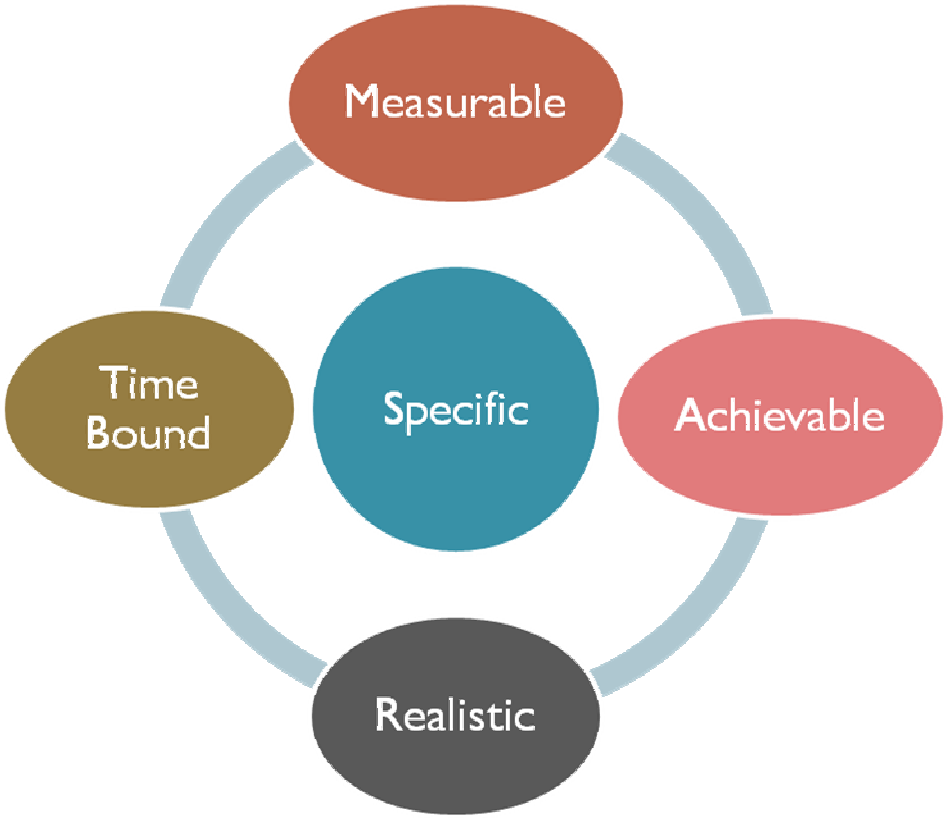
- ✓ Demand supply gap
- ✓ Edge over competitors
- ✓ Cost effectiveness
- ✓ Improved specifications

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

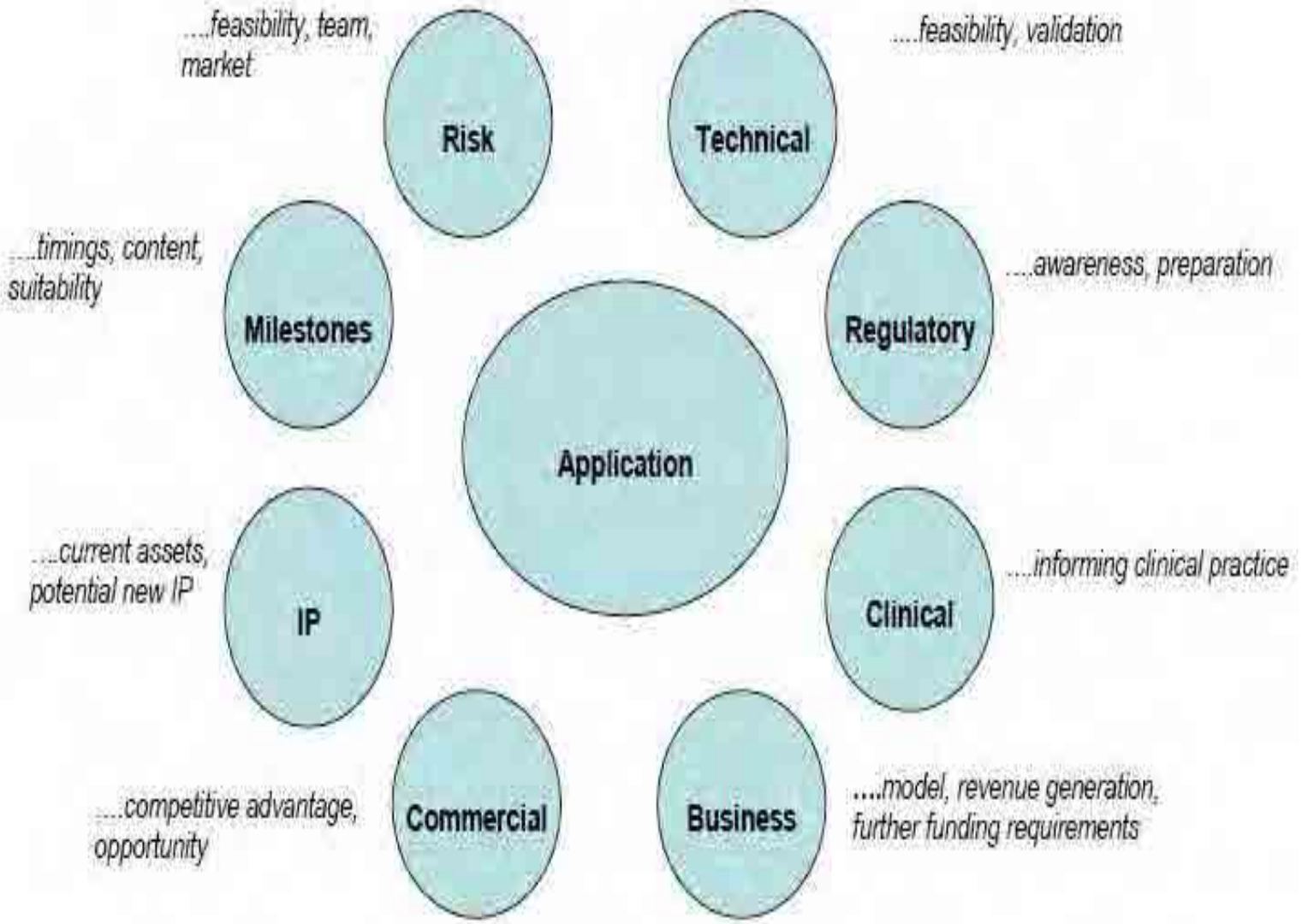
  (NDA/ MoU/ MTA/ License Agreements etc)

- Resumes of PI's & Scientific Team
- Patents Status (FTO reports / Prior art search)
- Financial Statements of the company

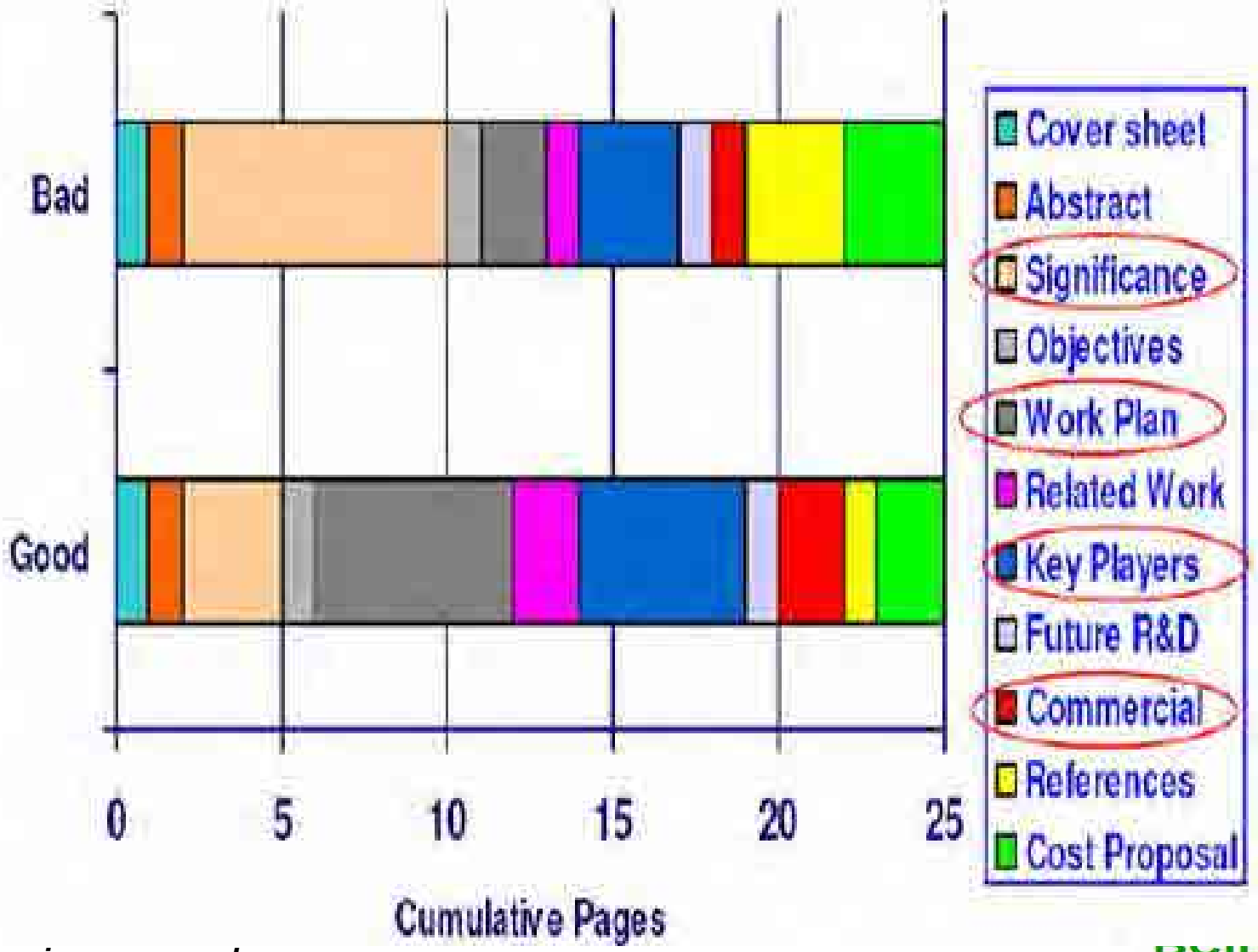
Summary

- ✓ 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



Source: g-jggreenwood.com

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 !

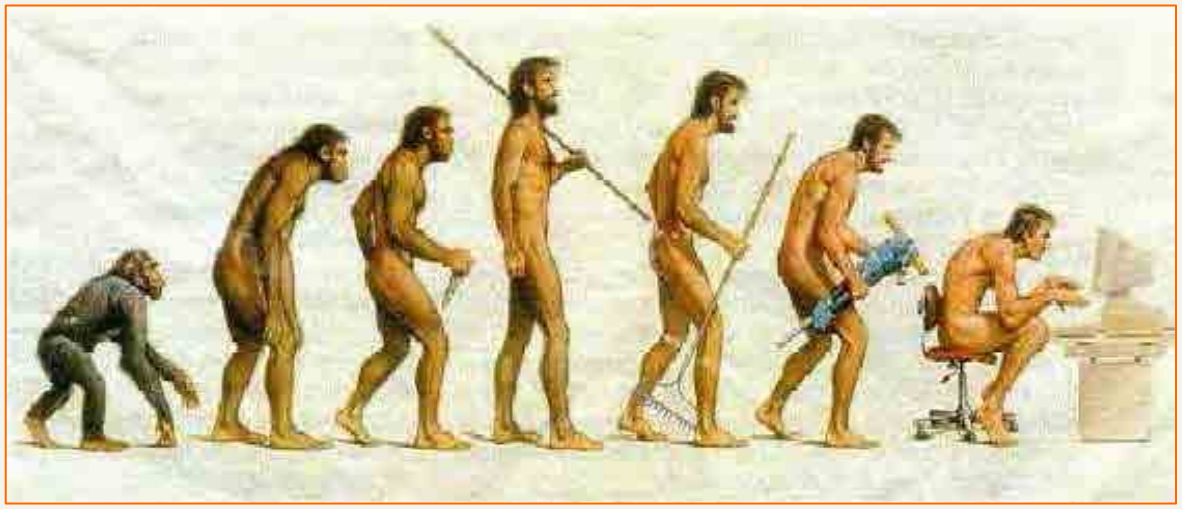
Funds for innovation

- Grant proposal

Dr. M. UDAYAKUMAR
Professor
Department of Crop Physiology
UAS, GKVK, Bangalore 560 065

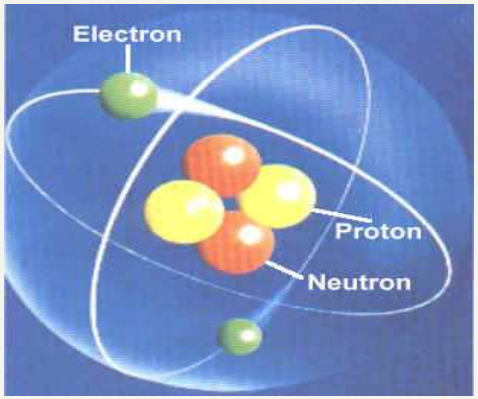
Funds for Innovation

- Innovation has been the steering force for progress



Civilized society always excited with

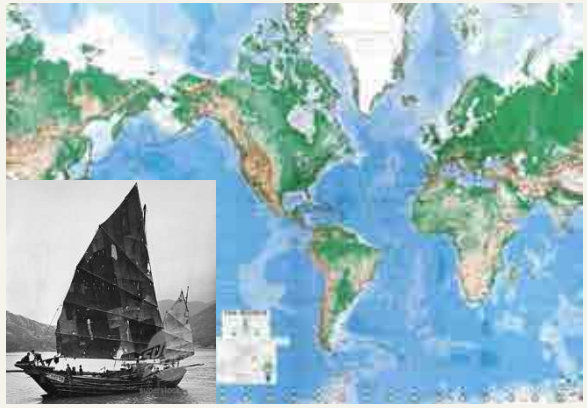
Discovery

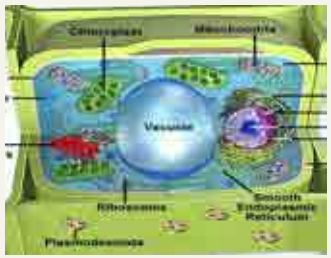


Invention

Innovation

Discoveries are always exciting ! !





Invention

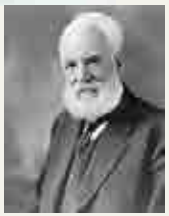
A creation (a new device or process) resulting from experimentation / discovery

Steam engine

James Watt

Windmill

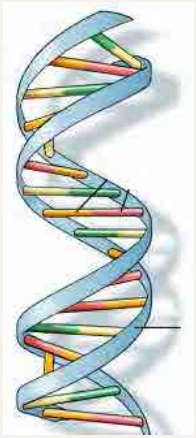
Phone



Graham Bell

Innovation

Invention when improves some product, process or service for the public, then that invention transforms into an innovation.



Bt cotton

Research and development is no more for inquisitiveness

R & D is for societal benefit

It is need driven

Need

Ideas
&
Approaches

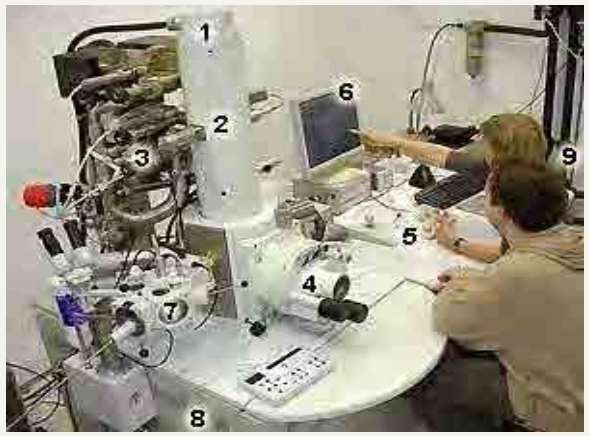
Funding

Drives the Invention and Innovation

Why funding ?

Infrastructure

Man power



Instruments

Knowledge acquisition

Interaction

Where the funds come from ?

Is the modern society

keen to promote science ?

Innovation ?

YES

At whom we look for funding?

R & D organizations

mainly public sectors

(Institutions/universities)

- Made significant contribution in knowledge generation and discovery and to some extent inventions

Translating the discovery/inventions to innovative product/process For social benefit is the missing link

Industry

Drives the innovations to develop products / processes

Several funding agencies to promote science

DST,
DBT,
DAE,
MOES,
ICMR,
UGC

Discovery, ….
Invention

Do we have agencies to promote invention / innovations by private sectors?

Innovation

leading to product / process development

Has phenomenal impact on economy & social benefit

Innovation by industry

needs to be nurtured & supported

What are funding agencies supporting this cause

- **TDB – DST**
  (Mandate is different)

- **Are there any others?**

BIRAP

Biotechnology industry research assistant programme

A unique initiative to promote growth of Indian biotech industry

BIPP (Biotechnology industry partnership programme) is a crucial component of BIRAP

BIPP

Biotech industry partnership programme

Provides support to innovative programme of the industry

To get the support from any funding agency

It is crucial

a) Areas of funding by the agency

b) Problem identified should meet the aim /goal (philosophy) of the agency

BIPP - Categories of Programmes

Bt cotton

BRL-1

Containment facilities

- 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

The first step of the inventor

is

a) Problem identification

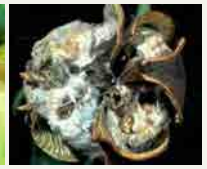
b) To develop the project proposal

i) to convey the philosophy of the project

ii) the relevance

iii) likely deliverables to solve a specific problem

Grant proposal writing and its presentation has phenomenal significance

Proposal needs to address

-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


The proposal need to be developed

Keeping in view the evaluation criteria of the project

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

Identification of the problem

- It should be relevant
- There must be innovative approach to address the problem

Case study:

Major constraints to realize the potential yields of cotton

Yield losses due to

- *H.armigera* (20 – 60%)
- sucking pest (22 -35 %)
- weeds (15 – 30%)

Improving Bt-cotton

for sucking pests and effective control of weeds is useful

Criteria - Significance

Relevance and significance of the proposed project

- The problem is of great concern
- Addressing the problem will have economic benefits to the society
- out come of the project solve the problem

Case study:

Bollworm

Sucking pest

Weeds

- Reduce yield loss
- ↓ Cost of cultivation

Insect resistant plant

Improving insect tolerance and effective control of weeds has phenomenal significance

Criteria – commercial potential / societal relevance

How to address the problem
review the status/options
justify the approach proposed

Case study:

What are the options to improve the tolerance ? …

- Identifying resistant genotypes
- Integrated pest management (IPM)
- Genetic improvement
  - Transgenics
  - Molecular breeding

What is the status in the literature on these aspects

a) Present status of IPM
b) relevant resistant sources/ constraints
c) Are there validated insecticidal proteins / genes
d) Which is the effective herbicide – do we have options to improve resistance to herbicide

Scientific strategy

What is the scientific strategy to address the problem

- **Based on the existing scientific options**
- **Should be noval / innovative**
- **Implementable in time lines**

Case study:

- **There is no known sources of resistance**
- **Improving insect and herbicide resistance by transgenic approach is relevant**
- **Identify/relevant genes coding for insecticidal proteins**
- **(*Cry1Ac* & Garlic Lectin) and**
- **herbicide tolerant genes (*igrA*)**
- **co expressing by multigene constructs**

Criteria –scientific merit

Two options

✓Stack the genes by crossing
by developing individual transgenics

- Bt cotton
- lectin cotton
- herbicide tolerance cotton

✓Transfer a cotton genotype
- with multigene cassette with all the three genes

Multigene Construct is advantages
because
“one locus” no segregation

Criteria –innovativeness

TITLE of PROPOSAL

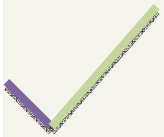
- The project title should be short, concise, and preferably refer to a certain key project result or the project activity

- 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 cotton for International markets" - Title is diffused



"co-expression of insecticidal protein cry1Ac, lectin and herbicide resistance gene igra to improve multiple biotic stress tolerance" – Title is more specific

It is clear from the title that simultaneous expression of specific genes is the focus to improve biotic stress tolerance in cotton. And thus, to address important constraint from insect and weeds.

Novelty of the scientific strategy

New approaches to achieve the goal using already validated approach

What is the novelty….?

- **Simultaneously developing resistance to both *H.armigera* and sucking pests**
- **Value addition by managing the weeds**
- **Avoid antibiotic marker for selection**
- **All the genes is in single locus**
- **Cost effective / time saving**

Criteria –innovativeness

What is the invention step in the project

Develop a new approach / process to exploit the existing scientific knowledge

Case study:

The function of cry1Ac, Lectin and igrA is known

a) **Developing a strategy for developing multigene construct for co expression of *cry1Ac*, Garlic lectin and *igrA***

b) **Approach for transforming the multigene construct**

c) **Suitable protocols for characterization of transgenics**

Preliminary work done

Scientific data to support the proposed concept / scientific strategy

- ✓ It could be from the literature

- ✓ In-house - Experiments

Case study:

- ➢ Relevance of the proposed study
- ➢ Proof to support abilities to develop multigene constructs
- ➢ Proof to demonstrate the availability and ability to study bioeffecacy

Goal & objectives

Goal – To develop a product/process by addressing a constraint

Case study:

Goal - " Improving resistance to insect pest and herbicide"

Objectives:

What is proposed to achieve adapting a well defined plan of work or methodology

Case study:

-Development of multigene construct with *Cry1AC, GL (Garlic lectin)* and *IgrA*

-Development of transgenics with multigene construct and characterization of putative transformants

-Evaluation of transgenics for better performance based on bio-efficacy

Criteria –approach

Plan of work should address

a. Conceptual frame work

b. Design of the experiments

c. Methodologies

a) To generate product/ process

b) Test the product process

d. Components to be outsourced

Conceptual frame work

Genes

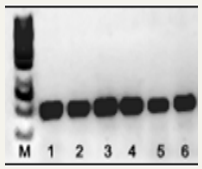
AGTCAAGGCACATACA
CTTCAGTCCGGTACTACT
GTTGTTAGAGGACCCGG
ATTCACGGGAGGAGAC
ATTCTTCGTCGTACAAGTG
GAGGACCCTTTGCTTACA
CTATCGTTAACATCAATG

Transformation

Characterization

Gene construct

Transformants



Characterization

Events

Field evaluation

Criteria –approach

Work plan

Elements of work to be implemented as per the proposed objectives

It is desirable to plan for work elements as objective wise

Case study:

transgenic development and evaluation

Objective: multigene construct

-Method and steps to develop construct

Objective: development of transgenics and their characterization

-Protocols to be adapted and proposed selection

-number of events to be generated

-Evaluation of trasngenics

- **Molecular characteristion**
- **Insect infestation / ex[poser**

Objective: evaluation of the Bio-effecacy of transgenics

- Bioassays against insects

- Bioassay against herbicide

Criteria –approach & methodology

Expertise and infrastructure

Crucial to implement the objectives

- Critical assessment
- To bring in expertise by hiring
- Develop required infrastructure as the essential component of the project budget

- likely collaborators

Collaboration and public private partnership

In-spite of focused objectives and approaches often projects are not considered

Because of lack of expertise and infrastructure in proposed / specified area

We need to find collaborators for facilities and expertise

– we should work together

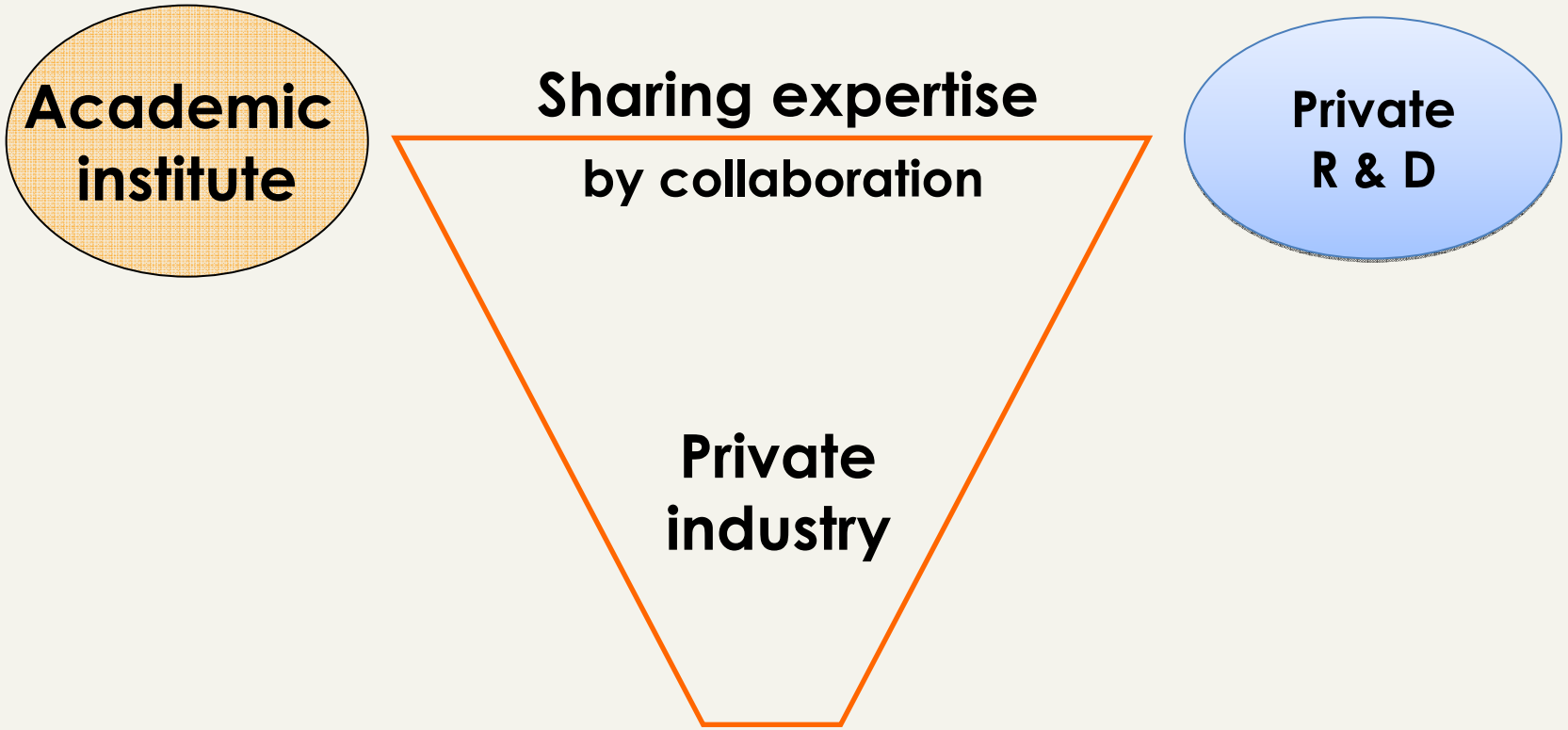
Diverse expertise is needed

to address the research programmes

collaboration is the key

Recent concept is

Knowledge economy partnership



Time lines

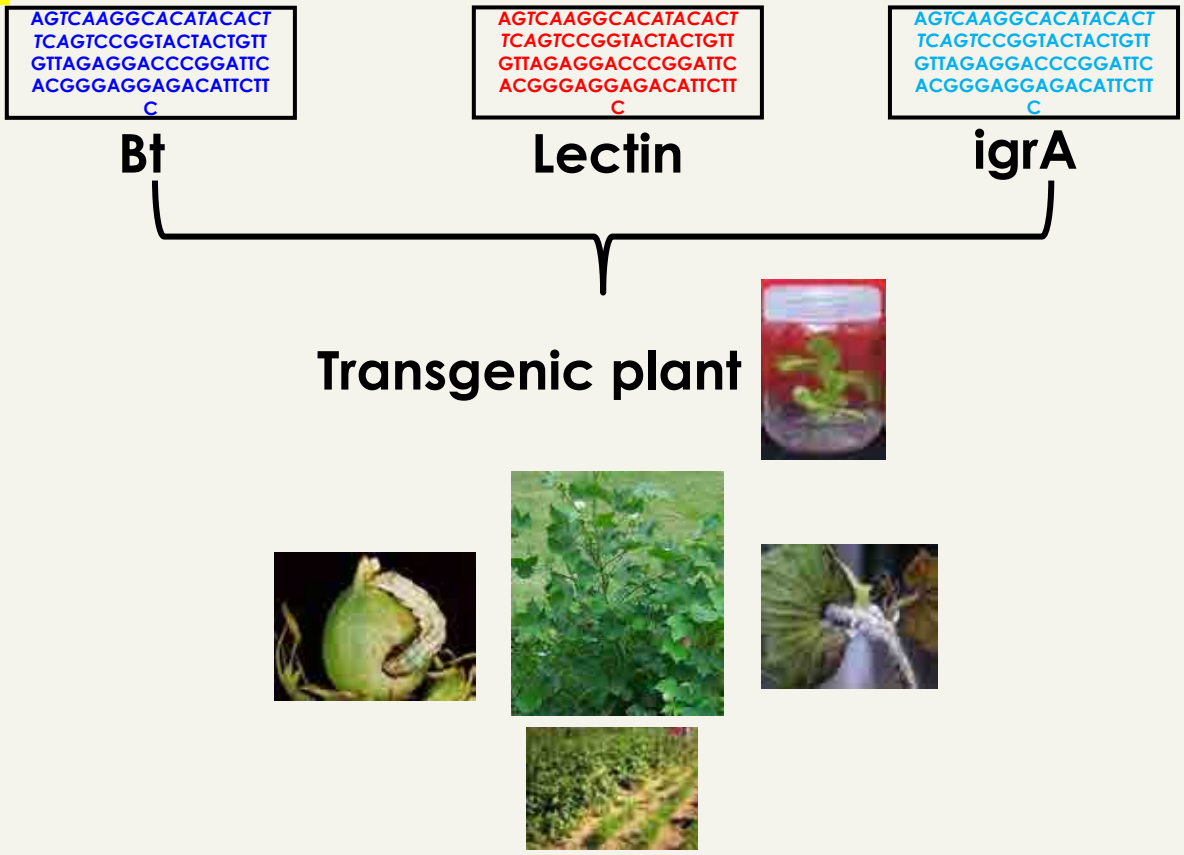
- It is crucial to be realistic
- Transformation and development of transformants is species specific
- Bio-efficacy tests involves rising the plant material
- Number of transformants/events that needs to be evaluated in confinement facility

Innovativeness of the project

Does the project generate noval concept?

From the existing scientific knowledge / inventions developing a product

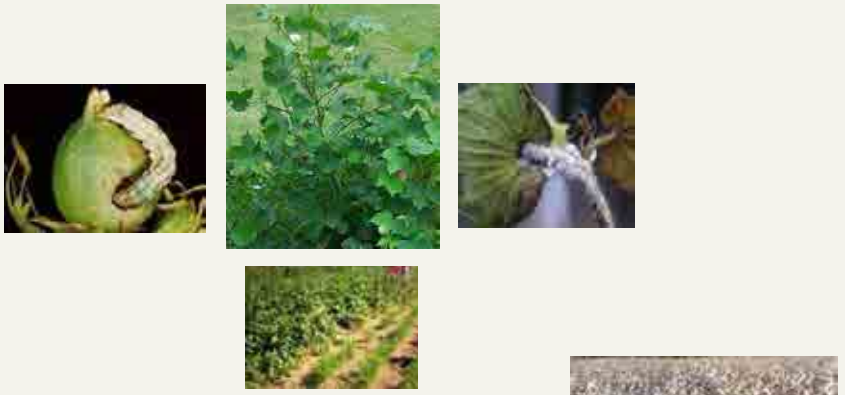
Case study:



Out come/ deliverables

✓ **Multigene expressing cassettes with specific genes**

✓ **Transgenic events with multiple stress tolerant**



Cotton transgenic event with Improved productivity

Other aspects

Budget

Man power

Should match

the work elements

Equipments

Infrastructure

} Required for the project experiments

Consumables

contingency

} Justify based on the planned programme

IP

Important for transgenic work
even for the molecular breeding

FTO – for

- genes / construct etc

- QTL , QTL donors

Abstract / summary

Most important component

Should be concise **Should be one page**

It should cover

- **Need / relevance / importance**
- **Brief description of strategy / approaches**
- **Goals & objectives**
- **The amount of funding that is being sought**
- **Expected out come and also success indicators**

Funds for innovation

In-summary

- **Industry drives the innovations to develop products / process**
- **Besides noval ideas**

  Funding drives the innovations
- **BIRAP - BIPP**

  Initiative to promote biotech industry
- **Grant proposal and its presentation has phenomenal significance**
- **A comprehensive proposal – needs to be developed**
  - **Problem / relevance**
  - **Approach to inplement**
  - **Out come / deliverables**

Thank you

Department of Biotechnology
Ministry of Science and Technology

HOW TO WRITE AN EFFECTIVE GRANT PROPOSAL

BCIL Biotech Consortium India Limited

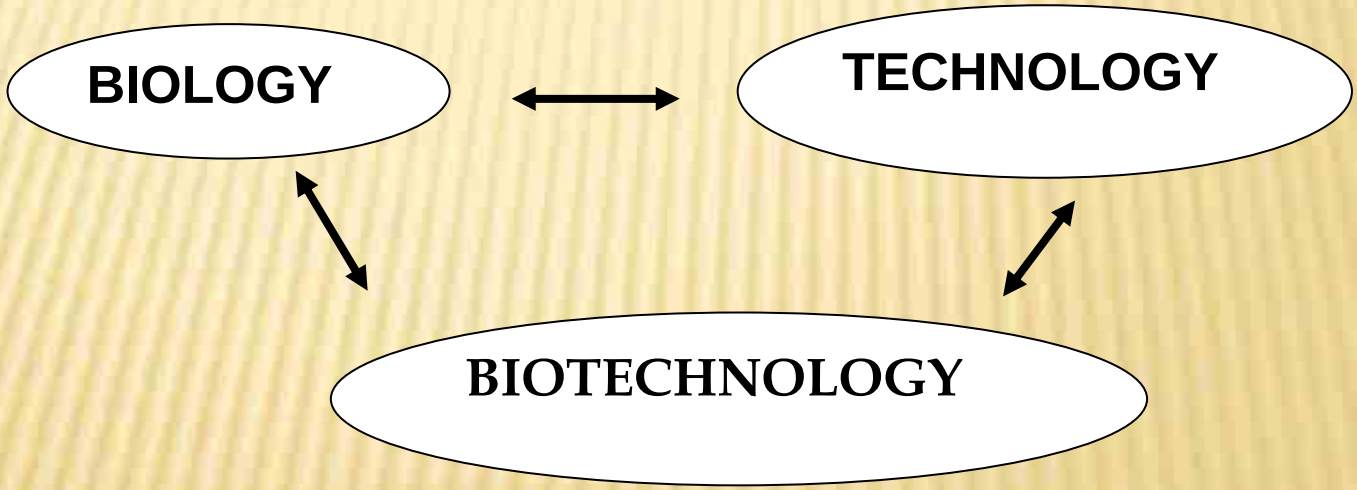
BIRAP
The Biotechnology Industry Research Assistance Program
Incubating. Discovering. Innovating

Sathguru
Catalysing Success

BIOTECHNOLOGY

Technological exploitation and control of biological processes

VII Int. 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**

Century	Definition
19	Fermentation
20	Bio-chemical engineering
21	Bio-molecular 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
   - heterologuos therapeutic protein
   - gene delivery vectors/DNA vaccine

Estimated species diversity in nature

Group of Organisms	Estimated number of species	Characterized number of species (% 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	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

Four primary classes of biological molecules

- Proteins
- Nucleic Acids
- Carbohydrates
- Lipids

- **Proteins as a class are ideal for biological application**
- **Practical challenges are usually encountered with other three classes**

Diverse biological applications of the proteins

1. Therapeutics (hormone, interferon)
2. Enzymes [catalyst]

   high value product, value addition
3. Diagnostic reagents
4. Vaccines
5. Biomarkers
6. Monoclonal antibodies
7. Transgenic systems

MAIN COMPONENTS OF THE APPLICATION

1. Title of the proposal
2. Novelty / innovative quality
3. Preliminary work performed
4. National importance
5. Objectives
6. Milestones with timelines
7. Budget
8. General lacunae in the proposals
9. Evaluation process
10. After the sanction of the project

Title of the proposal

Appropriate title with clear expression and concept

- ✓ Company ABC submitted a proposal to develop a novel immunoassay for HPV using the flash type chemiluminiscence format and magnetic particle matrix

- ✖ Novel immunoassay format
- ✖ Diagnostic kits for detection of Human Papiloma Virus
- ✖ Immunodiagnostic kit using magnetic particles

Novelty / innovative quality

Area: Immuno-diagnostics

1. **Novel markers for the disease/serotypes**
2. **Ways and means to produce and characterize the markers**
3. **Improvement in 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)

- Should clearly define how the core element of the proposal can address the existing gap

- 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

INNOVATION

Innovation in industry addresses a technical challenge, reduces time and/or cuts costs

1) Indirect ELISA:

Several primary antibodies but a single secondary antibody – linked to an enzyme

2) Paramagnetic beads for separation of analytes

Efficient washing

3) A homogeneous immuno-assay

No washing step to remove unused analytes

4) Anti-HIV HTS assay

The assay should distinguish between anti-viral and cytotoxic molecules

Innovation in Biosimilar Product (Insulin)

Noble prize was awarded for insulin on four different occasions

1. **Different expression system**
   (*E. coli* / *Lactobacilus* / yeast / CHO / fungus)

2. **Different version of *insulin***
   (normal / long-lasting / fast-acting / peg-insulin)

3. **Novel ways of purification and refolding**

4. **Novel ways of delivering insulin**
   (oral / mucosal / single-dose)

PRELIMINARY WORK PERFORMED
(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

- Preliminary data supporting the working hypothesis must be provided
  - Proof-of-the-concept data as tables, graphs etc
- The functional roles of the collaborator and the company must be clearly delineated
- For projects of exploration
  - Scientific justification
  - Preliminary experimental data should be provided

NATIONAL IMPORTANCE AND RELEVANCE

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

Various studies have established that oncogenic Human Papilloma Virus (HPV) is associated with almost all cases of cervical cancer.

Simultaneously, outside Africa, India harbors the highest number of people living with HIV known to increase the chances of acquiring and maintaining the oncogenic HPV.

The high incidence of cervical cancer due to HPV is huge in India – 76.7%. Lack of high throughput automated immunoassay systems and reagents – a serious problem.

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.

NATIONAL IMPORTANCE AND RELEVANCE

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

Anti-HIV medicines:

1) Several against RT and protease
2) Few against integrase
3) None to Tat-TAR

OBJECTIVES

Objectives should be “SHARP“ and “QUANTIFIABLE”

- Design
- Feasibility
- Optimization
- Validation

- ✓ Development of XYZ labelled magnetic particles as a universal matrix for different assay formats for different analytes
- ✓ Flash type chemiluminiscence reporting for enhanced sensitivity and improved signal to noise ratio

---

State clearly 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 amenable for monitoring, time-bound and specific

BUDGET SUPPORTED WITH PROPER QUOTES

Neither inflated nor under-estimated

Equipments:

- As per the need of the proposal
- High end equipment specific to the proposal

Manpower:

- as per Govt. norms

Consumables:

- only for the proposed work

Outsourcing:

- minimized to the extent possible

Travel and contingency:

- should be properly justified

After securing the project

1. Execution and Accountability

- *Adhere to the timelines*
- *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*

GENERAL LACUNAE IN PROPOSALS

- Lack of technical competence:
  - The collaborating partners lack technical competence and/or expertise in the area of proposal
- Lack of preliminary data:
  - Proof-of-the-concept data not provideded
- Noncompliance with regulatory requirements:
  - Without completion of requisite data and regulatory clearances the next stage proposal submitted
- Wrong format of application:
  - Clinical Trial project submitted in R&D category form
- Essential information kept confidential:
  - Specific structure/class of the molecule, genes expressing specific proteins are not revealed
- Impractical goals:
  - 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
Total Marks	100

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)

Recombinant Insulin

Insulin Requirement: 500 mg/person/year (type I Diabetes)

World 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

Penicillin

4 Amino acids → $ 25/Kg

Insulin

51 Amino acids → $ 300/Kg
Assuming Insulin 100 times more complex than Penicillin
Cost of production should have been $ 30,000/Kg

Hepatitis B

227 Amino acids → $ 1,300/Kg
Assuming HBsAg 1,000 times complex than Penicillin
Cost of production should have been $ 1,000,000/Kg
That is $ 1/mg = US$ 0.02/dose (20 μg)
Rs 1.00/20 μg (one single dose)

Vaccine development

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 pre-clinical evaluation**
4. **Facility for clinical supply**
5. **Manufacturing facility**
6. **Supply chain with stability analysis**
7. **Assay development**
8. **Clinical trials (assay for protection)**
9. **Regulatory frame work**
10. **Marketing/Pharmaco-vigilance**

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

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

Vaccines provide a cost effective means for health care treatment for Infectious diseases

Best examples: Small pox eradication

Investment

Two Decades: $ 25 million / year (Expenses)

Total of $ 500 million

Results

Lives saved **40 Million / Two decades**

$ 275 million / year on quarantine and treatment

Total savings $ 6,500 million

Hepatitis B Surface Antigen (HBsAg)

- Need three injections (0, 1 and 6 month)
- Recombinant Yeast produced (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 OD_{600} culture)

2. Purification

Around 30-50 % recovery, avoid tag
look for soluble aggregates

3. Formulation and stability

Adsorption/ new adjuvants/excipients/delivery

Want to move faster : go alone

Want to move farther : go together

[BCIL/BIRAP]

Meeting your strategic goals – BIPP is your gateway

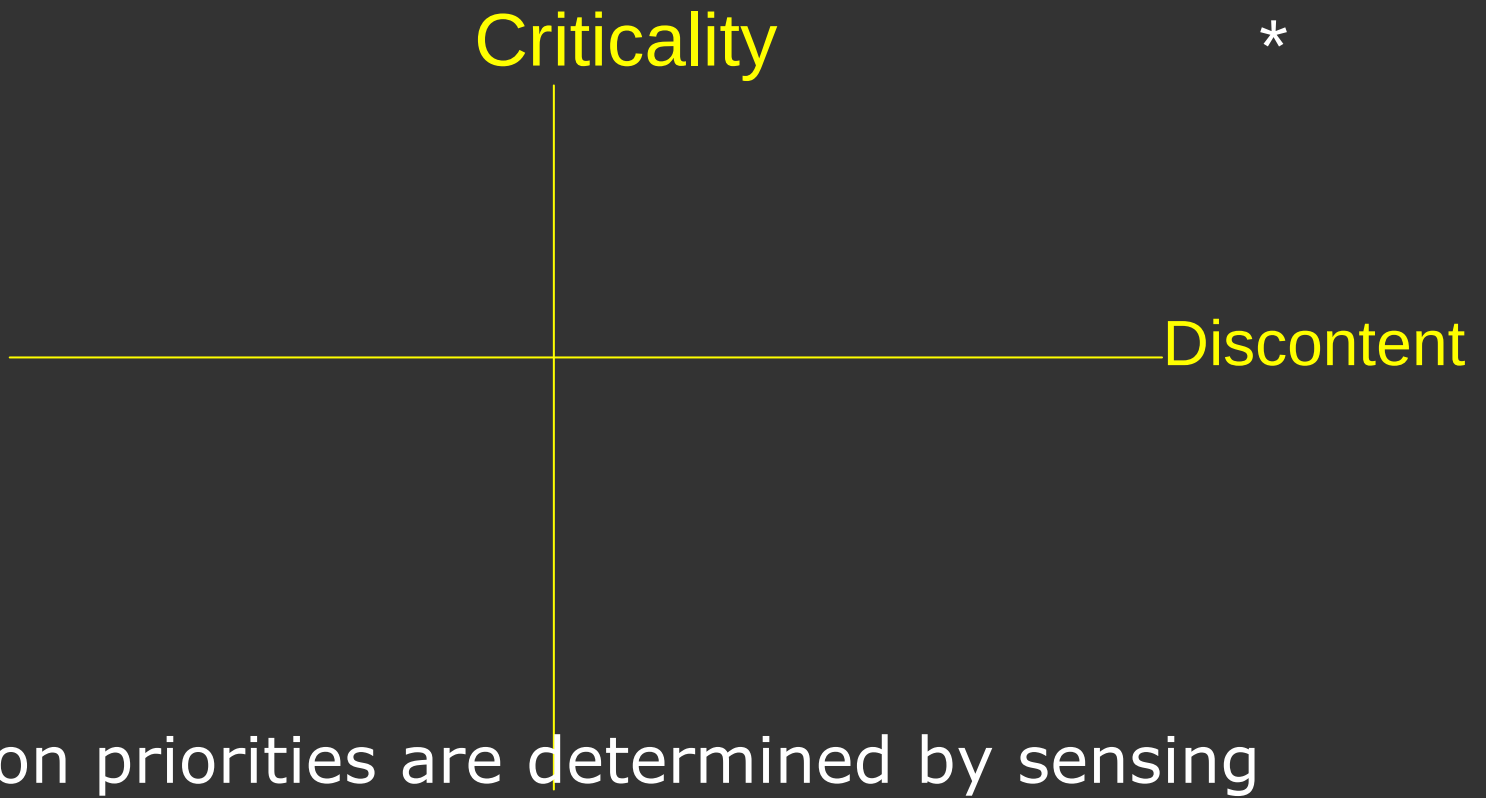
Sathguru Management Consultants

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

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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.

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- 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.

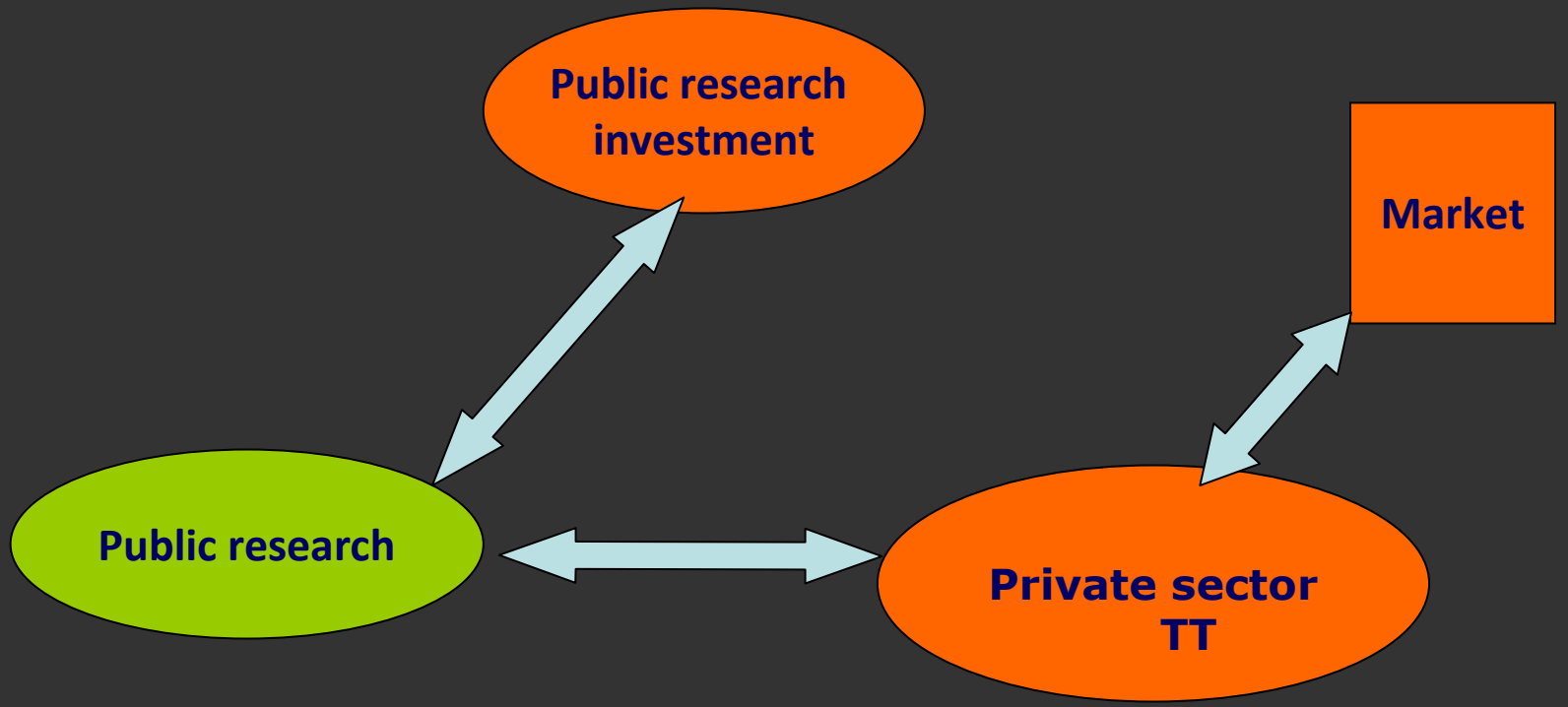
YOU CAN'T ACCESS BROADER MARKETS WITHOUT PLATFORM TECHNOLOGIES

COLLABORATIVE RESEARCH

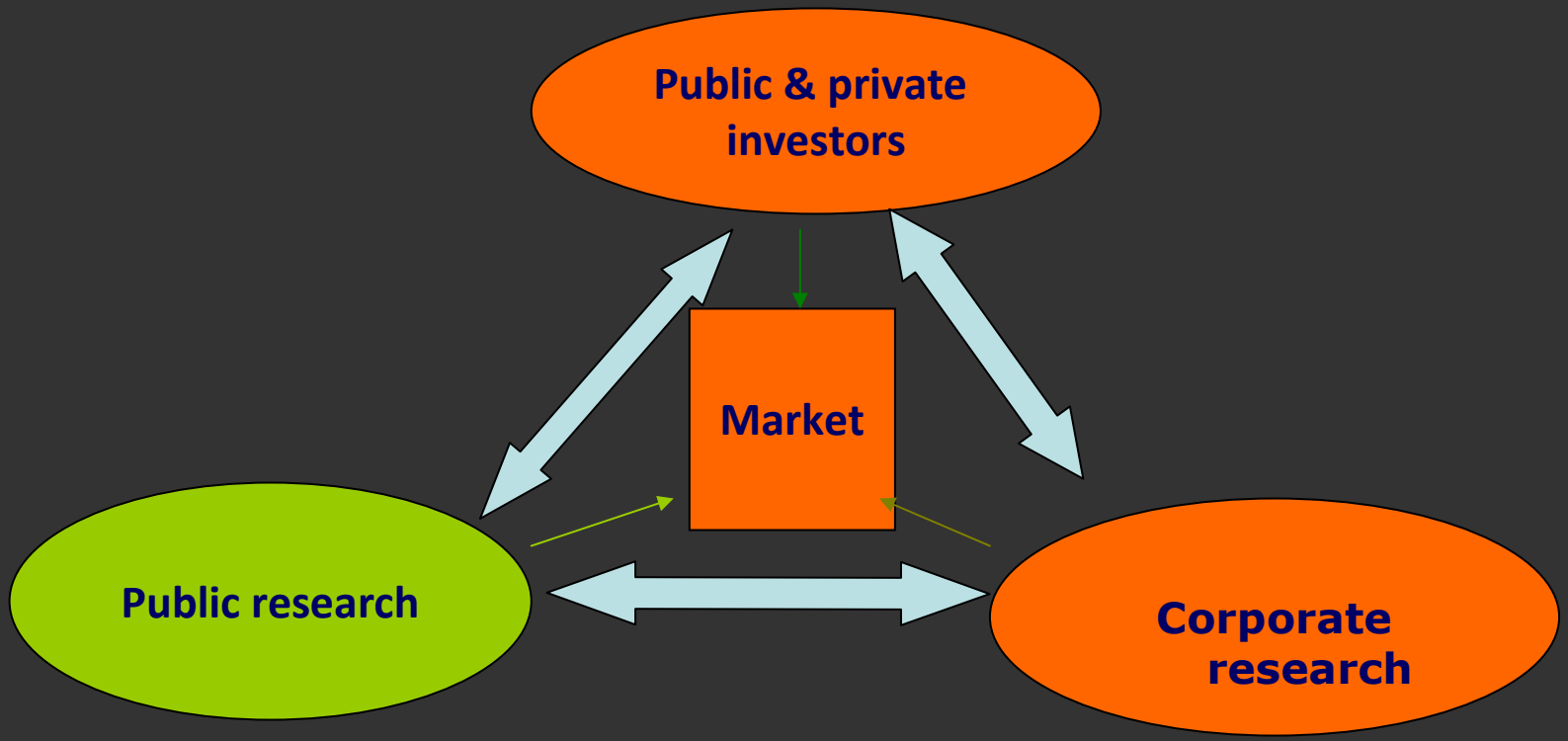
- Bridge the technology – market gap.
- Multi-partner role.
- Resource augmentation potential.
- Public – private research partnership.
- New orientation to Corporate Research ability and focus.

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.



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.**

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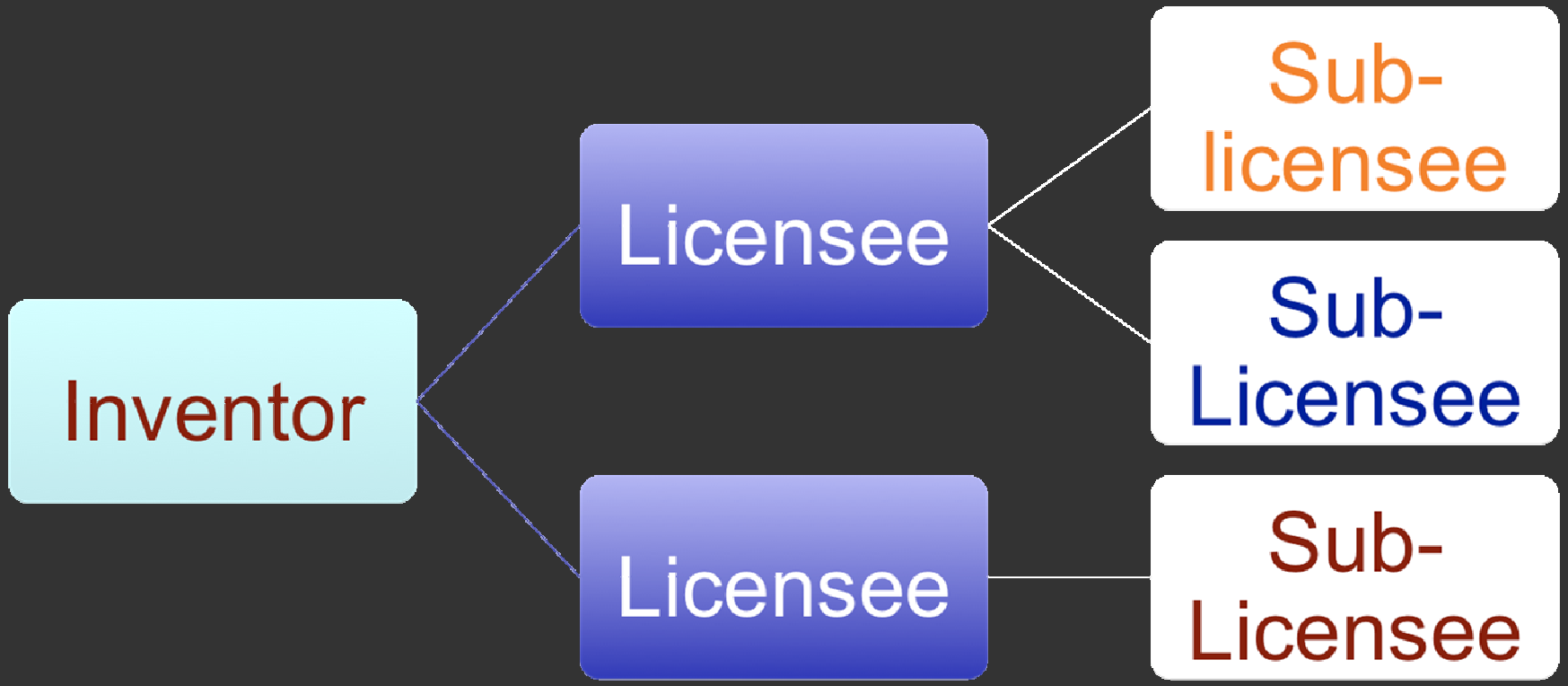
Stage 4 – Combine execution effectiveness and strategy

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.

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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?
- Tltle 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

- Challenge
- Alternative analysis
- Solution
- Execution.

IP at all stages

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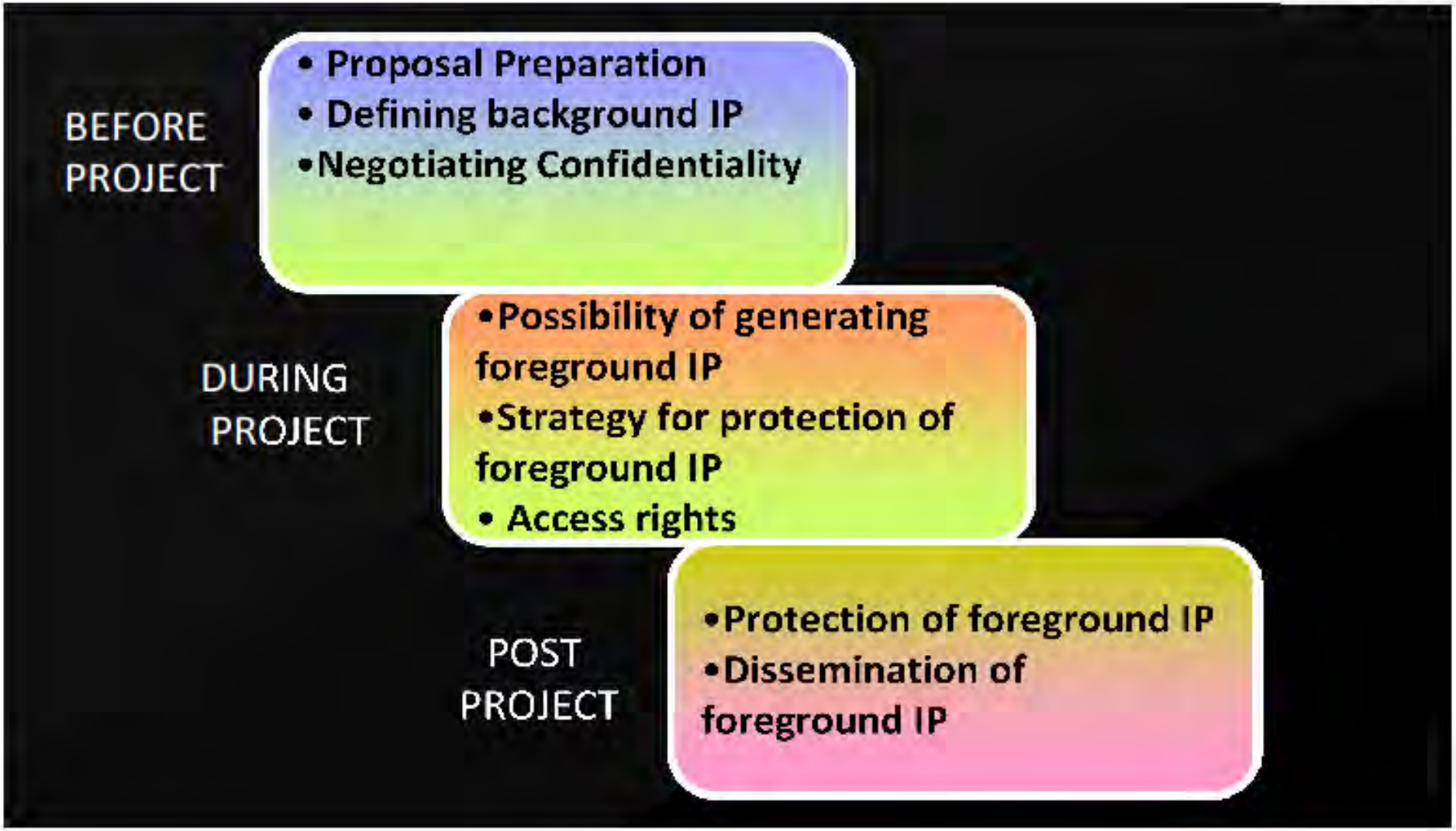

Addressing IP Issues in a Grant Proposal

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- 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.

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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.

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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.

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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

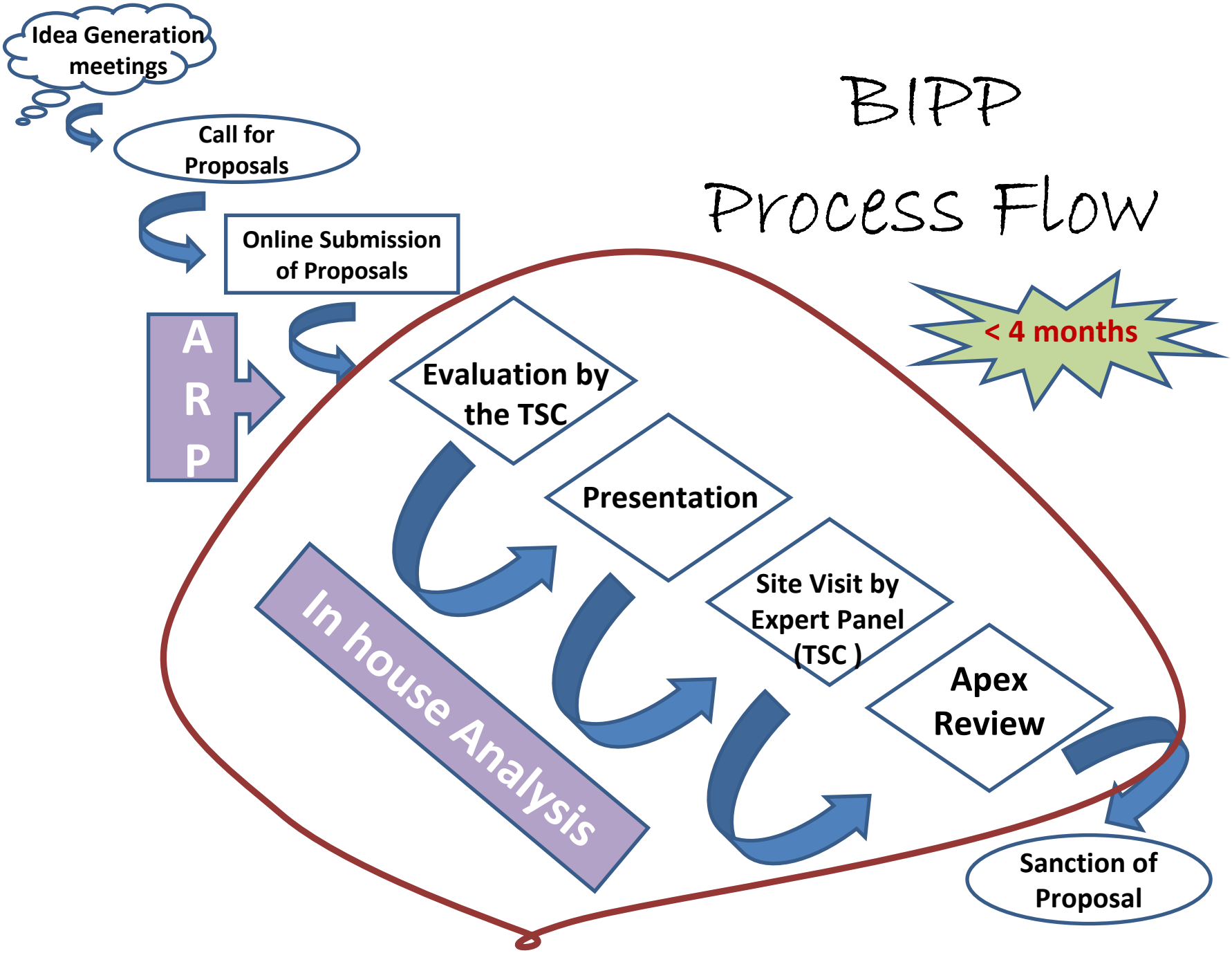
Ms. Shilpy Kochhar

Assistant Manager

Biotech Consortium India Limited (BCIL)

BIPP

Process Flow



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

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	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

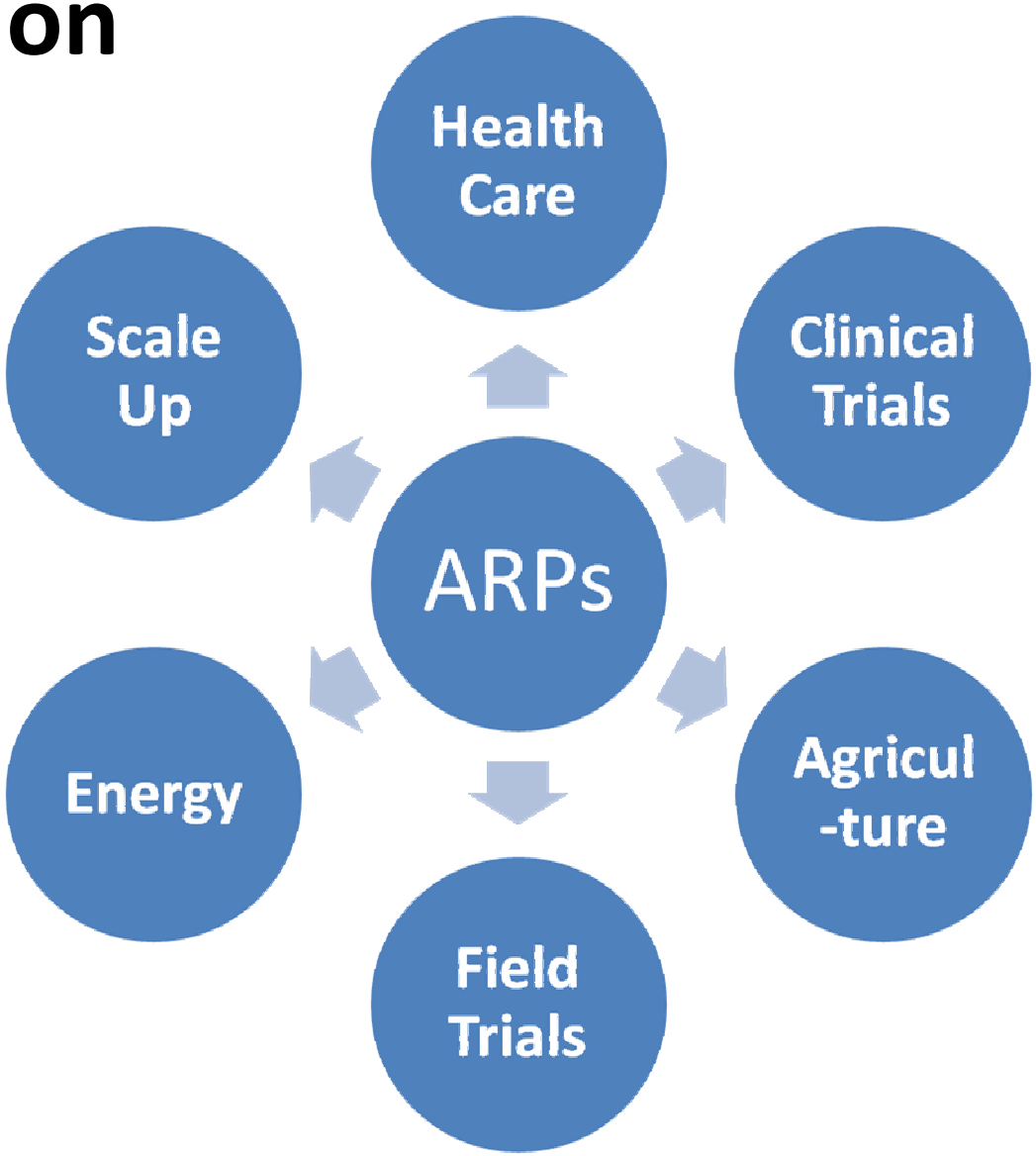
- DSIR recognition for the in-house R&D lab **mandatory** for the primary applicant as well as for all company type collaborators
- In case, DSIR is unavailable, it is mandatory to have **applied to DSIR** before proposal submission
- **For incubatees**:
- DSIR recognition of the incubator is considered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

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*

Any other need based specialized review



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

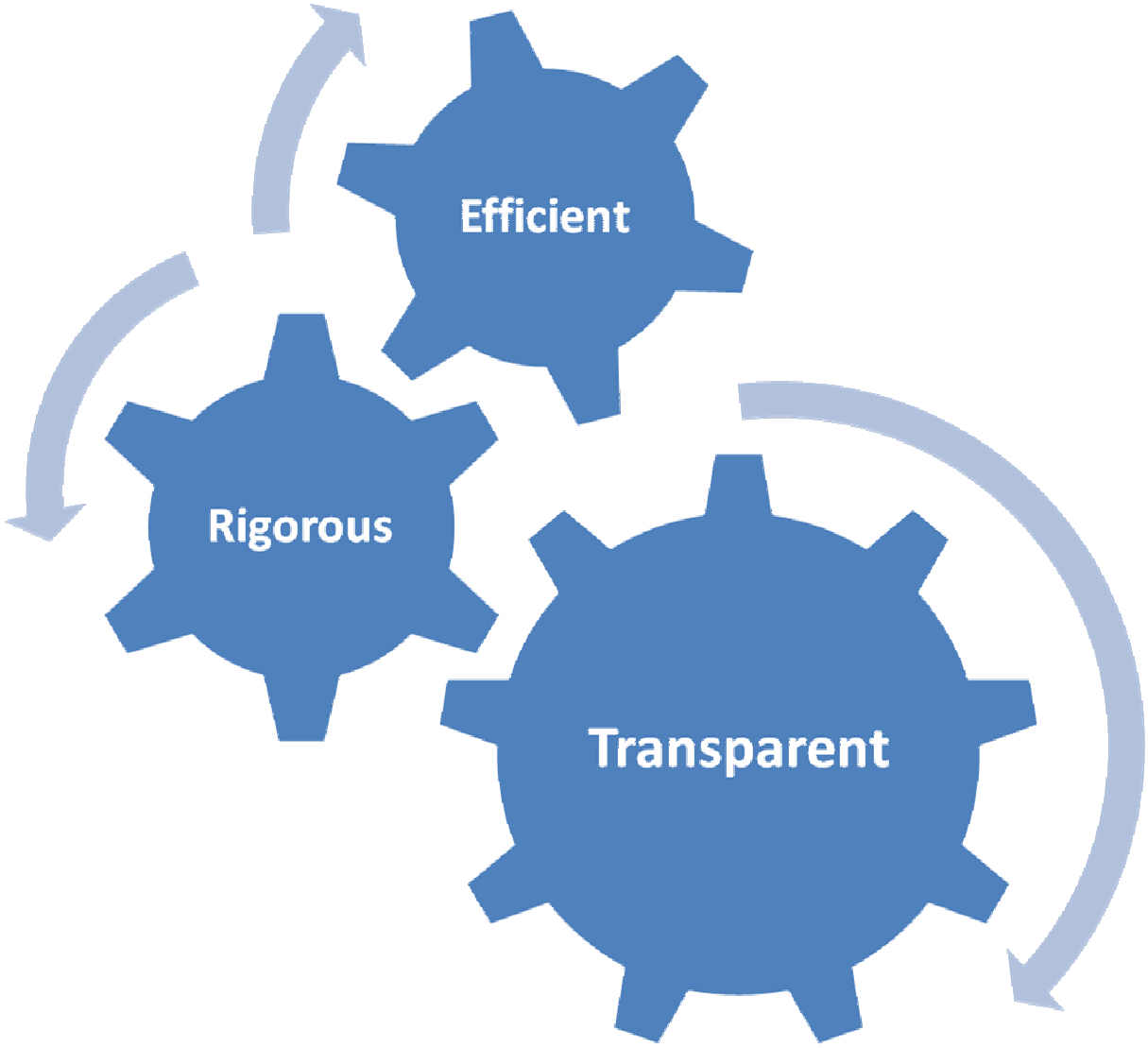
In case of short term projects, at least one site visit is ensured.

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 ?????