NETWORK OF LABORATORIES FOR SAFETY ASSESSMENT OF GM CROPS: ISSUES AND CHALLENGES

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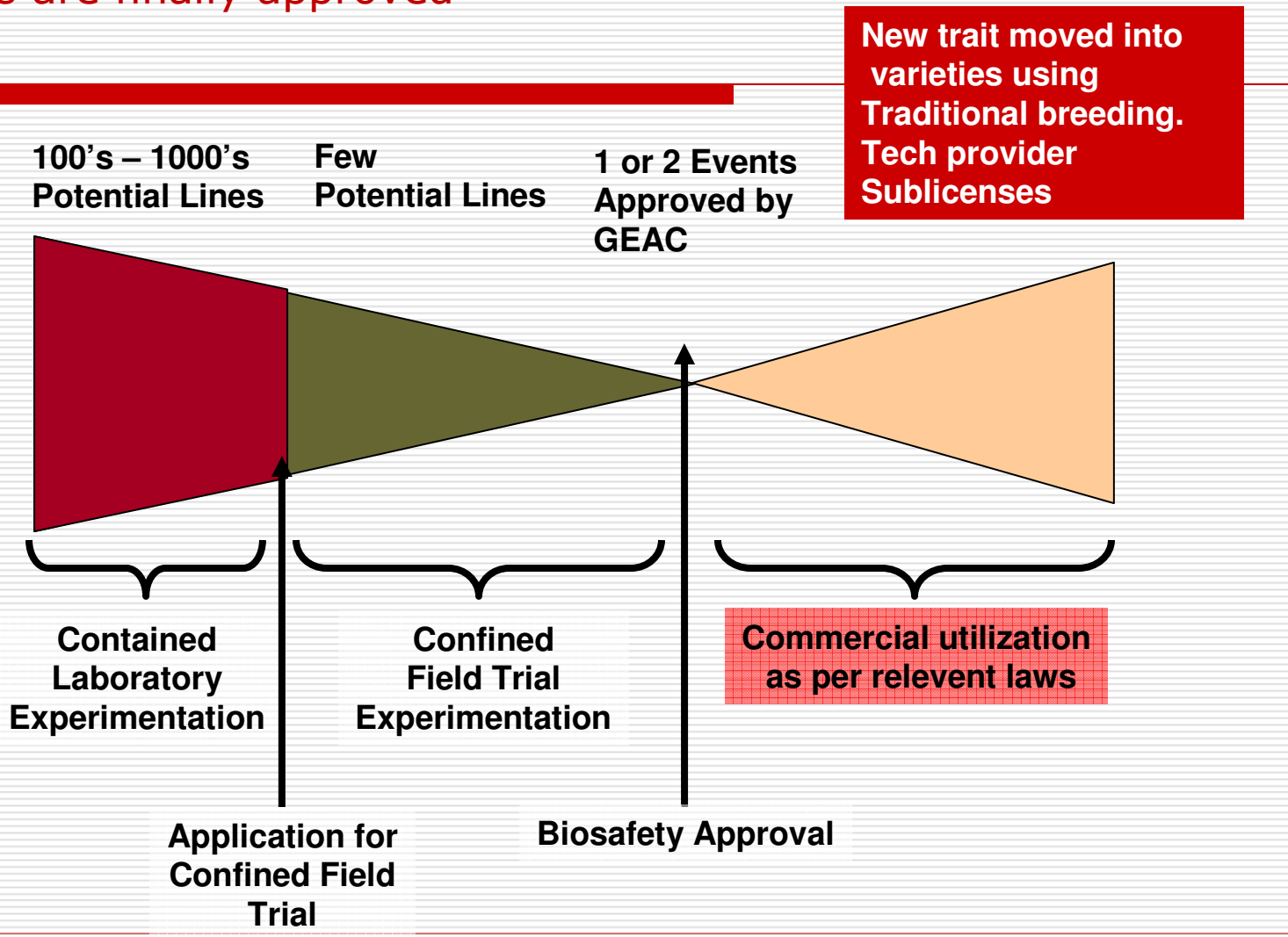
REGULATORY GUIDELINES FOR SAFETY ASSESSMENT OF GM CROPS

- Recombinant DNA Safety Guidelines, 1990
- Revised guidelines for research in transgenic plants & guidelines for toxicity and allergenicity evaluation of transgenic seeds, plants and plant parts, 1998
- Guidelines and Standard Operating Procedures (SOPs) for Confined Field Trials of Regulated, Genetically Engineered (GE) Plants - 2008
- Guidelines for the Safety Assessment of Foods Derived from Genetically Engineered Plants - 2008
- Protocols for Food and Feed Safety Assessment of GE crops - 2008

EVENT BASED APPROVAL SYSTEM OF A GE PLANT

Extensive safety assessment required; only limited lines under confined field trials are finally approved



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SAFETY CONSIDERATIONS

Core Characterization

Gene(s)

- Source(s)
- Molecular characterization
- Insert / copy number / gene integrity

Protein(s)

- History of safe use and consumption
- Function / specificity / mode-of-action
- Levels
- Toxicology / allergenicity testing

Food/Feed Composition

- Proximate analysis
- Key nutrients
- Key anti-nutrients
- Animal performance assessment

Environmental

- Host organism
- Safety to non-target organisms
- Soil degradation, toxicity
- Outcrossing, weediness

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Safety studies and Confined field trials

- Studies that should be completed before Biosafety Research Level I (BRL-I) trials are undertaken
- Field studies that should be completed during BRL-I and/or Biosafety Research Level II (BRL-II) trials
- Non-field studies that should be completed in parallel to BRL-I and BRL-II.

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STUDIES TO BE COMPLETED BEFORE INITIATING BRL-1 TRIALS

STUDIES TO BE COMPLETED	Food & Feed Safety Assessment			Environmental Risk Assessment		
	Before first field trial	Field studies	Non-field studies*	Before first field trial	Field studies	Non-field studies*
Description of the genetically engineered plant						
Biology of the non-transgenic host plant						
Donor organism information						
Bioinformatic analysis: potential toxicity and allergenicity						

run concurrently with field trials

Contd/-

Recommendations for staged completion of specific information and data requirements for the safety assessment of GE plants

STUDIES TO BE COMPLETED	Food & Feed Safety Assessment		Environmental Risk Assessment	
	Field studies	Non-field studies*	Field studies	Non-field studies*
Acute oral safety limit study				
Pepsin digestibility assay				
Protein thermal stability				
Subchronic feeding study in rodents (if required)				
Livestock feeding study (if required)				
Molecular characterization				
Inheritance of introduced trait				
Stability of introduced trait				
Expression of introduced protein(s)				
Compositional analysis				
Reproductive and survival biology				
Impact on non-target organisms: Tier I testing				
Impact on non-target organisms: Tier 2 testing				

run concurrently with field trials

STUDIES/INFORMATION THAT SHOULD BE COMPLETED BEFORE INITIATING BRL1 TRIALS

- **Description of the GE Plant**
- **Description of the Biology of the Non-Transgenic Host Plant**
- **Description of the Genetic Modification(s)**
- **Assessment of Possible Toxicity and Allergenicity :** homology of the newly expressed protein with known protein toxins, anti nutrients and allergens using bioinformatics
- **Conformation of Inheritance of the New Trait(s) Over Multiple Generations:**

FIELD STUDIES THAT SHOULD BE COMPLETED DURING BRL I AND/OR BRL II TRIALS

- **Include both in-field experiments and Studies that require plant material collected from field trials**
  1. Confirmation of expression levels of new proteins
  2. Data about reproductive and survival biology as compared to non transformed counterpart
  3. Impact on non target organisms
  4. Compositional analysis of key components
  5. Live stock feeding performance studies

NON-FIELD STUDIES THAT SHOULD BE COMPLETED

- During the period that confined field trials will be undertaken, other non-field studies necessary to meet information and data requirements for the environmental risk assessment of GE plants should also commence.

1. Molecular characterization of the GE plant
2. Assessment of possible toxicity
3. Assessment of possible allergenicity

Assessment of Possible Toxicity and allergenicity

- Pepsin digestion of each newly expressed protein.
- Structural, functional and biochemical equivalence of the non-plant expressed protein with the plant expressed protein, if a host other than plant is used for production of the protein.
- Acute oral toxicity study.
- Sub chronic feeding study.
- Testing in immunological assays, where sera are available (if required).

COMPOSITIONAL ANALYSES OF KEY COMPONENTS

- **For all other parts of the GE plant and its conventional counterparts that may be used as food or livestock feed, provide the following:**

  Proximate composition e.g., ash, moisture content, crude protein, crude fat, crude carbohydrate;

  Content of true protein, non-protein nitrogenous material (e.g., nucleic acids and aminoglycosides), amino acid profile.

  Quantitative and qualitative composition of total lipids.

COMPOSITIONAL ANALYSES OF KEY COMPONENTS (CONTD.)

Composition of the carbohydrate fraction e.g., sugars, starches, chitin, tannins, non-starch polysaccharides and lignin;

Qualitative and quantitative composition of micronutrients, i.e., significant vitamin and mineral analysis;

Presence of naturally occurring or adventitious anti-nutritional factors e.g., phytates, trypsin inhibitors, etc.;

Predictable secondary metabolites, physiologically active (bioactive) substances.

IMPACT ON NON-TARGET ORGANISMS

- Tier 1 studies: Laboratory-based, non-target organism studies using test diets incorporating concentrations of the target protein at, or above, the maximum estimated environmental exposure. Representative non-target organismsTier 1 testing are:
  - **Mammalian *e.g.*, mouse**
  - **Avian model**
  - **Freshwater fish**
  - **Aquatic invertebrate**
  - **Non-target arthropods:**
    - **Honey bee larvae and adults (*Apis mellifera*)**
    - **Lady beetle (*Hippodamia convergent*)**
    - **Green lacewing (*Chrysopa carnea*)**
    - **Parasitic hymenopteran (*Brachymeria intermedia*)**
    - **Collembola**
    - **Earthworm (*Lumbricus terrestris)***

LIVESTOCK FEEDING PERFORMANCE STUDIES

- Livestock feeding trials as required on a case-by case basis as per the DBT publication “Protocols for Food and Feed Safety Assessment of GE Crops”

Present status of pre approval testing in India

- The tests undertaken in private testing labs, contract research organisations and national institutions are accepted by regulatory agencies
- The private testing labs and CROs are either accredited by National Accreditation Board for Laboratories or GLP Compliance Committee under DST

Issues and Challenges

- Specific guidelines required for handing GM crops and products

Example : in June 2007, the NABL published "Specific Guidelines for Biological Testing Laboratories",as a supplement to ISO/IEC 17025 and applicable to laboratories using techniques in areas related to toxicology, veterinary science, biochemistry, molecular biology and cell culture. These guidelines provide specific guidance for both assessors and for laboratories carrying out biological testing and set out the specific requirements that a biological testing laboratory has to meet.

Issues and Challenges

- Safety parameters highly dependent on the crop/trait/use etc., multidiscplinary expertise required to develop testing protocols
- Need for active interaction between technology developers, testing labs and regulators

  Safety testing protocols provided by regulators are generic and specific action would depend on crop/trait/intended use

Issues and Challenges

- Capacity building in labs required with respect to handing GM crops
- National labs need special training with respect to maintaining GLP and other testing standards

SUGGESTIONS

- To develop a network of organisations to facilitate complementary services for fulfilling comprhensive testing requirements

- To implement an accreditation system for referral laboratories that provide testing services for the safety assessment of GM crops and foods derived from these. The accreditation system should be specific for pre-commercial (*i.e.*, pre-approval) testing.

SUGGESTIONS

- Stipulation of data quality standards for all of the types of studies submitted to support the safety assessment of GMOs and these specific requirements.
- Submission of proof of accreditation by GLP or NABL to the regulatory agencies.
- To maintain and publish a roster of accredited organisations as this information will be of value to both the regulatory agencies as well as product developers wishing to use accredited laboratories.

THANK YOU!