DATA QUALITY IN SAFETY ASSESSMENT OF GE CROPS:

ISSUES AND CHALLENGES

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SAFETY ASSESSMENT OF GE CROPS

Applications for the commercial approval of a GM crop are usually supported by risk assessments conducted using scientific methodology and with the purpose of facilitating decision-making.

- The risk assessments are **planned** taking into account the national regulatory framework
- The risk assessments are conducted on a **case-by-case** basis, taking into consideration the **crop/trait combination** and the **receiving environment**.
- The data used to support this assessment is carefully generated to ensure that it fulfills the country regulatory requirements and addresses all the relevant questions for that particular GM crop .

DATA GENERATED TO SUPPORT SAFETY ASSESSMENTS

- Product Developers are required to generate required data during product development and this includes :

  - Data generated during research and development
  - Data gathered in regulatory studies
    - Laboratory studies
    - Field studies
  - Post-commercialisation data

Data generation

- Data collected in the analysis phase are crucial to the outcome of the risk assessment and ultimately the decision taken by regulatory authorities

- Useful data of sufficient quality may already exist:
  - Scientific literature
  - Previously conducted studies
  - New studies carried out especially for the risk assessment

Present status of pre approval testing in India

- The food and feed safety assessment tests are 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
- The confined field trials and any other environmental safety sudies are being done by product developers , sometimes in association with SAUs or agriculture research institutions

Challenges

- Safety parameters highly dependent on the crop/trait/use etc., multidisciplinary 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

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
- 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.

Planning data generation during safety assessment

- To take into account available literature
- Clearly understand the data requirements and work on objectives of studies
- Plan in such a way so that maximum information can be collected during experiments
- Present analysis of experimental studies along with available information , history of safe use and decisions by other regulatory authorities

EXAMPLE : Assessing Changes in Weediness Potential – What is "Weediness"?

- Weediness is the measure of a plant's ability to successfully colonize a managed and/or unmanaged ecosystem
  - A plant out of place
- Weediness generally depends on the selective advantage conferred by *many genes acting in combination*
- Some properties of the "ideal weed" (Baker 1965)
  - Discontinuous germination and great longevity of seed
  - Rapid growth to flowering
  - Long, continuous and high seed production under range of environments
  - Self-compatible, but not obligatorily self-pollinated or apomictic
  - Cross pollination by wind or unspecialized pollinator
  - Special adaptations for short- and long-distance seed dispersal

Examples of Reproductive and Survival Biology Parameters that can be Measured in field trial

- Growth habit and morphology
- Days to emergence
- Seedling vigour / early growth
- Days to flowering/pollen shed
- Duration of flowering/pollen shed
- Pollen morphology and viability
- Days to maturity
- Seed/fruit production (yield)
- Plant population at harvest
- Seed germination (lab and/or field)
- Observations on susceptibility to natural infestation/infection with common pests/diseases

Typical Conclusions that can be Drawn from Phenotypic Data

- *The agronomic performance and phenotypic data generated for Event-A derived hybrids and their corresponding near isogenic non-transgenic control hybrids suggest that the genetic modification resulting in Event-A did not have any unintended effect on plant growth habit and general morphology, lifespan, vegetative vigour, flowering and pollination, grain yield, or disease susceptibility.*
- *These data support the conclusion that Event-A derived hybrids are unlikely to form feral persistent populations, or to be more invasive or weedy than conventional maize hybrids, and would not display higher rates of outcrossing than unmodified maize.*

Example : Gene Flow

- The movements of genes and organisms over the landscape are natural processes that only came to public attention in the assessment of GM crops
- Transfer of "GM genes" (transgenes) cannot occur in isolation of the other crop genes: the entire crop genome is subject to transfer at the same time
- The process of genetic modification does not allow the transgenes to move any more freely than any other gene: stability of the insertion into the genome is assessed during product development
- *Does "gene flow" need to be studied in confined field trials?*

In the Absence of Significant Differences in Plant Morphological Parameters, Repeating Gene Flow Studies is Unlikely to be Informative

It is the Consequences of Pollen-Mediated Gene Flow that Require Analysis

Data Analysis

- In any case where there is the potential for pollen-mediated gene flow, it is important to *consider the consequences, not the frequency*
- Is the introduced trait similar to a trait currently found in sexually compatible relatives in the environment?
- Does the introduced trait have potential to increase fitness or confer selective advantage?
  - Impact on establishment and spread of wild relatives?
  - Is this potential any different from the potential due to an existing trait?
- *This type of impact analysis is more important than empirical data on gene flow frequency*

Using available data

- Local product developed 'de novo'
  - No prior pre-market risk assessment
  - All risk assessment data need to be developed locally
- Products/simillar products already approved and being tested for local deployment
  - Prior risk assessment and commercialization in country of origin
  - Wealth of existing data that may be utilized
  - Questions that need considering –
    - What makes the local receiving environment uniquely different?
    - What new/other risk hypotheses require testing?
    - What data are transportable – i.e., foreign data that can be used for the local assessment?
    - What additional or new data are actually required?

Important Considerations for Already-Approved GE Plant Events in other countries

- A wealth of data / studies supporting environmental, food, feed safety in the country of origin
- Prior risk assessment reports and regulatory decision documents by competent authorities in the country of origin
- A history of safe use (familiarity) –
  - Cultivation by farmers
  - Use in livestock feed
  - Use as food
- *There must be a way to capitalize on this experience, data, and familiarity without going back to "square one"*

Data quality considerations

- Focus on Appropriateness, accuracy, integrity, transparency
- Avoid Your scientist *vs*. my scientist; your study *vs*. my study

Data quality

- Appropriateness: The degree to which data are relevant and applicable to a particular exposure assessment.
- Accuracy: The degree to which measured, calculated, or modeled values correspond to the true values of what they are intended to represent.
- Integrity: The degree to which the data collected and reported are what they purport to be.
- Transparency: The clarity and completeness with which all key data, methods, and processes, as well as the underlying assumptions and limitations, are documented and available.

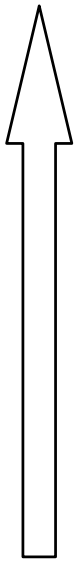
Data acceptability by regulators

- Data acceptability is determined by comparing the type and quality of data with the minimum criteria necessary
- Acceptability criteria to be determined by regulations and notified by regulatory authorities (guidance)

Data quality specifications

- "Hallmarks of data quality" have been notified by WHO in 2008 and the same could be applied to safety assessment of GE plants
- e.g. OGTR's Risk Analysis Framework addresses the quality of evidence
- The provision of such guidance about data quality assists both the product developer and strengthens the robustness of the risk assessment

Ranking of types of information and their relative values as evidence (OGTR 2009)

	Reliability	Appropriateness
 **Increasing value**	Validated studies conducted according to international protocols meeting defined standards.	Experimental data on the GMO and/or parent organism in the Australian environment.
	Peer reviewed literature – strongly supported reports, models, theories.	Experimental data on the GMO and/or parent organism overseas.
	Peer reviewed literature – single report, model, theory.	Experimental data on modified traits in other organisms.
	General biological principles.	Experimental data on related, surrogate systems.
	Opinion of an expert familiar with the GMO, parent organism, modified traits, ecology.	
	Other technical reports, specialist literature (for example, beekeeping), government reports, etc.	
	No information to indicate a problem.	
	Unsubstantiated statements.	

Concluding Comments

- Quality data facilitates the safety assessment by regulators
- It helps in peer review and reproducability
- It helps in accepatibilty of data acrooss boundaries and transportability
- However the focus should be on n "need to know" not "nice to know"
- Need for practical guidelines for RA and a "robust" regulatory structure
- …But locally affordable and locally relevant

How to get from here

To here?

THANK YOU!