Low Level Presence: Present Situation and Market Implications

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Risk Assessment

The Plant Biotechnology and Biosafety Workshop

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Outline

- Introduction to low level presence
- GM food safety assessment
- Low level presence in GM food
- Environmental risk assessment
- Low level presence in seed
- International efforts to address LLP in food and seed

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What is “low level presence”?

- “Some adventitious mixing is unavoidable”
- Low levels of GM events that have been approved in the country of origin and that are present in shipments to importing countries that have yet to approve these events
- Zero tolerance for unapproved events is the regulatory norm
- Does not refer to events that have not been authorized for commercialization anywhere

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Sources of LLP

- Asynchronous approvals
  - Most likely cause of LLP
  - At least one cultivating country has already authorized a GM event while other importing countries have not
- Isolated foreign approvals
  - A cultivating country has authorized a GM event, but its developer does not seek approval in importing countries
- Result: Trade disruptions

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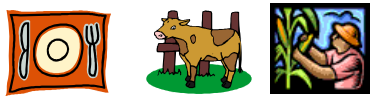
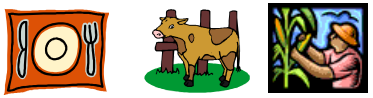
Example times to approvals

- Canada: 20-24 months 
- USA: 24-30 months  FDA: 12-18 months 
- Japan: 36 months (~ 1 year taken up with the stage-3 field trial in-country)  ()
- EU: 42-48 months 
- China: 30-36 months (only 3 application dates per year, March 1, July 1, and Nov 1; in-country field trial) 
- Mexico: 9-12 months assuming prior USA or Canada approval 
- Australia & New Zealand: 9 months 
- Brazil: 8-12 months 

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Traditional views of food safety

- Historically, our beliefs about the safety of foods have been based almost entirely on tradition and cultural experience
- In practice, very few of the foods we eat today have been subject to any toxicological studies and yet they are generally accepted as safe
- Even foods that contain toxins or anti-nutrients or allergens have been considered safe through a long history of use
  - Consider potatoes, tomatoes, peanuts, eggs, milk products, wheat products, strawberries and other fruits, fish, shellfish, etc.

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GM food safety assessment

- At the heart of the safety assessment process is the principle that GM foods CAN be compared with traditional counterparts that have an established history of safe use
- This comparison can be based on an examination of the same types of risk factors for both (e.g. toxins, potential allergens, key nutrients, anti-nutrients).

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Codex 2003 Plant Guideline

- Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant DNA-Plants
- The Guideline supports the Principles for the Risk Analysis of Foods Derived from Modern Biotechnology.
- Addresses safety and nutritional aspects of foods consisting of, or derived from, plants that have a history of safe use as sources of food, and that have been modified by modern biotechnology to exhibit new or altered expression of traits.
- It does not address animal feed or animals fed with the feed.
- It does not address environmental risks.

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Framework of the GE food safety assessment

- Description of the rDNA plant
- Description of host plant and its use as food
- Description of donor organism(s)
- Description of the genetic modification(s)
- Characterization of the genetic modification(s)
- Safety assessment:
  - Expressed substances
  - Assessment of potential toxicity and allergenicity
  - Compositional analyses of key components
  - Evaluation of metabolites
  - Food processing
  - Nutritional modification
  - Other considerations (e.g. marker genes)

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Annexes to the Codex Plant Guideline

- Annex 1: Assessment of Possible Allergenicity (2003)
- Annex 2: Food Safety Assessment of Foods Derived from rDNA Plants Modified for Nutritional or Health Benefits (2008)
- Annex 3: Food Safety Assessment in Situations of Low-Level Presence of rDNA Plant Material in Food (2008)

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Defining LLP in food in Annex 3

- "Low levels of recombinant DNA plant materials that have passed a food safety assessment according to the Codex Guideline for the conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants in one or more countries may on occasion be present in food in importing countries in which the food safety of the relevant recombinant-DNA plants has not been determined."

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Importance of the Codex Plant Guideline

- Created a robust, scientifically sound and internationally accepted approach to the safety assessment of GM foods
- Has facilitated harmonization as many countries have used the Codex Principles and the Plant Guideline in new or revised national regulations or guidance
- Very helpful for the resolution of LLP in food situations

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Environmental risk assessment (ERA)

- No "Codex equivalent" organization
- Key intergovernmental players
  - Organisation for Economic Cooperation and Development (OECD)
  - International Plant Protection Convention (IPPC)
  - Cartagena Protocol on Biosafety

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Environmental risk assessment

- What is risk assessment?
  - The process of establishing information regarding acceptable levels of a risk and/or levels of risk for an individual, group, society, or the environment (Society for Risk Analysis)
- What is risk?
  - Risk = hazard x exposure

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Sources of potential harm

- Concerns that are consistently addressed across different regulatory systems:
  - Will the GM plant become a weed of agriculture or invasive of natural habitats?
  - Will gene flow to sexually compatible relatives result in established populations of weedy or invasive hybrids?
  - Will there be an adverse environmental impact on non-target organisms?
  - Will there be an adverse impact on biodiversity? (usually addressed by a weight of evidence approach based on the first three sources of potential harm)

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Defining “LLP in seed”

- Seed that contains a low level of a GM event that has been authorized for commercial cultivation (following an environmental risk assessment) in one or more countries but not in the country of import

Seed includes…

Scenario 1: Viable plant material imported for FFP

Scenario 2: Seed for planting

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ERA of LLP in seed

- ERA of LLP in seed should follow the accepted risk assessment paradigm
  - Risk = hazard x exposure
  - Trait - host plant - receiving environment
- Use problem formulation to identify plausible risk hypotheses
  - Utilize information and data from existing ERAs (and literature)

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Commercial approval in one or more other countries implies that…

- No evidence that the reproductive biology of the plant was altered, thus the potential for weediness or invasiveness is unchanged
- Impacts of gene flow to sexually compatible relatives in that geography considered minimal
- No anticipated environmental impact on non-target organisms in that geography
- No anticipated impact on biodiversity in the cultivating country

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Let's apply what we know…

- ERA of LLP in seed should explicitly take into account:
  - The extensive body of knowledge gained from ERA of GM events for unconfined release
  - The experience and knowledge gained from cultivating GM crops
  - The mitigating impact afforded by low-level exposure

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Examples sources of information

- Biology documents
  - OECD consensus documents
  - Country biology documents
- CERA monographs on the environmental safety of novel proteins
  - PAT, CP4EPSPS, Cry1Ab, Cry1Ac, Vip3Aa, Cry34Ab/Cry35Ab
- Risk assessments and decision documents published by regulatory authorities
- Databases
  - OECD BioTrack
  - BCH
  - CERA's GM Crop Database

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Options for addressing ERA of LLP in seed

Option 1: ERA based on a subset of data, relevant only to plausible risk hypotheses

- Case-specific
- Provides flexibility for country-specific exemptions (e.g., crops that will not persist in the receiving environment; familiar proteins with a history of environmental safety)
- Generation of in-country data is not required

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Options for addressing ERA of LLP in seed

Option 2: Acceptance of scientific opinion prepared by the regulatory authority in the country where the GM event has been approved for cultivation

- Recognizes the harmonized nature of ERA guidance
- No new ERA required by the country of import

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Options for addressing ERA of LLP in seed

Option 3: No requirement for any ERA for LLP in seed scenarios

- Recognizes that to date no GM crop plants have had adverse environmental impacts (e.g., EC DG Research. 2010. "A Decade of EU-funded GMO Research")

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Options for addressing ERA of LLP in seed

- Scientifically defensible
- Compliant with Parties obligations under the Cartagena Protocol
- Allows regulatory authorities to focus human, financial and institutional resources in a manner that is commensurate with risk

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How to address LLP in the longer term

- The best approach to avoiding LLP situations is to promote the synchronicity of approvals
- This will require harmonization of time standards and will be greatly facilitated by harmonization of requirements and approaches for risk/safety assessment.

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International Engagement on LLP

- 1st International Meeting on LLP
  - Vancouver, Canada in March 2012
  - LLP in food
  - International Statement on Low Level Presence
- 2nd International Meeting on LLP
  - Rosario, Argentina in September 2012
  - LLP in food and seed

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International Engagement on LLP

- OECD Working Group on the Harmonization of Regulatory Oversight in Biotechnology
- "Low Level Presence of Transgenic Plants in Seed and Grain Commodities: Environmental Risk/Safety Assessment , and Availability and Use of Information"

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