



CANADIAN SEED TRADE ASSOCIATION POSITION PAPER

Trace Level Safety Assessment Process for Biotechnology-Derived Material in Seed, Food and Feed

December 4, 2002

Current Situation:

The “Troubles with Thresholds” paper by Bill Leask of the (CSTA) Canadian Seed Trade Association (Nov. 2000) noted that “for decades, national seed certification procedures have been largely harmonized to facilitate international trade of seed. Adventitious (unintended, trace) levels of foreign material and genetic off-types are always present in seed lots and most certification standards specify the acceptable levels for seed purity and genetic purity.”

Why Should We Care?

Unintended, trace levels of foreign material are common and well accepted in society provided that there are no safety concerns. Without a policy and trace level safety assessment process the standard or threshold for biotechnology-derived products has become zero or zero detection. This lack of policy and assessment process has negatively impacted seed, grain and food trade.

Some current examples of current trace level allowances, provided there are no safety concerns, are:

- ? Number 1 Grade Corn may contain up to 2% foreign material
- ? Sugar Free product may contain up to 0.5% sugar per serving
- ? Decaffeinated Coffee may contain up to 3% caffeine
- ? Unapproved pesticide may be present at *de minimus* levels up to 0.1 ppm
- ? Organic Food may contain up to 5% non-organic

Outcome and Scope of this Paper:

There is an urgent need to develop a trace level safety assessment policy plus a review and approval process for unintended, trace levels in seed, grain, food and feed. Two types of situations may be addressed:

- 1) Single occurrence risk assessment for compliance; and
- 2) Continuous unintended, trace level risk assessment for trade.

Different safety assessments may be completed relative to the potential exposure of these situations.

In the United States, the White House Office of Science and Technology Policy has released on August 2, 2002 ‘Proposed Federal Actions to Update Field Test Requirements for Biotechnology Derived Plants and To Establish Early Food Safety Assessments for New Proteins Produced by Such Plants.’ This proposal is aimed to address the potential for the occurrence of intermittent, low-levels of biotechnology derived genes or gene products from crops under development for food or feed prior to full safety assessment.

In Canada, this paper proposes to broaden the scope of trace level (adventitious presence) safety assessments to address early assessment at a defined trigger acreage (eg. 100 ha) for confined field trials or potential imported products from research or approved products in another OECD country. The scope is broader than the U.S. since many crops or plants may not be grown in Canada eg: Cotton, Papaya etc.

This enhanced regulatory oversight will continue the government protection of public health and the environment plus enhance public confidence in biotechnology regulations. Trace level safety assessments will support trade and minimize the potential of seed, grain, food or feed recalls from unintended, trace levels of proteins or biotechnology derived material by providing an approval or safety assessment process.

Definitions:

Trace level safety assessment replaces the terminology adventitious presence in order to be more descriptive and improve understanding.

Adventitious presence or trace levels refers to the unintended, incidental occurrence of trace levels of plant material or protein, from crops developed through modern biotechnology, in seed; grain; livestock feed; or food as a result of natural, mechanical or human means (examples are pollen flow or unintended commingling during production or processing).

“Plant material” or “biotechnology-derived material” means proteins and other expression products [and the genetic material necessary for their production] in a plant improved through modern biotechnology.

Issues:

There is not an international standard, threshold or tolerance for adventitious presence (trace levels) and the few national standards, thresholds or tolerances vary from country to country, both in terms of the levels that are set and what they measure.

- US and Canada lack a national policy for adventitious presence and have no standard, threshold or tolerance for products that are not cleared domestically for commercial introduction -- "0" by default.
- EU has proposed a 1% level for approved and pending (not denied) applications, for Feed and Food approval, and review by a scientific committee within the EU. Experimental field trials are not addressed.

- Countries such as Switzerland, Australia, Brazil, Korea and Japan have adopted standards ranging from 0.1% to 5% (labeling and food/feed application).
- Japan MAFF has proposed a 1% level for unapproved biotechnology products in animal feed. No provision for food.
- All field trials of new crop varieties could raise adventitious presence issues -- this includes crops improved by conventional breeding as well as modern biotechnology.
- Some regulators view detection of DNA as an indication of the presence of the new expressed protein.
- Detection and sampling capabilities -- not risk of harm -- are being used to establish adventitious presence or tolerance levels.

Tiered Approach to Safety Assessment:

A key underpinning of safety assessment with appropriate data requirements is the well accepted approach of risk = hazard x exposure.

The CSTA Seed Thresholds and Detection Methods Seminar on Dec. 11, 2001 developed a tiered approach proposal for adventitious presence or trace level approval process.

Trace Level Presence Category		Example
I	Known Risk/Safety Approved Domestically	GT73 Off-Type in Canola Variety
II	Partially Known Risk/Safety Unapproved but approved in another OECD Country	Corn or Cotton events approved in U.S. Approved protein from another crop
III	Unknown Risk/Safety Research Events	Unfamiliar events or proteins from Confined Field Trials
IV	Molecular Farming Tiered levels of risk/safety assessment based upon trait.	
IV.1	Known Low Risk	High oleic acid trait
IV.2	Partially Known Low Risk	High laurate trait from other crops
IV.3	Unknown Risk	Unfamiliar trait in research
IV.4	High Risk	Pharma Trait

Concept:

1. This paper proposes a procedure for enhanced regulatory oversight of biotechnology-derived plant material (proteins and genetic material necessary for protein production) that may be present at very low, trace levels, in seed or commodity grain crops through “adventitious presence.” This proposal defines “adventitious presence or trace level” as the unintended presence of biotechnology-derived plant material in seed, grain, or food products at trace levels through naturally occurring pollen flow or unintended commingling during the production process.
2. This proposal seeks to provide a regulatory mechanism for review and approval of trace levels of biotechnology derived products with a Defined risk assessment exposure level (threshold or tolerance) based upon a) good agricultural practices, or b) potential trace levels *vis a vis* traditional commodity quality standards. Currently biotechnology products can be approved for confined field trial research (*de minimus* exposure) and full commercial release using a 100% exposure risk assessment. Trace level allowances and regulatory approval systems are currently provided for pesticide residues, food additives, and foreign material in seed, feed, and food with defined tolerance levels. This paper proposes additional regulatory review and an approval framework for trace level allowances by commodity using a defined minimal exposure risk assessment. Minimal exposure can be achieved by compliance with either confinement practices for field trials or good agricultural and best management practices for materials not approved for commercial use in Canada. The proposal does not require one threshold for all commodities but rather allows assessment of a Defined Trace Level by commodity.
3. Under this proposal, the technology provider could submit data and information to the appropriate agencies for assessment when the field testing of a commodity grain crop reaches a predefined level (eg 100 ha). Even if these crops are not commercialized, if their biotechnology-derived plant material is later discovered in seed, grain, or food products at trace levels, that adventitious or trace level presence would have been reviewed by the appropriate regulatory agencies and would have received regulatory safety assessment.

Trace Level Presence:

4. Biotechnology-derived plant material that has not been cleared for commercialization may occur at trace levels either in a biotechnology-derived crop that has otherwise received regulatory clearance, or in a conventional crop. This can occur at extremely low levels, in the field while biotechnology-derived crops are being field tested, as well as during seed handling and processing. Under the following proposal, the regulatory agencies would review issues associated with unintended trace level presence at a relatively early stage. For crops that reach a sufficient stage of development, an appropriate subset of environmental and food/feed safety data and information regarding the biotechnology-derived plant varieties containing the specific protein would be reviewed by the appropriate regulatory agencies while field tests are ongoing.

5. The trace level presence of biotechnology-derived plant material may occur because of the natural process of pollen flow, or by inadvertent commingling of seed. This plant material may ultimately be detected in seed, harvested grain, or processed food products. Current good agricultural practices and processing facilities practices cannot provide 100% genetic purity, nor is such a standard possible in a widespread and complex biological system.
6. Experts looking at trace level or adventitious presence in the U.S., Canada, Argentina and the International Seed Trade Federation have determined that setting a standard for adventitious presence of biotechnology-derived seed at less than 1% is not practicable, and the European Commission's Scientific Committee on Plants has stated that 1% may not be practicable for traits that are widely commercially adopted.

Appropriate Data Set

7. Years of scientific analysis and experience with experimental and approved crops have demonstrated the risks associated with biotechnology-derived crops are similar to those associated with crops developed using conventional breeding and selection. Nevertheless, when up to 100% of a crop variety could contain biotechnology-derived plant material, the current broad and extensive set of data submitted for a product's regulatory assessment remains appropriate. Because seed or grain containing biotechnology-derived plant material poses even less risk when found at trace levels, the submission of a more limited data set, earlier in the development process, would be appropriate for assessment of the unintended trace level presence of biotechnology-derived plant material in seed or grain.
8. The presence of biotechnology-derived plant material at negligible levels would be expected to have minimal effects relative to areas of concern to the reviewing regulatory agencies. Changes in the nutritional value of food produced from grain containing biotechnology-derived plant material at negligible levels would not be meaningful, due to the small percentage of the total nutritional intake that the trace levels of biotechnology-derived plant material would comprise.
9. Under this process, developers would submit a relevant data subset regarding the biotechnology-derived plant material (trait) present in the crop being tested, through a list of defined transformation events. The specific data to be included in such a submission would vary depending on the agencies' familiarity with the relevant crop and protein being tested. This data would be reviewed by CFIA and Health Canada. The data would provide the reviewing agencies sufficient information to assess the relevant environmental, health and safety issues that could arise through the trace level presence of the defined biotechnology-derived material. This review and approval could be for a single occurrence or continuous trace level presence.

Data Submission Procedure :

10. When the field testing of a crop that produces a particular protein reaches a trigger acreage, (eg. 100 ha) containment and good agricultural practices may no longer serve to eliminate the possibility of trace level presence. At this point, developers would provide data regarding the biotechnology-derived plant material to the relevant regulatory agencies. In addition, the developer could also voluntarily provide data for trace level assessment to address potential import concerns from another OECD country.

11. At the trigger acreage or voluntary notification, the developer would supply CFIA with data regarding the encoded protein; a list of events encoding the protein; the familiarity of the host crop and protein; and whether the protein's unintended trace level introduction in the crop through these events would either confer selective advantage on the crop in the environment, or would otherwise increase the crop's potential to become a plant pest.

At the trigger acreage or voluntary notification, the developer would submit to Health Canada:

- an assessment of the history of safe use of the introduced protein (or a related protein);
- information on the function, specificity and mode-of-action of the expressed protein;
- bioinformatic assessment of relatedness to known protein toxins and allergens; and
- digestive fate data for the expressed protein.

Safety Assessment Considerations:

12. A pro-active approach to unintended trace levels in seed, grain, feed and food is appropriate to support trade and establish tolerances. Several key considerations are needed.
 - Risk of a previously approved protein, proteins with a history of safe use, or proteins that are closely related or substantially similar to a previously approved protein would not have a concern of secondary effects if they occur in trace levels.
 - If the occurrence is in trace levels and it is unintended, then there is less concern regarding nutrition effects.
 - If the protein had minor changes from a previously approved protein, then the most important consideration would be allergenicity.
 - Resources must be addressed to develop, administer and enforce a trace level policy.