Canada's Perspective on Research Needs for Safety Assessments of the Next Generation of Novel Agricultural Products

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Overview

- Baseline Data
- Animal Biotechnology
- Next Generation of Crops
- Toxicology/Allegernicity
- Stacks
- Breeding
- Risk Communication

Baseline Data

- In most cases, the safety assessment of a new product is based on a comparative approach and, when necessary, actual toxicological data
- Baseline data on appropriate comparators is crucial
- ILSI: http://www.cropcomposition.org/
  - Robust tool as it permits user to obtain data per crop based on region, year, method of analysis, etc
  - Limited to corn, cotton and soybean
    - *Need data on other major food and feed crops (e.g., canola)*
  - Limited to nutrients and antinutrients
    - *We also have to consider allergens*

Baseline Data

- Food/feed safety
  - In line with work undergoing at OECD, the database should be eventually expanded to cover other relevant crops with consensus documents
  - At the 17th OECD Meeting of the Task Force (TF) for the Safety of Novel Foods and Feeds : progress made on Sugar cane consensus document, revision of soybean and canola
  - Future work may cover common beans, pulses, mushrooms

OECD update

- Animal biotechnology: salmon, beef and dairy cattle, swine
  - OECD work on consensus document on the biology of Atlantic salmon, no work yet on composition
  - A Data Call to be organised in order to collect information and interest for launching an "Exploratory Work" on composition data relating to animal products.
- Data quality
  - Data relevance, good sources, traceability of the information, natural variation, methodological variation, data interpretation by users, etc).
  - The TF recommended for the Bureau to explore how the "Instructions for Authors" could be updated and completed in terms of the quality of data, and to report back at the next TF meeting.

Animal Biotechnology

- Methodology challenges
- Baseline data will be an issue
- Petitioners will be faced with low number of samples (low in fish, lower in mammals)
  - How many animals must be tested to get relevant data?
- What tissues?
- What components (nutrients, allergens, hormones, bacterial flora, drug residues, etc)?

Animal Biotechnology

- Feed: bones, skins, impact of rendering
- Integration of animal health
- Methods to support traceability of biotechnology-derived animals in the food and feed chains

Next Generation of Crops

- Nutritionally enhanced crops
  - Effects on metabolic pathways leading to new metabolites
    - Impact on nutrient balance, especially for livestock feed
  - Effects of post-harvest factors (ex. processing)
  - Bioavailability
  - Exposure assessment
  - Upper safe limits

- Abiotic stress resistance (drought, salt, etc)
  - New stressed/environmental induced metabolites to consider (goes back to baseline data)
  - New levels of contaminants

- Crops without a history of safe use in food or feed (e.g., biofuels)

Next Generation of Crops

- Evaluation of potential pleiotropic effects introduced into "second generation" plants developed through genetic engineering or conventional mutagenesis.

- New approaches to obtain novel traits
  - RNAi
  - Transcription factors
    - Target specificity
    - May change expression of hundred of genes

Toxicology/Animal models

- Whole foods
  - General toxicology studies are unlikely to contribute meaningfully to hazard characterization
  - Animal studies may be appropriate to answer targeted questions about a novel food, ie. strong hypothesis-based studies on relevant health effects as opposed to descriptive toxicology

Toxicology/Animal models

- Allergenicity
  - Research efforts have yet to yield a cell culture system or animal model which can consistently distinguish allergens from non-allergens.
  - Current animal models will be difficult to adapt and validate for the purpose of identifying unknown novel allergen(s) in whole foods and are not expected to have regulatory applications in the near future.

Allergenicity of Novel Proteins

- Better tools to predict allergenicity (e.g., animal models, bioinformatic approaches)

- Threshold of allergenicity
  - Of known allergens, as a comparator
  - Of the novel protein

- Better tools would support safety assessments - weight of evidence approach

Acute Toxicity Studies on Novel Protein

- Acute toxicity studies currently supplied in support of safety of novel proteins
- These may not be useful as the sole support for lack of toxicity
  - Lack of appropriate controls
  - Too few animals
  - Inability to establish a NOEL with a satisfactory margin of safety for the predicted exposure (e.g., noting that exposure levels of some plant parts in livestock feeds may be very high).
- Need better tools for assessing real effects to include:
  - More accurate assessment of extent of exposure
  - Longer term feeding trials when exposure may be significant
  - Better understanding of the biological significance of mild adverse effects observed in some acute studies

Equivalence of Novel Proteins vs. Test Proteins

- What is the minimum data requirements to satisfy equivalence?
- If there are slight differences in amino acids homology, enzyme kinetics etc., how significant are these differences in terms of the equivalency of the test material used to do the toxicological studies?
- How to address scenarios when it is difficult to obtain proteins from the plant (e.g., Intractable chloroplast bound proteins, low level protein expression)

Stacks

- HC policy on stack:
  - Notify only if there is introduction of novelty due to the stacking
  - Onus is on developer to ensure there is no changes caused by the stacking of traits
  - Post market approach similar to other food commodities

Stacks

- CFIA Feed policy on stacks
  - Potential that stacked traits may interact to produce new traits
    - e.g., two traits affecting the same metabolic pathway)
  - Novel protein expression and metabolites may differ between stacks and parental lines
    - Can impact on exposure assessment
  - CFIA notification required for all stacks
  - CFIA may request data and/or rational to demonstrate that the stack is not novel thus not requiring pre-market assessment (i.e., equivalence to parental or conventional lines).

Stacks

- ILSI- IFBiC work on stacked events
  - Define in which situation the safety assessment of a stack could be warranted
  - Looked at insertional effects
  - Potential interactions scenarios
  - Impact of breeding

- Health Canada and CFIA are looking forward to the results of this work.

General questions on breeding

- Responsibility of breeder to identify novel crops requiring premarket assessment
- 4 documented examples of crops where breeding "led" to a health and safety issue
  - Lenape potatoes, cucurbitacin E in squash, two cultivars of zucchini in Australia, high psoralene celery
- Are there some sort of Best Practices breeders use in order to verify safety? If not, can these be developed?

Risk Communication

- Public Opinion Research work in US and Canada on animal biotech/clones indicates low public acceptance of agrifood applications of these technologies

- Regulators and Industry will need to develop strong risk communication approaches to communicate on these issues

For more information concerning Novel Foods and Novel Feeds in Canada

Novel Foods

Health Canada Web address:

http://www.hc-sc.gc.ca

HC-Novel Foods Web address :

http://www.novelfoods.gc.ca

Novel Feeds

CFIA Web address:

http://www.inspection.gc.ca

CFIA - Feed Web Address:

http://www.inspection.gc.ca/english/anima/feebet/feebete.shtml

Questions?

Canada

Past Regulatory Research

- Gene transfer & fate of transgenes/ proteins in the GI tract
- Pleiotropic effects in modified plants
- Allergens & other biological hazards (lit review)