Substantial Equivalence

(DBT guidelines; ILSI- IFBiC- Argentina 2013)

B Sesikeran MD,FAMS

Former Director

National Institute of Nutrition-ICMR-Hyderabad

Chairman RCGM

Unintended effects

* By the insertion of defined DNA sequences(intended), additional traits could, in some cases, be acquired or existing traits could be lost or modified (unintended effects).
* **It is an inherent and general phenomenon and not specific to GMOs**
* Can occur more so in conventional breeding or mutation breeding.

COMPOSITIONAL ANALYSES OF KEY COMPONENTS

* Key nutrients or key anti-nutrients of those components in a particular food that may have a substantial impact in the overall diet.

* Major constituents (fats, proteins, carbohydrates as nutrients or enzyme inhibitors as anti-nutrients)

* Minor compounds (minerals, vitamins).

Normal Variation In Composition

* Wide variation in the composition of any crop (conventional or otherwise) is normal, unavoidable and NOT a safety concern in a balanced diet
* Variation is driven by: climate & microclimate, variation from location to location and year to Year
* Environmental variation – soil, pest pressure, sunlight, location within a field
* seed genetic variation
* The composition of 2 plants taken from the same field will vary compositionally due to variations in microclimate and microenvironment

Safety Assessment Approaches
Andrew Bartholomaeus
School of Pharmacy, University of Canberra-presentation from ILSi IFBiC- Argentina 2013

Purpose of Compositional analysis

- Assess how similar is the GM crop to what is considered to be the conventional “safe” crop

–Deviations outside natural variability may indicate need for further evaluation

Key toxicants or toxicologically significant compounds known to be inherently present

* (e.g. solanine in potatoes if the level is increased, selenium in wheat) and allergens.

* A comparison with the GE plant grown under its expected agronomic conditions may need to be considered (e.g. application of an herbicide) in some cases.

Key toxicants or toxicologically significant compounds known to be inherently present

The statistical significance of any observed differences should be assessed in the context of the range of natural variations for that parameter to determine its biological significance.

* The comparator(s) used in this assessment need to be ideally the near isogenic parental line.
* In practice, this may not be feasible at all times, in which case a line as close as possible should be chosen.

Information required

* Literature from a range of standard cultivars that are in commercial production for the same purposes and grown in the same geographical areas as those typically found in the Indian market may also be provided for assessing the nutritional relevance of any unintended effect.

Trial sites

* The location of trial sites needs to be representative of the range of environmental conditions under which the plant varieties would be expected to be grown.

* The number of trial sites need to be sufficient to allow accurate assessment of compositional characteristics over this range.

* Trials have to be conducted over a sufficient number of generations to allow adequate exposure to the variety of conditions met in nature

Trial sites

* Each trial site is required to be replicated to minimise environmental effects, and to reduce any effect from naturally occurring genotypic variation within a crop variety,

* Sampling of adequate number of plants and the methods of analysis need to be sufficiently sensitive and specific to detect variations in key components.

Pre Conditions for analytes

* Applicant needs to provide the criteria used to select the nutrients analysed and the rationale for the exclusion from analysis of any nutrients and other substances listed

Test Material ?

* Appropriate analyses must be performed on

all the parts of the plant that may be used as food in India.

eg: If the intended uses of a transgenic corn event include the oil and the meal, samples of both corn oil and cornmeal should be analysed for the appropriate nutrients

Proximate composition

* 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

Fats & Carbohydrates

* Quantitative and qualitative composition of total lipids, i.e., saponifiable and nonsaponifiable components, complete fatty acid profile, phospholipids, sterols, cyclic fatty acids and known toxic fatty acids;

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

Micro nutrients, Anti Nutritional Factors, Bio actives etc

* 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, other detected substances.

If there is a difference

* The statistical significance of any observed differences will be assessed in the context of the range of natural variations for that parameter to determine its biological significance.

* If the composition of the GM food is judged not to be nutritionally equivalent to that of its parent and commercial varieties, i.e., significant differences (statistical and biological) exist in the nutrient data, additional nutritional data may be required on a case-by-case basis.

Nutritional Modified Plants

* All aspects of nutritional quality will be evaluated based on modern nutritional principles, standards and guidelines aimed at meeting human nutritional needs. The bases of evaluation include:

* 1. Nutrient intake recommendations;

* 2. The role of the food in the diet of the population;

* 3. The role of diet and nutrition in reducing the risk of developing a diet-related disease and health promotion.

Nutritional Change- intended or unintended

* The first phase of nutritional evaluation will be based on the nutrient composition data.

* If there is a finding of unusual or unanticipated components or levels of nutrients or nutritive substances, the food may need to be subjected to further analysis and assessment.

* The safety of a major increase in the level of a nutrient or other bioactive component would need to be assessed in a similar way to the safety assessment of an intended nutritional change

INTENDED NUTRITIONAL MODIFICATIONS

* Foods derived from GE plants that have undergone modification to intentionally alter nutritional quality or functionality need to be subjected to additional nutritional assessment to assess the consequences of the changes and whether the nutrient intakes are likely to be altered by the introduction of such foods into the food supply.

INTENDED NUTRITIONAL MODIFICATIONS

* Estimate the likely intake of the food derived from the GE plant.
* The expected intake of the food should be used to assess the nutritional implications of the altered nutrient profile both at customary and maximal levels of consumption.
* Basing the estimate on the highest likely consumption provides assurance that the potential for any undesirable nutritional effects will be detected.

INTENDED NUTRITIONAL MODIFICATIONS

* Impact of consumption on specific population groups - infants, children, pregnant and lactating women, the elderly and those with chronic diseases or compromised immune systems.

* Based on the analysis of nutritional impacts and the dietary needs of specific population subgroups, additional nutritional assessments may be necessary.

* Ascertain to what extent the modified nutrient is bioavailable and remains stable with time, processing and storage.

INTENDED NUTRITIONAL MODIFICATIONS

* The intended modification in plant constituents could change the overall nutrient profile of the plant product and this change could affect the nutritional status of individuals consuming the food.

* Unexpected alterations in nutrients could have the same effect.

* Although the GE plant components may be individually assessed as safe, the impact of the change on the overall nutrient profile needs to be determined.

Summary- ILSI Argentina July 2013

* **Compositional Analysis**

* It is necessary to revisit and understand the purpose of compositional analysis in the light of the state of the knowledge about natural variability, genome plasticity and the experience with GM technology

* Is it to identify unintended effects? Ensure nutritional content? Monitor toxins?

* Revisiting the purpose of compositional analysis may provide scope to reframe compositional analysis to focus only on critical nutrient compositional dataset.

Summary- ILSI Argentina July 2013

- There is a need to extend the composition databases to include local data and information on GM crops, new crops, and data obtained by alternative analytical methods.

- It would be helpful if Best Practices documents were developed on Quality Guidelines for Regulatory Sciences (vs GLP) for composition and other studies. This would greatly help local and public sector developers.

Thank You