SOT ISSUE STATEMENT

Food and Feed Safety of Genetically Engineered Food Crops
Approved by SOT Council, November 2017

The first genetically engineered (GE) food crop (tomato) was introduced in 1995, followed by the successful development and commercial release of maize, soybeans, cotton, canola, potatoes, papaya, alfalfa, squash, and sugar beets with specific new genetic traits. While there has been ongoing public debate about potential adverse impacts due to consumption of foods produced from these GE crops (i.e., genetically modified organisms [GMOs]) on human or animal health, the safety of each new event has been evaluated and communicated to regulatory authorities and all necessary regulatory approvals secured prior to their commercial release. Genetic engineering is a process to introduce specific genetic changes to improve common crop varieties in specific ways not achievable by conventional breeding. In many cases, this has been accomplished by the insertion of DNA sequences from unrelated sources into the genome of food crops specifically to endow them with biological activities that they otherwise would not possess. The most well-established GE crops express proteins that provide the plants with selective insecticidal activity or tolerance to certain herbicides. All plants used as human food or animal feed include varieties with marked genetic differences due to conventional breeding over hundreds to thousands of years or through intentional but undirected mutagenesis. These processes usually result in large-scale genomic changes in the resulting crops. Crop safety has been traditionally assured by plant breeders by examining the agronomic characters of the resulting crops and the testing of crop nutrients. However, new GE crops are tested and evaluated with much greater scrutiny.

Many GE events have achieved tremendous commercial success in the ensuing 20 years, especially those in soybeans and maize where more than 90% of harvests in the US include one or more GE traits (e.g., insect resistance or herbicide tolerance, both agronomic traits) to benefit crop cultivation which improves farming efficiency and can reduce or help maintain overall food costs. During that time, there has been no verifiable evidence of the potential for adverse health effects.

While this evidence supports the safety of these products to many in the scientific community (Nicolia et al. 2014), it has not satisfied the concerns of some scientists and many consumers (Pew Research Center 2015). Some countries have passed mandates requiring labeling of foods containing any ingredients from GE crops with labels stating, "contains ingredients from genetically engineered crops" or "contains GMO." Some consumers may view the labels as an indication there are concerns that GE crops and foods obtained from them are unsafe or at least

that there is uncertainty about their safety. Data from scientific studies have overwhelmingly demonstrated that foods obtained from GE crops are as safe and nutritious as foods obtained from non-GE (i.e., conventional) crops. Historically, the primary reason for labeling foods was to inform consumers about their contents so that they could make choices for safety, nutritional, or personal reasons. Labeling for allergens is quite specific to the allergenic ingredient. Concentrations of sugar, salt, and fats are identified on the packaging labels for this purpose. Accordingly, labeling food packaging as "contains GMO" is accurate in that it describes the process used to produce the food product (or perhaps one or more components within), but it does not necessarily inform about the specific change or the safety of the food. The mere possession of any label suggests to some consumers that the food is somehow novel in that it contains DNA and that it therefore presents some type of health risk. Furthermore, the absence of such a label or possession of a label such as "Non-GMO" or "GMO free" could be interpreted as somehow being safer even though, in all likelihood, the safety of product bearing such a label has not been evaluated. This document covers an extensive review of the safety data that has been published related to the safety of GE crops and the foods obtained from them.

Key Observations

1. Although commonly consumed foods are safe based on historical use, no foods are *absolutely* safe. This means that individual foods can present some risks for individuals either based on their natural constituents since they are from genetically diverse organisms or from the presence of contaminants. As an example, individuals with food allergies are sensitized to naturally occurring proteins present in the food to which they are allergic. To prevent allergic reactions, they must avoid consuming the food to which they are allergic. However, persons that are not sensitized to allergenic food proteins can freely consume the same foods without risk.

2. The safety evaluation process for proteins expressed in GE crops considers the following aspects:

   a. History of safe use of the source of the introduced proteins/genes in addition to the anticipated use or exposure to the proteins themselves. Therefore, many of the genes applied in GE crops are from sources that do not present an obvious risk, such as plants themselves or ubiquitous soil bacteria rather than from pathogenic bacteria.
   b. Bioinformatics comparison of the sequence identity of new proteins to known allergenic proteins to determine if they could be similar enough to present a risk for direct or cross reactivity in sensitive individuals. In some cases, performance of additional tests, such as *in vitro* serum IgE binding tests or clinical elicitation, have been conducted using sera from subjects with specific allergies. These methods have been effective and have prevented the introduction of allergenic proteins into GE crops.

    c. Evaluation of the sequence identity of a new protein, expressed by the transgene, is compared to proteins with known toxic effects. As with allergenicity, these methods are used to identify proteins that might present a risk of toxicity and are likely to require specific additional testing, depending on the characteristic of any matched "toxin."

    d. When appropriate, evaluation of potential metabolites of enzymes introduced in new GE events to determine if they present a potential for risk.

    e. Evaluation of expression of the protein in parts of the GE crop that are commonly consumed.

    f. Consideration of the normal processes used to prepare materials of the crop for consumption (e.g., cooking, processing, or extraction) on the stability of the expressed protein.

    g. Evaluating stability of the protein *in vitro* in pepsin at acid pH (1.2 or 2) and standardized conditions to which it would be exposed upon consumption. If appropriate, incubation with pancreatin is used as a surrogate for the possibility of digestion in the small intestine.

Collectively, data to date have identified no evidence of adverse health or nutritional effects from commercially available GE crops or from the foods obtained from them

3. The concept of "substantial equivalence" forms a starting point for evaluating the safety of foods from GE crops. This represents a comparative analysis between the GE crop and an appropriate non-GE, conventional comparator crop to identify any significant differences and/or unintended effects. Notably, the context of the modification of GE crops needs to be considered alongside conventional plant-breeding techniques that also involve modification to the genome of the plant and, potentially, various nutrients. Importantly, the extent of the changes to an organism resulting from natural or induced mutations followed by conventional breeding far exceeds the magnitude of changes typically produced by genetic engineering with the introduction of one or a few specific DNA constructs and editing tools (Ladics et al. 2015). Any observed differences are then evaluated in the context of potential for hazards. These analyses include evaluation of the nutrients and anti-nutrients of the host plant/organism to determine whether introduction of the new DNA altered the composition. Many feeding studies with laboratory and livestock animal models have been conducted and published to evaluate overall nutritional qualities. To date, such studies have not revealed any evidence that foods from GE crops present a risk for adverse health or nutritional effects, but they have helped demonstrate overall suitability based on the species of the crop.

4. Tests that have so far not proven to be predictive for evaluating the safety of food produced from GE crops include:

    a. General 'omics profiling for potential changes in protein expression, genome/transcriptome, and metabolite expression.
    b. Animal model testing for allergenicity.

5. Discussions regarding the labeling of foods as containing "GMO" or "GE ingredients" are likely to continue due to consumer demand, but it is not relevant regarding food safety. Evidence accumulated to date demonstrates that biotechnology itself does not present a risk and that the foods produced from current commercial GE crops are as safe and nutritious as those from non-GE sources. Plants with clear differences in risk or safety compared to currently consumed varieties (e.g., introduction of an allergenic protein or removal of an allergen) should have labeling requirements.

References

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