Pocket K

Substantial Equivalence of GM and Non-GM Crops

ISAAA
International Service for the Acquisition of Agri-biotech Applications

Global Knowledge Center on Crop Biotechnology

One of the primary requirements in commercializing a genetically modified (GM) crop is the proof of its substantial equivalence with its non-GM counterpart. In other words, substantial equivalence means that a new product such as a GM crop must be the same as the non-GM crop except for the traits that were enhanced, added, or removed through genetic engineering.

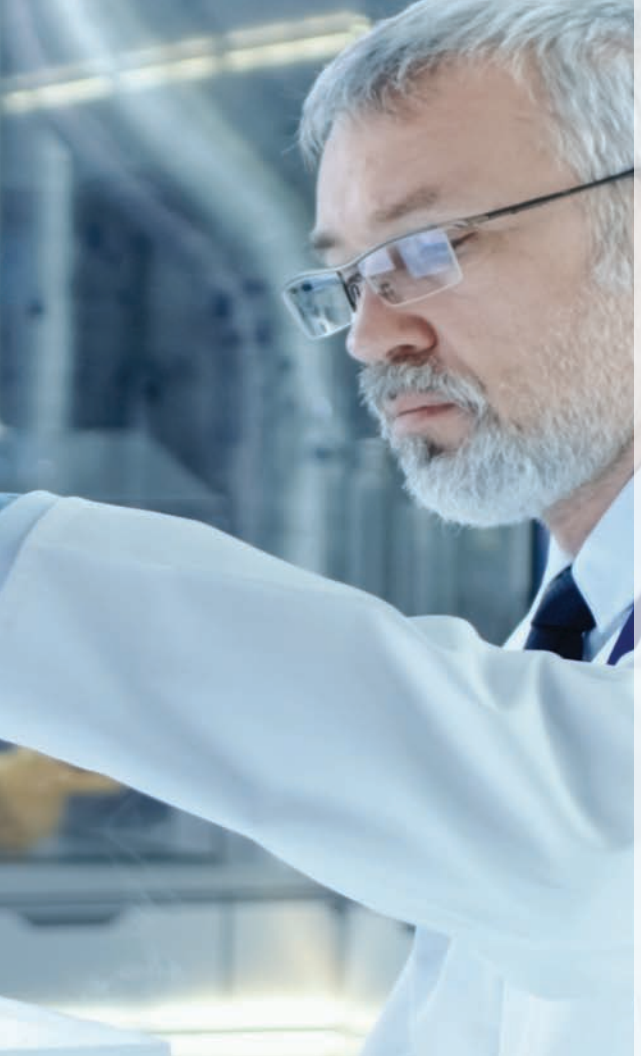
The concept of substantial equivalence

The concept of substantial equivalence was developed even before biotech crops were commercialized. It was first mentioned in the publication of the Organization for Economic Cooperation and Development (OECD) in 1993, developed by around 60 experts from 19 OECD countries that have been deliberating about evaluation of GM food safety. The experts were all nominated by governments, and most of them were regulatory scientists working in government agencies and ministries that are tasked to ensure consumer safety.[1]

OECD is an intergovernmental organization that promotes policies that will improve the economic social well-being of people around the world. In June 1999, G8 leaders gathered in a summit in Cologne, Germany, requested OECD to "undertake a study on the implications of biotechnology and other aspects of food safety." Thus in 2000, the OECD Edinburgh Conference on Scientific and Health Aspects of Genetically Modified Foods was held.[2]

Based on the discussions in the Edinburgh Conference, OECD released another document highlighting the importance of the concept of substantial equivalence as a tool for analyzing safety of novel foods, including GM foods. It was also mentioned in the document that substantial equivalence is not a quantitative criterion or a hurdle, but a framework for thinking. The concept is continually being modified and updated according to the issues that come up from time to time.[2]

Another institution that set the standard on GM food safety is Codex Alimentarius Commission (CAC). It was founded by Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) to develop food standards, guidelines, codes of practice, and other relevant documents under the FAO-WHO Food Standards Programme, which aims to protect consumers' health, fair food trade, and harmonization of food standards. The Codex Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants CAC GL 45-2003 includes a paragraph on substantial equivalence:



"The concept of substantial equivalence is a key step in the safety assessment process. However, it is not a safety assessment in itself; rather it represents the starting point which is used to structure the safety assessment of a new food relative to its conventional counterpart. This concept is used to identify similarities and differences between the new food and its conventional counterpart. It aids in the identification of potential safety and nutritional issues and is considered the most appropriate strategy to date for safety assessment of foods derived from recombinant-DNA plants. The safety assessment carried out in this way does not imply absolute safety of the new product; rather, it focuses on assessing the safety of any identified differences so that the safety of the new product can be considered relative to its conventional counterpart."[3]

Thus, substantial equivalence cannot replace safety assessment. It serves as a guide for regulatory scientists who conduct safety assessments. By evaluating the safety of the new product compared to its traditional counterpart, differences can be identified and further assessed through nutritional, toxicological, and immunological tests.[1]

Testing substantial equivalence

The testing for substantial equivalence of GM and non-GM crops entails a two-step process which has been agreed internationally by Codex, FAO, OECD, and WHO, and involves the quantification of selected molecules, in a so-called ‘‘targeted approach.’’ First, the GM crop is assessed for agronomic, morphological and chemical characteristics, such as macro- and micro-nutrients, anti-nutrients and toxic molecules. The results of these standard initial tests will determine if there’s a need for further testing for nutritive value. A difference that falls within the range of the normal variability for the crop is considered safe. However, if the compositional differences are beyond the range, further evaluations must be conducted with respect to their safety.[4]

Choosing appropriate comparators

One of the primary considerations in analyzing compositional analysis is choosing the suitable comparators. For example, in analyzing a new GM soybean variety, three approaches are followed in selecting the suitable comparators. In the first approach, the new variety of soybean will be planted alongside genetically closely-related varieties and the resulting values of certain parameters will be compared. Data composition of commercial varieties can also be used for comparison. The second approach is to use publicly available data about the composition of closely-related varieties. The third approach is suitable for GM crops with improved product quality. For soybean with improved fatty acid content of its oil, it may be appropriate to compare the component to the composition of its oil with another crop producing oil with good fatty acid content.[5]

Testing of glyphosate tolerant soybean varieties

Glyphosate tolerant soybean is the most planted GM crop worldwide.[6] It is commonly used in the animal feed industry as seed, oil, and meal. An extensive study of composition of two glyphosate tolerant soybean varieties (GTS 40-3-2 and 61-67-1) and a control parental soybean variety (A5403) was published in the *Journal of Nutrition*.[7] The soybean plants were planted in 13 fields for two years (1992-1993). The seeds were evaluated through various analyses including proximate analyses (protein, fat, fiber, ash, and carbohydrates), amino acids, and fatty acids. Anti-nutrients, the natural compounds that interfere with the absorption of nutrients, such as trypsin inhibitors, lectins, isoflavones, starchyose, raffinose, and phytate were also evaluated in both soybean seeds and toasted meal. Proximate analyses were also conducted for deffated toasted meal, defatted nontoasted meal, protein isolate and protein concentrate. Results showed that the

composition of control and glyphosate tolerant soybeans were substantially equivalent except for the proximate analyses of some nutrients (ash, fat, and carbohydrates). However, the differences found were miniscule and considered to be biologically insignificant. Thus, it was concluded that the glyphosate tolerant soybean varieties were equivalent to the conventional soybean variety.

Substantial equivalence shows an extensive global consensus of scientists on GM crop assessment. Based on the 10-year meta-analysis of GM crop safety studies, substantial equivalence accounts for 6% of the scientific records collected in GE food and feed. Most of these publications were released by GM crop developers, to fulfill the pre-commercialization requirements in approving countries.[4]

Declarations of biotech safety

Twenty one years after the first biotech crop was commercialized, 284 scientific organizations and over 3,000 studies have declared a solid and clear consensus that GM crops do not provide more risk than those that have been developed by conventional breeding techniques.[6,8] The following declarations essentially highlight the value of substantial equivalence in characterizing the safety of biotech crops:

WHO released a document on frequently asked questions about the safety of GM foods. According to WHO, GM foods currently available on the international market have passed safety evaluations and are not likely to present risks for human health. The document also stressed that there are no effects on human health resulting from human consumption of GM food by the general population in the countries where they have been approved. WHO recommended for continuous conduct of safety evaluations based on the Codex Alimentarius

principles which include assessment of substantial equivalence with non-GM counterparts.[9]

The National Academies of Sciences, Engineering, and Medicine of the U.S. conducted an extensive study on GE crops and found that new technologies in genetic engineering and conventional breeding are blurring the once clear distinctions between these two crop-improvement approaches. The special committee found that "no substantiated evidence of a difference in risks to human health between current commercially available genetically engineered (GE) crops and conventionally bred crops, nor did it find conclusive cause-and-effect evidence of environmental problems from the GE crops."[10]

The UK Royal Society also said that foods derived from GM plants are safe. In their publication, *GM Plants: Questions and Answers*, they addressed the studies claiming that consumption of GM foods caused damage to human or animal health. They said that these claims were not about the GM method itself, but about the specific gene introduced into the crop, or about agricultural practices linked with the crop, such as use of herbicides. The statistical analysis and methodology of such studies have been questioned by experts. The Royal Society stated in the publication that "all reliable evidence produced to date shows that currently available GM food is at least as safe to eat as non-GM food."[11]

Food Standards Australia New Zealand (FSANZ) declared that "To date, gene technology has not been shown to introduce any new or altered hazards into the food supply, therefore the potential for long term risks associated with GM foods is considered to be no different to that for conventional foods already in the food supply. As a consequence, FSANZ does not consider that long term studies are generally needed to ensure the safety of GM foods."[12]

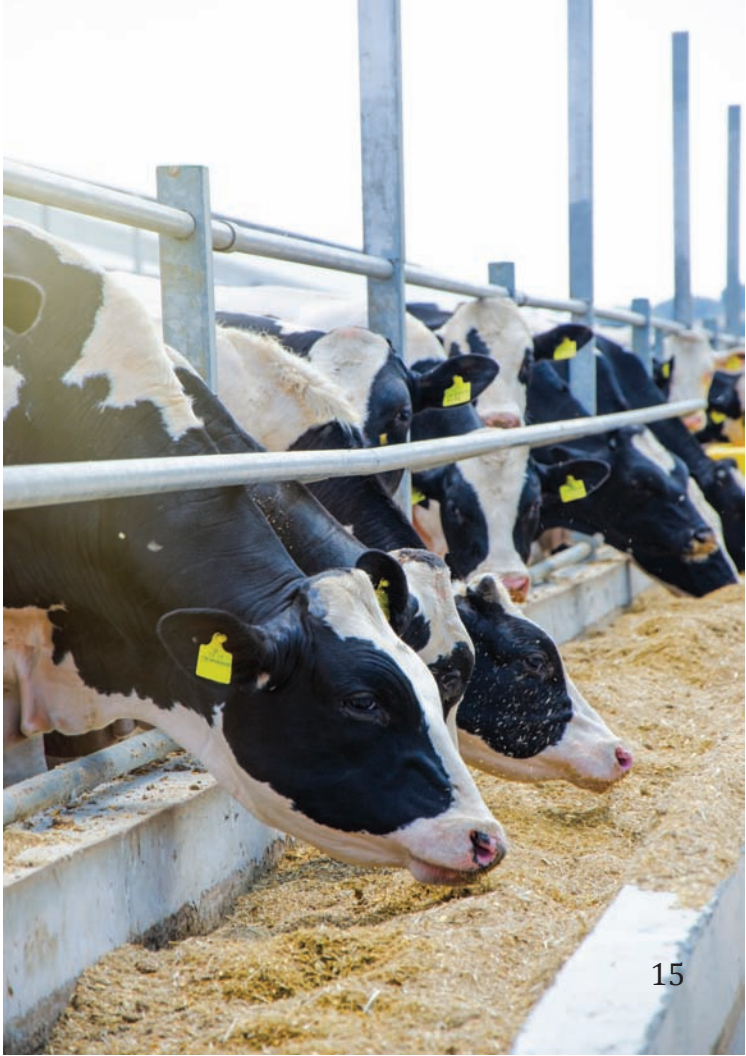
Based on a decade of EU-funded GMO research, the European Commission concluded that "biotechnology, and in particular GMOs, are no more risky than conventional plant breeding technologies." This conclusion is drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research, and involving more than 500 independent research groups. [13]

The Union of German Academics of Sciences and Humanities also said that “In consuming food derived from GM plants approved in the EU and in the USA, the risk is in no way higher than in the consumption of food from conventionally grown plants. On the contrary, in some cases, food from GM plants appears to be superior in respect to health.”[14]

In November 2017, the Society of Toxicology (SOT), a professional membership association of more than 8,200 scientists from the U.S. and abroad released an issue statement on food and feed safety related to genetically engineered (GE) crops. The issue statement has five key observations on safety, substantial equivalence, and labeling. The Society affirms the safety of GE crops amidst ongoing public debate about potential adverse impacts of GE crops on human or animal health, saying that each new event has been evaluated by regulatory authorities and all necessary regulatory approvals were secured before their commercial release. It was emphasized in the statement that “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.”[15]

The American Association for the Advancement of Science (AAAS) Board of Directors issued a statement on labelling GM foods. The statement underlines the evidence of GM crop safety as declared by respected organizations worldwide. According to AAAS, consuming foods containing ingredients derived from GM crops is no riskier than consuming the same foods containing ingredients from crop plants modified by conventional plant improvement techniques. The statement also mentioned the results of a meta-analysis of long-term animal feeding studies comparing GM crops and their non-GM counterparts, which concluded that they are nutritionally equivalent.[16,17]

These statements from the most respected organizations worldwide, together with new statements released every year, is indeed a scientific consensus that the GM crops available in the market are as safe as their non-GM counterparts. With its long history of safe use, FAO and other institutions have recognized the value of biotechnology in meeting the needs for foods, products and services for the rapidly growing global population.[3]



References

[1] Kearns, P. and P. Mayers. 1999. Substantial Equivalence is a Useful Tool. https://www.nature.com/articles/44260.
[2] OECD. 2000. Genetically Modified Foods. http://www.oecd.org/sti/biotech/geneticallymodifiedfoods.htm.
[3] FAO. 2008. GM Food Safety Assessment Tools for Trainers. http://www.fao.org/3/a-i0110e.pdf.
[4] Nicolia, A., A. Manzo, F. Veronesi, and D. Rosellini. 2012. An Overview of the Last 10 Years of Genetically Engineered Crop Safety Research. http://www.agrobio.org/bfiles/fckimg/Nicolia%202013.pdf.
[5] Laurena, A.C. 2005. Feed Safety of Agricultural Plant Products Derived through Modern Biotechnology. In Science-based Reviews: Issues and Concerns of Modern Biotechnology (Tecson, E.M.) pp. 59-91, FAST-PSHC Foundation, Manila, Philippines.
[6] ISAAA. 2016. Global Status of Commercialized Biotech/GM Crops: 2016. http://isaaa.org/resources/publications/briefs/52/download/isaaa-brief-52-2016.pdf.
[7] Padgette, S.R. N.B. Taylor, D.L. Nida, M.R. Bailey, J. MacDonald, L.R. Holden, and R. L. Fuchs. 1996. The Composition of Glyphosate-tolerant Soybean Seeds is Equivalent to that of Conventional Soybeans. Journal of Nutrition 126(3):702-716.
[8] Norero, D. 2017. GMO 20-year Safety Endorsement: 280 Science Institutions, More than 3,000 Studies. https://geneticliteracyproject.org/2017/06/19/gmo-20-year-safety-endorsement-280-science-institutions-more-3000-studies/.
[9] WHO. 2014. Frequently Asked Questions on Genetically Modified Foods. http://www.who.int/foodsafety/areas_work/food-technology/Frequently_asked_questions_on_gm_foods.pdf?ua=1.
[10] The National Academies of Sciences, Engineering, and Medicine. 2016. Distinction Between Genetic Engineering and Conventional Plant Breeding Becoming Less Clear, Says New Report on GE Crops. http://www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=23395.
[11] The Royal Society. 2016. GM Plants: Questions and Answers. https://royalsociety.org/~/media/policy/projects/gm-plants/gm-plant-q-and-a.pdf.
[12] FSANZ. 2016. Safety Assessments of GM Foods. http://www.foodstandards.gov.au/consumer/gmfood/safety/Pages/default.aspx.
[13] European Commission. 2010. A Decade of EU-funded GMO Research. https://ec.europa.eu/research/biosociety/pdf/a_decade_of_eu-funded_gmo_research.pdf.
[14] FBAE. 2009. Are There Health Hazards for the Consumer from Eating Genetically Modified Food? http://www.fbae.org/2009/FBAE/website/special-topics_are_there_health_hazards.html.
[15] SOT. 2017. SOT Issue Statement: Food and Feed Safety of Genetically Engineered Food Crops. https://www.toxicology.org/pubs/statements/SOT_Safety_of_GE_Food_Crops_Issue_Statement_FINAL.pdf.
[16] AAAS. 2012. Statement by the AAAS Board of Directors on Labeling of Genetically Modified Foods. https://www.aaas.org/sites/default/files/AAAS_GM_statement.pdf.
[17] Snell, C. A. Bernheim, J. Bergé, M. Kuntz, G. Pascal, A. Paris, A. Ricroch. 2012. Assessment of the Health Impact of GM Plant Diets in Long-term and Multigenerational Animal Feeding Trials: A Literature Review. https://www.sciencedirect.com/science/article/pii/S0278691511006399.

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