

Recommendations for Science-Based Safety Assessment of Genetically Modified (GM) Plants for Food and Feed Uses

Stephen Waters^a, Adela Ramos^b, Angela Hendrickson Culler^c, Penny Hunst^d, Lawrence Zeph^e, Rachel Gast^e, Debbie Mahadeo^c, Jordan Sottosanto^d, Scott Huber^e, Guomin Shan^b, Suma Chakravarthy^{f,*}, Laurie Goodwin^{f,**}

^aWaters International Consulting, Bousval, Belgium

^bCorteva Agriscience™, Johnston, IA

^cBayer, Crop Science Division, Chesterfield, MO

^dBASF Corporation, Research Triangle Park, NC

^eSyngenta, Crop Protection, LLC., Research Triangle Park, NC

^fCropLife International, Washington, DC

Abstract

Since the commercial introduction of genetically modified (GM) plants in agriculture over two decades ago, technology developers and regulatory authorities have gained significant experience in evaluating their safety based on assessing potential impact to humans, animals and the environment. Over 3,500 independent regulatory agency reviews have positively concluded on the safety of GM plants for food and feed. Yet, divergent and increased regulatory requirements have led to delayed and asynchronous approvals and have restricted access to innovative products for farmers and consumers. With accumulated knowledge from safety assessments conducted so far, an enhanced understanding of plant genomes, and a history of safe use, it is time to re-evaluate the current approaches to the regulation of GM plants used for food and feed. A stepwise approach using weight-of-evidence should be sufficient for the safety assessment of newly expressed proteins in GM plants. A set of core studies including molecular characterization, expression and characterization of the newly expressed proteins (or other expression product), and safety assessment of the introduced protein, are appropriate to characterize the product and assess safety. Using data from core studies and employing a “problem formulation” approach, the need for supplementary hypothesis-driven or case-by-case studies can be determined. Employing this approach for the evaluation of GM plants will remove regulatory data requirements that do not provide value to the safety assessment, and provide a consistent framework for global regulation.

Keywords: genetically modified plant, food and feed, safety assessment, core studies, supplementary studies, risk, problem formulation, regulations

1. Introduction

The first genetically modified (GM) plants used as a source of food were commercialized in 1994 [17], and in 2018 GM plants were grown on over 190 million hectares across 26 countries [16]. Over the past 25+ years, technology developers and regulatory agencies have gained knowledge and experience from studying and assessing the safety of GM plant products. To date, more than 4,000 independent regulatory agency reviews issued by 70 countries have concluded on the safety of

GM plants, of which 3,524 reviews have been for food and feed use [16]. The approvals have unanimously found in each case that the GM plant in question was as safe as its conventional counterpart. Moreover, global economic gain of 186 billion USD over 21 years, and savings of 27.1 billion kilograms of CO₂ emissions in 2016 [15], have been realized as a result of the commercialization of GM plants.

While the 1,000+ years of safe use of conventionally-bred agricultural plants demonstrate that plants developed in this manner are generally safe for human and animal consumption, the introduction of GM plants generated questions about their safety despite the similarities in the development of both conventional and GM plants. In a typical commercial breeding program, hundreds of thousands of plants are produced and tested in hundreds of environments over many years to select

*This work was performed when Suma Chakravarthy was employed by CropLife International. Present affiliation: United States Department of Agriculture, Animal and Plant Health Inspection Service, Riverdale, MD.

**Corresponding author: Laurie Goodwin,

Email: laurie.goodwin@croplife.org, Phone: 202-365-5059

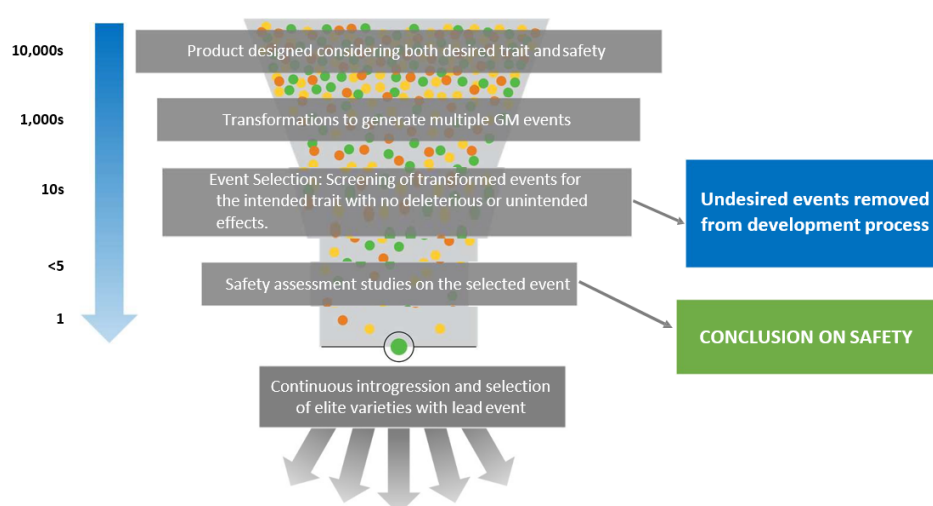


Figure 1: Screening process for the selection of the lead GM event for further safety assessment and introgression into elite varieties

a commercially viable, new variety. The screening out of undesired and unintended agronomic effects is an integral part of the breeding process for both conventional and GM varieties, and acts as a mechanism to reduce or eliminate undesirable plants and events from the development process. The extensive screening and selection process during variety development has led to a general recognition that conventional breeding of food crops does not present a risk to human or animal health.

During the development of new GM varieties, transgene(s) are typically introduced into an easily transformable host plant to produce thousands of GM events [21, 22]. Following an initial safety screen that is performed during the design phase, the GM events themselves are subject to an extensive screening process that includes molecular profiling, assessments of trait efficacy, and observations for unintended agronomic phenotypes [21]. At this point, for sexually propagated crops, one or more lead events are selected for introgression into elite germplasms. Introgression typically involves multiple backcrosses with locally-adapted germplasm. Following these backcrosses, more than 99 percent of the DNA in the GM variety is derived from the local germplasm [22]. The trait introgression process, along with the lead event selection process, substantially reduce any possibility of unintended effects in commercial GM varieties [22]. For vegetatively-propagated crops (e.g., sugarcane, potatoes, perennials), alternative selection and breeding strategies may be required [1]. An overview of the commercial development process for new sexually propagated GM varieties is shown in Figure 1.

Despite the rigorous breeding and selection process, record of safety, environmental benefit, and increasing familiarity with GM plants, their development and commercialization has, in some cases, been under increasingly stringent regulatory oversight and new safety data requirements. Many of these new regulatory requirements are not scientifically justified and do not add value to a safety assessment. Advances in science and

accumulated experience should be considered during the safety assessment process. As discussed below, some existing data requirements and/or data that do not add value should be removed from regulatory oversight. This would reduce and provide consistency to product development timelines, greatly benefiting industry, including small and public sector developers. Another pragmatic approach to the regulation of GM plants employs the recognition of safety assessments completed in other regions through a significantly streamlined approach to the safety assessment process or through the mutual recognition of safety assessments. This approach maintains a high level of safety for human/animal health and the environment, while reducing regulatory timelines and enabling timely access to technology.

This paper presents the aligned view of the authors and recommends study designs and scientific data appropriate for the initial safety assessment of GM plants for food and feed use. These recommendations are modified from earlier guidelines and recommendations for the safety assessment of GM plants containing newly expressed proteins (e.g., [5, 9]).

1.1. Current food and feed safety assessment for GM plants

With the commercialization of GM plants, the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) held consultations on biotechnology and food safety in 1990 and 1996, and the Codex Alimentarius Commission (CAC) published guidelines for the conduct of food safety assessments in 2003 [3, 4]. The Codex Alimentarius (Codex) recognized the need for a focused approach for the safety assessment of foods produced from GM plants, differing from the classical safety assessment approaches for discrete hazards that may be present in foods, such as food additives or pesticide residues. Codex also recognized the need for a comparative approach, and the concept of “substantial equivalence” was emphasized as an important first step in the safety assessment process to identify differences and sim-

ilarities between the new food (GM plant) and its conventional counterpart. Codex recommended that the safety assessment include an evaluation of both intended effects (consideration of the safety of any newly expressed proteins, NEPs, or intended metabolic changes) and unintended effects (identifying any new or altered hazards). These comparisons were to be made relative to an appropriate conventional counterpart with a history of safe use (HOSU).

Codex Alimentarius principles and guidelines have served as a valuable and consistent standard for the development of national and regional safety assessment guidelines and regulations since their introduction. However, those guidelines should be supplemented by the familiarity and established history of safety of GM plants over the past 25 years. Additionally, the divergent implementation of these guidelines by regulatory authorities has, in some cases, led to excessive data requirements prior to regulatory approval. The unique requirements of different agencies have resulted in significant delays in regulatory approvals, leading to asynchronous approvals globally. Notable areas of divergence from Codex include requirements for animal feeding studies without a testable risk hypothesis; expanding compositional analysis requirements, statistical approaches and appropriate comparators; extensive allergenicity assessments of introduced proteins and endogenous allergens in whole foods; and requests for excessive molecular and protein characterization data. Regulatory authorities in some countries where GM plants or their products are imported, but not cultivated, also require submission of agronomic and environmental data that are not relevant to the assessment of safety of the GM plant and its products for animal and human consumption. Additionally, some countries require specific studies that have already been conducted in another country or region to be repeated locally, adding further time, complexity, and cost to the approval process, when data from existing studies in other countries are fully applicable to these countries.

Although all countries agree that the primary purpose of regulation is the protection of human and animal health and the environment, divergent approaches to the regulation of GM plants globally have had major impacts in other policy areas. For example, asynchronous approvals have resulted in delays in commercial launches of innovations [18], despite the benefits of the cultivation of GM plants being well documented. The divergent approaches to current global regulation of GM plants hinder innovation as well as the wider adoption of the technology, resulting in loss of significant economic and environmental benefits. In fact, a recent report estimated that the value of corn production and soybean production in major export countries would increase by 4.3 billion USD and 4.9 billion USD, respectively, between 2018 and 2022 if GM plant approvals were achieved in a more timely manner [14].

Some regulatory authorities have revised their oversight of GM plants as a result of their familiarity with GM traits and plants and extensive experience with their regulation. In Japan, some previously approved agronomic traits (for example, traits conferring herbicide tolerance) stacked through conventional plant breeding are now subject to a simplified risk assessment [25]. Japan also excluded GM crops that do not have wild rel-

atives in Japan from mandatory field trial requirements if they contain familiar traits [26]. Canada has reduced the requirement of certain agronomic data needed for the approval of a GM trait which has ‘sufficient similarity’ to a previously approved GM trait [7]. The USDA recently proposed modernization of its biotechnology regulations to exempt GM plants obtained through certain genetic engineering techniques and some previously approved traits from regulation [24].

In 2017, the U.S. National Academy of Sciences recommended an updated approach to the regulation of future products of biotechnology to address the needs of, “*supporting innovation, protecting health and the environment, promoting public confidence in the regulatory process, increasing transparency and predictability, and reducing unnecessary costs and burdens*”. The recommendations also suggested an expedited, simplified process for products containing previously assessed traits (i.e., familiar products) [19].

1.2. Recommendations for future food and feed safety assessments for GM plants

Despite recent developments in the regulatory approaches followed in some countries, complex and unnecessarily burdensome regulatory requirements continue to underscore the importance of a science-based testing paradigm for safety assessments. With the vastly enhanced understanding of plant genomes since the publication of the Codex principles and guidelines over 15 years ago, as well as more than two decades of experience in the development, commercialization and safety assessment of GM plants, it is time to re-examine approaches for the safety assessment of GM plants used as food or feed.

A weight-of-evidence (WOE), stepwise, and science-based approach that uses a set of core studies to evaluate the safety assessment of GM plants is recommended. Depending on the nature of the introduced trait, intended use, and data obtained from core studies, supplementary (hypothesis-driven or case-by-case) studies may be required to fully evaluate the safety of the GM plant. Figure 2 provides a schematic overview of the studies required to ascertain the safety of GM plants as proposed in this article, distinguishing between core studies and supplementary studies.

1.3. Core studies for food and feed safety assessment

Safety assessment of GM plants used as sources of human and/or animal nutrition requires a collection of information about the host plant and donor organism from which the GM trait is derived, history of food and feed use (if applicable), and detailed knowledge of the GM trait [4]. In this article, the following core sets of studies are recommended to characterize the product and assess safety, namely: (1) molecular characterization of the GM event; (2) expression levels and characterization of the NEP or other expression product (e.g., double-stranded RNA); and (3) safety assessment of the introduced protein (or expression product). These studies are discussed in more detail elsewhere [2].

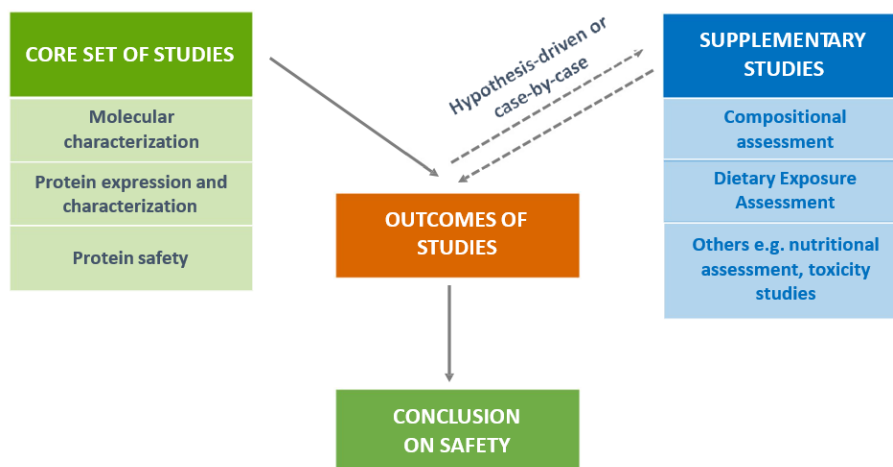


Figure 2: Schematic overview of the studies necessary to assess the safety of GM plants for food and feed uses. Core studies are a set of studies necessary for a science-based risk assessment of a GM plant. These are suggested core studies for typical GM plants. There may also be alternative newly expressed substances (e.g. RNAi). Supplementary studies are studies to be conducted upon identification of information and/or hypothesis that indicates increased risk to human or animal health. The conduct of these studies depends on the nature of the introduced trait, intended use and data obtained from core studies.

1.4. Supplementary hypothesis-driven or case-by-case studies and study design

Data obtained from core safety assessment studies can be used to determine which additional studies may need to be conducted before fully characterizing the product and evaluating the safety of a GM plant for food and feed. A “problem formulation” approach should be employed [23, 28] to address specific safety questions relevant to the nature of the GM product. The problem formulation approach generates risk hypotheses arising from the nature of the trait and the genes introduced to confer the new trait. Evaluation of the potential risks is then conducted according to the science-based process established by Codex. Risk analysis is a stepwise process requiring hazard identification, hazard characterization, exposure assessment, and risk characterization [11]. In simpler terms, risk is a function of hazard and exposure (Figure 3). Understanding the mode of action (MOA) of the expression product also provides meaningful information on potential hazards. To employ problem formulation, the study design must be testable and specifically address the questions or concerns raised to enable developers and regulators to efficiently assess risk and evaluate the safety of the product.

Extensive compositional analysis has historically been considered a core study. However, over 25 years of safety assessments evaluating composition data have demonstrated a lack of notable difference between GM plants and conventional comparators, especially in the context of the natural variability that already exists between plant varieties [8, 27]. As discussed by Herman and co-authors, there is enough scientific evidence today to merit a shift to conducting compositional analysis as a supplementary hypothesis-driven study [13]. In some cases, nutritional and dietary exposure assessments are performed to fulfill regulatory requirements. These studies should also be supplementary and performed if required upon hazard or expo-

sure identification. Similarly, for traits intended to improve the nutritional profile of grains (e.g., increased oleic acid), changes in the levels of other grain components (e.g., other fatty acids) should be assessed through supplementary studies.

1.5. Risk evaluation

Risk evaluation requires consideration of potential “hazards”, as well as an evaluation of likely “exposure” to the evaluated substance [20]. Even in commonly-consumed foods, there are hazardous substances. Some foods, for example kidney beans, tomatoes, and potatoes, contain naturally-occurring toxins that could be “hazardous” to our health (e.g. phytohemagglutinin, tomatine, solanine/glycoalkaloids). However, various means (e.g. plant breeding and variety selection, proper storage and/or preparation, cooking, etc.) have been used to mitigate “exposure” to these toxins and thereby reduce the risk to an acceptable level. Safety assessments of new foods produced from GM plants should focus on new or altered hazards as they pertain to the NEP, rather than trying to identify every potential hazard associated with that food [3]. The safety of food substances *per se* is regulated through other food regulation mechanisms [12, 6]. A WOE and stepwise approach should be followed for assessing the safety of newly expressed substances (protein or DNA) in GM plants, delineating the safety/risk assessment into its components of hazard and exposure in alignment with Codex principles [3, 5]. In cases where no new hazards are identified, or where there is no human or animal exposure to identified hazards, there would be no new risk or need for a full safety assessment. For example, in the case of a highly purified food ingredient, such as sugar or oil produced from a GM plant where there would be no exposure to a newly expressed substance, a hazard assessment is not scientifically justified. When a full safety assessment is necessary, both hazard and exposure must be evaluated to understand risk. Figure

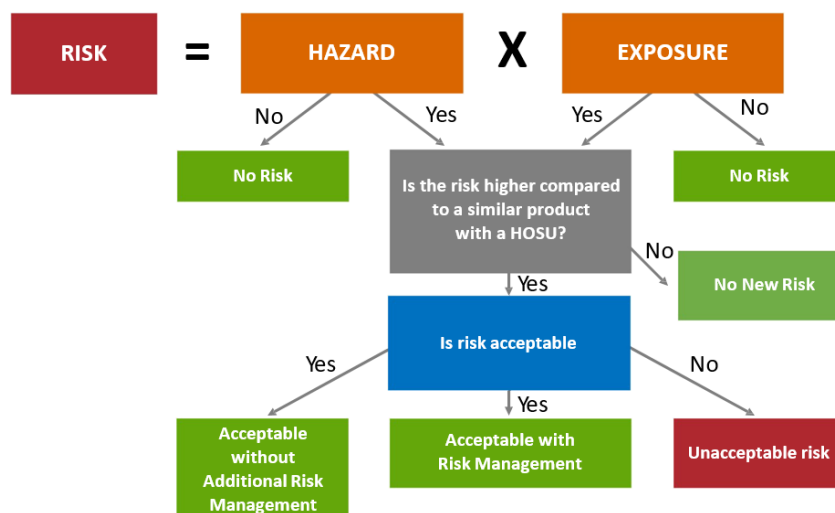


Figure 3: Risk evaluation process and possible outcomes [10]. Risk is a function of the probability of an adverse health effect and the severity of that effect, consequential to hazard(s) in food. Hazard is a biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect. Exposure is the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant.

3 highlights the risk evaluation process and the three possible outcomes of risk evaluation:

- No risk/no new risk
- Acceptable risk with or without risk management
- Unacceptable

2. Conclusions

The development of GM technology in agriculture was rightly accompanied by the development of regulatory safety guidance at the international level through the Codex Alimentarius. With the knowledge, experience, and HOSU gained from over 25 years of developing, commercializing, and consuming GM plants, it is time to re-evaluate current approaches to their regulation. A stepwise and science-based method using a set of core studies and a problem formulation approach to determine the necessity for supplementary studies for the safety assessment of GM plants used for food and feed is proposed for all GM plants. These studies, outlined in Figure 2, are described in further detail by Brune et al. [2].

The recommendations are based on extensive global experience and an enhanced understanding of plant genomes and genetic diversity. Further, the extensive screening process for new GM events and the plant breeding/trait introgression process together significantly reduce the possibility of unintended effects in commercial varieties. Removal of regulatory requirements that do not provide value to the safety assessment would reduce product development timelines, which would enable smaller and public sector developers to bring diverse agricultural innovations to the marketplace. It would also lower the cost barriers to working on non-traditional crops and traits and make product

launch timelines more predictable. With the increasing repertoire of GM plant products anticipated in the future, a science-based regulatory paradigm will enable innovation and delivery of products that will have a positive impact on the global economy, the environment, and food security sustainability.

3. Declaration of Conflicting Interest

All the authors of this paper are currently employed by, or have been employed by, the agricultural biotechnology industry.

4. Disclaimer

The findings and conclusions in this publication are those of the author(s) and should not be construed to represent any official USDA or U.S. government determination or policy.

5. Article Information

This article was received November 25, 2019, in revised form April 3, 2020, and made available online January 5, 2021.

6. References

- [1] Bisognin, D. A. (2011). Breeding vegetatively propagated horticultural crops. *Crop Breeding and Applied Biotechnology*, 11, 35-43. Retrieved from http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1984-70332011000500006&nrm=iso
- [2] Brune, P., Chakravarthy, S., Graser, G., Mathesius, C., McClain, S., Petrick, J. S., Sauve-Ciencewicki, A., Schafer, B., Silvanovich, A., Brink, K., Burgin, K., Bushey, D., Cheever, M. L., Edrington, T., Fu, H., Habex, V., Herman, R., Islamovic, E., Lipscomb, E. A., Motyka, S., Privalle, L., Ranjan, R., Roper, J., Song, P., Tilton, G., Zhang, J., Waters, S., Ramos, A., Culler, A. H., Hunst, P., Gast, R., Mahadeo, D., & Goodwin,

- L. (2021). Core and supplementary studies to assess the safety of genetically modified (GM) plants used for food and feed. *Journal of Regulatory Science*, 9(1), 45-60. doi: 10.21423/jrs-v09i1brune
- [3] Codex Alimentarius Commission. (2003, 30 June-5 July). *Appendix III, Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants*, and *Appendix IV, Annex on the Assessment of Possible Allergenicity*. Joint FAO/WHO Food Standard Programme, Twenty-fifth session. Food and Agriculture Organization of the United Nations, Rome.
- [4] Codex Alimentarius Commission. (2003). *Principles for the Risk Analysis of Foods Derived from Modern Biotechnology*. Joint FAO/WHO Food Standard Programme. Food and Agriculture Organization of the United Nations, Rome.
- [5] Codex Alimentarius Commission. (2009). *Foods derived from modern biotechnology*, Second edition. Food and Agriculture Organization of the United Nations and World Health Organization, Rome. Retrieved from <http://www.fao.org/3/a-a1554e.pdf>
- [6] Canadian Food Inspection Agency. (1985). *Food and Drugs Act*. Retrieved September 2019 from <https://laws-lois.justice.gc.ca/eng/acts/F-27/FullText.html>
- [7] Canadian Food Inspection Agency. (2018). *Appendix 5: Similar PNTs*. Assessment Criteria for Determining Environmental Safety of Plants With Novel Traits, Directive 94-08. Retrieved September 2019 from <https://www.inspection.gc.ca/plants/plants-with-novel-traits/applicants/directive-94-08/appendices/eng/1512662253920/1512662254595#app5>
- [8] Cong, B., Maxwell, C., Luck, S., Vestestad, D., Richard, K., Mickelson, J., & Zhong, C. (2015). Genotypic and Environmental Impact on Natural Variation of Nutrient Composition in 50 Non Genetically Modified Commercial Maize Hybrids in North America. *Journal of Agricultural and Food Chemistry*, 63(22), 5321-5334. doi: 10.1021/acs.jafc.5b01764
- [9] Delaney, B., Astwood, J. D., Cunny, H., Conn, R. E., Herouet-Guichene, C., MacIntosh, S., Meyer, L. S., Privalle, L., Gao, Y., Mattsson, J., Levine, M., & ILSI International Food Biotechnology Committee Task Force on Protein Safety. (2008). Evaluation of protein safety in the context of agricultural biotechnology. *Food and Chemical Toxicology*, 46(Supplement 2), S71-S97. doi: 10.1016/j.fct.2008.01.045
- [10] Food and Agriculture Organization of the United Nations & World Health Organization. (1999). *Principles and Guidelines for the Conduct of Microbiological Risk Assessment*. Retrieved from <http://www.fao.org/3/y1579e/y1579e05.htm>
- [11] Food and Agriculture Organization of the United Nations & World Health Organization. (2001). *Definitions for the Purposes of the Codex Alimentarius*. Retrieved from <http://www.fao.org/3/y2200e/y2200e07.htm>
- [12] Food Standards Australia New Zealand. (1991). *Food Standards Australia New Zealand Act 1991*. Retrieved September 2019 from <https://www.legislation.gov.au/Details/F2016C00156>
- [13] Herman, R. A., Chassy, B. M., & Parrott, W. (2009). Compositional assessment of transgenic crops: an idea whose time has passed. *Trends in Biotechnology*, 27(10), 555-557. doi: 10.1016/j.tibtech.2009.07.003
- [14] Informa. (2018, May). *The Impact of Delays in Chinese Approvals of Biotech Crops*. Retrieved from <https://croplife.org/wp-content/uploads/2018/05/Impact-of-Delays-in-Chinese-Approvals-of-Biotech-Crops-05-18-FINAL-1.pdf>
- [15] International Service for the Acquisition of Agri-biotech Applications. (2017). *Global Status of Commercialized Biotech/GM Crops in 2017: Biotech Crop Adoption Surges as Economic Benefits Accumulate in 22 Years* (Brief 53). International Service for the Acquisition of Agri-biotech Applications. Retrieved from <https://www.isaaa.org/resources/publications/briefs/53/download/isaaa-brief-53-2017.pdf>
- [16] International Service for the Acquisition of Agri-biotech Applications. (2018). *Global Status of Commercialized Biotech/GM Crops: 2018* (Brief 54). International Service for the Acquisition of Agri-biotech Applications. Retrieved from <https://www.isaaa.org/resources/publications/briefs/54/executivesummary/pdf/B54-ExecSum-English.pdf>
- [17] James, C., & Krattiger, A. F. (1996). *Global Review of the Field Testing and Commercialization of Transgenic Plants: 1986 to 1995, The First Decade of Crop Biotechnology* (Brief 1). International Service for the Acquisition of Agri-biotech Applications. Retrieved from <https://www.isaaa.org/resources/publications/briefs/01/download/isaaa-brief-01-1996.pdf>
- [18] National Academies of Sciences, Engineering, and Medicine. (2016). *Genetically Engineered Crops: Experiences and Prospects*. The National Academies Press.
- [19] National Academies of Sciences, Engineering, and Medicine. (2017). *Preparing for Future Products of Biotechnology*. The National Academies Press.
- [20] National Research Council. (2003). *Risk Management: The Principles Underlying the Design and Implementation of an Occupational Health and Safety Plan*. In *Occupational Health and Safety in the Care and Use of Nonhuman Primates*. The National Academies Press.
- [21] Prado, J. R., Segers, G., Voelker, T., Carson, D., Dobert, R., Phillips, J., Cook, K., Cornejo, C., Monken, J., Grapes, L., Reynolds, T., & Martino-Catt, S. (2014). Genetically engineered crops: from idea to product. *Annual Review of Plant Biology*, 65, 769-790. doi: 10.1146/annurev-arplant-050213-040039
- [22] Privalle, L. S., Chen, J., Clapper, G., Hunst, P., Spiegelhalter, F., & Zhong, C. X. (2012). Development of an Agricultural Biotechnology Crop Product: Testing from Discovery to Commercialization. *Journal of Agricultural and Food Chemistry*, 60(41), 10179-10187. doi: 10.1021/jf302706e
- [23] Solomon, K. R., Wilks, M. F., Bachman, A., Boobis, A., Moretto, A., Pastoor, T. P., Phillips, R., & Embry, M. R. (2016). Problem formulation for risk assessment of combined exposures to chemicals and other stressors in humans. *Critical Reviews in Toxicology*, 46(10), 835-844. doi: 10.1080/10408444.2016.1211617
- [24] U.S. Department of Agriculture. (n.d.). *About the SECURE Rule*. Retrieved November 2020 from <https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/biotech-rule-revision/secure-rule/secure-about>
- [25] U.S. Department of Agriculture Foreign Agricultural Service. (2015). *Japan's regulatory system for GE crops continues to improve*. Retrieved March 2019 from https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=Agricultural%20Biotechnology%20Annual_Tokyo_Japan_7-13-2015.pdf
- [26] U.S. Department of Agriculture Foreign Agricultural Service. (2017). *Japan 2017 Agricultural Biotechnology Annual*. Retrieved October 2019 from https://apps.fas.usda.gov/newgainapi/api/report/downloadreportbyfilename?filename=Agricultural%20Biotechnology%20Annual_Tokyo_Japan_11-16-2017.pdf
- [27] Venkatesh, T. V., Cook, K., Liu, B., Perez, T., Willse, A., Tichich, R., Feng, P., & Harrigan, G. G. (2015). Compositional differences between near-isogenic GM and conventional maize hybrids are associated with backcrossing practices in conventional breeding. *Plant Biotechnology Journal*, 13(2), 200-210. doi: 10.1111/pbi.12248
- [28] Wolt, J. D., Keese, P., Raybould, A., Fitzpatrick, J. W., Burachik, M., Gray, A., Olin, S. S., Schiemann, J., Sears, M., & Wu, F. (2010). Problem formulation in the environmental risk assessment for genetically modified plants. *Transgenic Research*, 19(3), 425-436. doi: 10.1007/s11248-009-9321-9