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Journal of Regulatory Science

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Regulatory Science

Journal of Regulatory Science 9(1) (2021) 38–44

Data Transportability for Studies Performed to Support an Environmental Risk Assessment for Genetically Modified (GM) Crops

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Abstract

Laboratory and field data generated on genetically modified (GM) plants in one country can inform the environmental risk assessment and support regulatory decision-making for GM plants being cultivated in another country. Well-designed studies that test clear risk hypotheses and that follow well-established methods allow for conclusions to be made about potential environmental effects from cultivation of a GM plant relative to its conventional counterparts. Following the principle of data transportability, if no biologically relevant differences between a GM plant and its conventional counterparts are observed in one country or region, data from these studies can be used to inform the risk assessment in another country, regardless of agroclimatic zone. Similarly, if biologically relevant differences are observed in studies conducted in one country, these data can be used to assess potential environmental harm in another country. Gathering additional data for the ERA in a different country or in expanded regions may increase the weight of evidence of environmental safety, but additional field study data are only warranted if specific hypotheses of risk remain after assessing risk based on the existing data, and if they would affect the outcome of decision-making. Transportation of product data across regions has been successfully used by multiple countries to eliminate redundancy, create regulatory efficiencies and enable timely realization of the benefits of GM plants.

Keywords: data transportability, environmental risk assessment, genetically modified plants, agroclimate

1. Introduction

Laboratory and/or field studies on genetically modified (GM) plants are conducted as part of an environmental risk assessment (ERA) to determine whether cultivation or incidental release of the GM plants could cause unreasonable environmental harm. Data that are developed as part of a science-based ERA for cultivation of GM plants should be driven by problem formulation and the identification of plausible pathways to harm [2, 30]. Problem formulation in the ERA for the cultivation of GM plants is based on information related to the receiving environment, the biology of the plant, the phenotypic similarity of the GM plant relative to its conventional counterparts, and the characteristics of the introduced trait [2]. These represent the core data for ERA and can be used to establish plausible relevant pathways to harm related to plant persistence, weediness or invasiveness, and gene flow. Any need for additional data for the ERA should be considered on a case-by-case basis, guided by problem formulation and development of risk hypotheses based on the core data and trait interactions with the environment [2]. For example, for a trait that has insect resistance properties, concentration data for the introduced gene product and non-target organism (NTO) laboratory hazard data may be necessary to understand potential effects beyond the target pest.

Sometimes, despite a lack of country-specific hypotheses of unique risks, regulatory agencies require local laboratory and/or field studies in a country intending to cultivate the GM plant. Some agencies also require local agronomic studies when the GM plant products (e.g., grain) is intended for import and will not be cultivated. For example, regulatory agencies in Japan have required local field studies for import approvals for some GM events, depending on the crop and trait (GM soybean re-

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quires a local field study to be conducted in Japan, but corn and cotton containing familiar traits do not). The regulatory agency in China (Ministry of Agriculture and Rural Affairs, MARA) accepts global data as part of the import permit application, and local field studies as well as other laboratory-based studies are then commissioned by MARA to be conducted by a local institution in China. The requirements to repeat studies in different countries lead to duplication of data and adds time and complexity to the regulatory process of GM plant approvals without providing additional information essential to the ERA [8]. The time added to the regulatory process delays accrual of benefits of new products to growers and consumers in both cultivation and import countries. Additionally, taxpayers bear the cost of unnecessary regulatory review of duplicative data. A more efficient approach for conducting a science-based ERA in a new location, known as data transportability (DT), consists of leveraging existing data generated in other places. This Policy Commentary explores the concept of DT and provides scientific justification for its use with both laboratory and field data employed in the ERA of GM plants.

2. Overview of Environmental Risks Assessed for GM Plants

Protection goals are derived by each country according to local laws and legislation; however, protection goals related to the environment tend to be broadly similar, such as protecting sustainable food production and biodiversity. Three core areas are typically considered as part of the ERA of GM plants [5, 12, 14]: assessment of weediness/invasiveness potential; assessment of the potential for and effects of transgene flow; and, for insect resistance traits, assessment of potential adverse effects on beneficial NTO populations. Problem formulation, which is based on knowledge of the receiving environment, biology of the plant, agronomic comparison of the GM plant to conventional counterparts, and the characteristics of the introduced trait, is used to assess whether sufficient information and data already exist to address these elements of the ERA and to develop specific hypotheses of harm relating to specific protection goals.

2.1. Weediness and invasiveness

Assessment of a plant's weediness potential considers whether the GM plant has increased weediness characteristics compared with the non-modified crop. An example of a specific hypothesis for harm related to weediness is that the GM plant has introduced traits that increase its ability to outcompete and reduce the abundance of a valued plant species in the environment, including other crops in the agroecosystem. Highly domesticated crops such as maize, cotton, and soybean have a long history of cultivation, and selective breeding has reduced or removed their weediness traits [24]. Many weedy traits, such as seed dormancy or shattering, are agronomically unfavourable and have been selected against in modern crop varieties. As discussed by [2], information about the receiving environment and the biology of the crop, understanding of the intended trait and how it may lead to increased weediness potential, and agronomic field data assessing the similarity of the GM plant to its conventional counterparts, allows for relevant pathways to harm related to weediness to be considered.

2.2. Effects of transgene flow to sexually compatible wild relatives

Gene flow can occur naturally among plants that are sexually compatible and sympatric. For the ERA of a GM plant, it is important to assess whether the introduced gene, if successfully introgressed into a wild relative population, could provide a selective advantage to that population to a greater level than other native genes in the cultivated species. As with weediness assessments, information about the receiving environment and the biology of the plant, an understanding of how the intended trait may lead to increased weediness potential of wild relatives, data on relative agronomic performance, coupled with an understanding of the potential for successful outcrossing and transgene introgression into a wild relative population, allows for relevant pathways to harm related to transgene flow to be considered.

A specific hypothesis for harm related to gene flow for GM soybeans that are to be cultivated in an area where wild soybeans are present would consider if the introduced trait in the GM plant become introgressed into the wild soybean population and confers a selective advantage. Cultivated soybean (*Glycine max*) is sexually compatible with wild soybean (*Glycine soja*), and genes from cultivated soybean can be found in wild soybean populations. An understanding of GM trait in cultivated soybean can be used to assess potential for selective advantage if the trait is introgressed in the wild soybean population. In many cases, introgression of a trait does not result in harm. For example, yield genes and abiotic stress tolerance genes that have been selected for through traditional breeding for generations have not been observed to provide a selectable advantage to wild soybean in North Asian countries such as Japan, China, Korea, and Taiwan, as evidenced by the lack of adverse effects on wild soybean populations in these countries after years of import of non-GM domestic soybeans with improved yield and stress phenotypes [9, 15, 16, 17, 18, 19, 20, 21, 22]. Therefore, it is reasonable to expect that GM traits that increase yield or abiotic stress would likewise not provide a selectable advantage to wild soybean. Similarly, it has been demonstrated that outcrossing by a GM soybean modified with an insect resistance gene from *Bacillus thuringiensis* (*Bt*) does not provide a selective advantage to wild soybean, based on the outcome of insect feeding damage surveys in wild soybean populations [10].

Agronomic endpoints related to reproduction (pollen viability, pollination rates, etc.), can be used to inform whether the trait has increased the potential for outcrossing, and information on the crop biology and the receiving environment can be used to inform the likelihood of outcrossing with sexually compatible wild relatives. There is rarely a plausible hypothesis that the trait in a GM plant has altered the outcrossing rates relative to the outcrossing rates of the non-modified crop. The only hypothetical exception to this would be if the GM trait alters

pollen dispersal or pollination rates, perhaps to increase crop yield. However, no such traits have been developed to date.

2.3. Effects on beneficial non-target organisms

Efficient crop production depends on valuable interactions between the crop and its biotic environment. For example, arthropod populations can be beneficial to agricultural production; many crops rely on insects for pollination; insect predators and parasitoids provide important ecosystem services by reducing the populations of insect pests that feed on the crop; some soil arthropods are important in processing decaying vegetable matter and maintaining soil function. Therefore, it is important to understand the potential for a particular GM trait to reduce the abundance of beneficial taxa representing core ecological functions (e.g., pollinators, predators, parasitoids, and decomposers). The need to generate data to assess the effects on NTOs typically only informs an ERA for GM plants with traits that confer insect protection (insecticidal trait), such as Cry proteins from *Bt* and traits based on RNAinterference (RNAi). The ERA of insect-protected crops includes an assessment of the effect of the trait on beneficial non-target arthropods (NTAs) that may be exposed to the trait and may be sensitive to it. As *Bt* proteins and RNAi are highly specific in their spectrums of activity, focused NTO testing under laboratory conditions is generally sufficient to detect meaningful effects (e.g., >50 percent mortality [29]) and higher tier studies (greenhouse or field study) are not conducted unless triggered by uncertainty in the tier 1 studies.

Beneficial microbial components of the agricultural environment, such as soil bacteria and fungi, could be considered within the ERA for GM plants if the introduced trait has antimicrobial activity, for example, through studies of soil microbial activity. However, no such traits have been developed to date and such studies are not warranted for existing GM traits.

3. Data Transportability (DT)

DT for the ERA of a GM plant can be defined as the use of data generated in one region or country to inform the ERA of the GM plant in another region or country. DT requires proper scientific justification to demonstrate that the data are suitable to inform the risk assessment. For example, studies should have clearly defined and relevant environmental risk hypotheses, follow well-established methods, have a suitable study design (e.g., adequate replication, randomization, and sampling), and use appropriate statistical analyses that are suitable for the environmental risk assessment.

3.1. Field studies

Agronomic field studies are typically conducted across multiple locations that are representative of the growing region in the country where the GM plant was developed. The purpose of these field studies is to assess the phenotypic and agronomic similarity between the GM plant and the conventional counterpart and to determine the concentration of an introduced gene product in different plant tissues and across multiple growth stages. If a GM plant and its conventional counterpart are observed across a range of environmental conditions in one country or region, these agronomic and concentration datasets can be used to support the risk assessment in another country, regardless of agroclimatic zone. Gathering additional data for the ERA in a different country or in expanded regions may increase the weight of evidence of environmental safety, but additional field study data are only warranted if specific hypotheses of risk remain after assessing risk based on the existing data, and if the additional field data would affect the outcome of decision-making.

3.1.1. Agronomic and phenotypic observation

Field studies for phenotypic/agronomic observations should not be designed or expected to characterize the agronomy of the GM plant in as much detail as possible in a given region or climate. Instead, field studies are used to identify any biologically relevant adverse changes to the GM plant as a result of the GM trait and compare these changes against a range of conventional counterparts grown in the same area and under the same conditions [26]. Agronomic field studies that follow current guidance (for example, [7]) are conducted in multiple locations that represent a diversity of the commercial crop growing areas, measure a standard suite of agronomic endpoints (some of which are relevant for the ERA), and are analyzed with appropriate statistical analyses to detect biologically-meaningful differences between GM plants and near-isoline control and/or representative reference lines. Environmental conditions, including climate, weather, and soil type, can influence how both GM and conventional crops grow. Changes in growth patterns of crops due to local environmental conditions are inherent and expected for both conventional and GM plants systems, but this natural variability is not indicative of environmental risk. There is a large range of agronomic properties that enable crops to grow in different environments with an established history of safety. Without a plausible mechanism based on the characteristics of the introduced trait, the potential for unintended or unanticipated harmful differences to occur in one environment and not in other environments is remote. In most cases, data from confined field trials can be transported across regions, regardless of agroclimatic conditions. When a plausible hypothesis can be developed for how the GM plant could result in harm in a different region, studies designed specifically to investigate the likelihood and magnitude of potential harm can be conducted [2]. For example, a cold hardiness trait may have an impact in temperate zones that may not be apparent in tropical areas, and additional testing in a temperate zone may be warranted. Other scenarios may exist where similarity of environments may be useful to justify the transportability of data, such as when there is an expectation that the expression of intended phenotype is heavily dependent on environment (e.g., drought tolerance) [8].

Selection against weedy traits during crop domestication is desired in modern crops, and agronomic endpoints that are related to weediness characteristics (for example, seed shattering, dropped ears) are typically measured in agronomic field studies. If the host plant (conventional crop) exhibits no weed-

iness characteristics, the GM trait is not related to weediness characteristics, and agronomic endpoints related to weediness characteristics are shown to be comparable to the non-modified plant, then no plausible hypothesis exists to support increased weediness potential of the GM plant, and the agronomic field study data collected in one country can and should be transported and used to inform the ERA in another country. On the other hand, if the host plant does exhibit weedy characteristics [23], and/or if the GM trait is observed to affect the agronomic endpoints that are related to weediness characteristics, the agronomic field study data collected in one country still can and should be transported and used to inform the ERA in another country. As discussed above, the comparative nature of well-designed field studies examines the GM plant in comparison to its conventional counterpart in a range of environments, and agronomic endpoints that are related to weediness characteristics should be able to be transported to inform the ERA in another region. If there remain additional plausible hypotheses for environmental harm related to weediness after considering the available transported agronomic field study data, additional studies to address those hypotheses may be warranted in another country, but the decision to request additional in-country data should be on a case-by-case basis to inform a hypothesis for harm that cannot be addressed with the available data from other countries.

As with weediness risk assessments, environmental risks associated with transgene flow to sexually compatible wild relatives can be assessed in one country using field study data from another country. Data and conclusions from field studies that demonstrate lack of biologically relevant differences in agronomic performance of the GM plant and its conventional counterpart across a range of environments can be used to inform the transgene flow risk assessment in another country.

i. Environmental exposure

For certain aspects of risk assessment, measures of exposure to environmental stressors can be necessary. These measures are warranted for assessment of risks to potentially sensitive NTOs like beneficial arthropods, on a case-by-case basis only when a potential hazard of a GM trait is identified by problem formulation, such as one that confers insect protection [2]. Potential exposure of NTOs are typically informed by measuring tissue specific concentrations of a gene product (newly expressed protein, dsRNA, etc.,) collected from field studies conducted under a range of field conditions. As with agronomic field study data, the concentration data for the gene products are collected from plants grown in multiple locations that represent the major growing areas for the crop, typically in the country of development. Protein or dsRNA concentration is measured in different plant tissues and different growth stages, and it can be used to estimate potential for exposure to NTOs (for example, a honey bee may be exposed to a protein/dsRNA expressed in maize pollen). Expression product concentration data and conclusions from studies conducted in one country are transportable to other countries for the purpose of assessing potential exposure to NTOs, and generating new expression data in one country should not need to be repeated to inform the ERA in another country.

ii. Laboratory data

When an NTO risk assessment for GM plants with traits that confer insect protection is needed, NTO testing should follow a tiered approach whereby laboratory studies are first conducted at high concentration of the GM gene product in the laboratory. Higher tier testing using GM plant tissue, greenhouse trials, or field studies to assess potential effects on NTOs are only warranted when they are triggered by effects seen in the lower tier laboratory assessment.

The transportability of laboratory data has been widely accepted by regulatory agencies globally for both GM plants [27, 28] and traditional chemistry testing [13, 25] because laboratory conditions are not intended to represent realistic environmental conditions. When laboratory studies are considered for use in a risk assessment or regulatory decision making, they should be evaluated for relevancy and reliability. Methods should be reconstructable, interpretable, reliable, and include appropriate statistical analysis. Test systems and study design should follow standardized and internationally accepted guidelines (e.g., Organisation for Economic Co-operation and Development, U.S. Environmental Protection Agency) or peer-reviewed published methodologies, when available. Finally, laboratory studies should be conducted under widely accepted quality criteria (e.g., good laboratory practices, International Organization for Standardization) to ensure reproducibility of the data. Numerous authors have set forth recommendations of laboratory testing to support the ERA of GM plants [3, 27]. Surrogate species are often used in laboratory testing, and surrogate species are selected based on relatedness to target pest and beneficial NTOs, amenability to testing under laboratory conditions, availability of standardized methods, etc. [4, 28]. The surrogate species concept is well-accepted, and testing at high concentration in the laboratory in the early tier hazard assessment (for example, 10X the concentration an NTO could be exposed to in the environment) provides a high margin of exposure and protection for other species that may be in the environment but not directly assessed in the laboratory. The data and conclusion from the laboratory hazard studies are transportable across regions due to the controlled nature of laboratory studies, validated, robust, and reproducible methods, and use of surrogate species. When triggered by the tiered testing approach, a field study may be conducted to assess the consequences of the hazard to NTOs under environmentally relevant conditions. As with other field study data, field NTO study data can be transported across regions if they are designed to detect meaningful differences in NTO abundance or function between the GM plant and its non-GM counterparts. Additional field testing should only be conducted in another country if there is a specific hypothesis for harm that cannot be addressed using all of the existing data, for example, if there is an NTO taxon of particular concern in one region that is not present in the original one, and familiarity with the GM trait and lower tier laboratory data are insufficient to assess risk.

For import-only scenarios (e.g., for food, feed, and processing) the potential exposure of individual NTOs to a GM plant is

low and the potential for population level exposure is negligible (i.e., seed spillage during transportation and/or Low Level Presence in conventional planting seeds) relative to cultivation scenarios, and therefore the risk to NTOs from import of GM grain is negligible when compared with the risk from cultivation of GM plants. In the case of import countries, the data and conclusions from the cultivation country should be considered, and additional data are not warranted to assess risk.

4. Data Transportability Case Studies

Garcia Alonso et al. [8] presented a case for the transportability of field study data for ERA along with a conceptual framework and process for both regulators and the regulatory community. This approach to DT relied on the similarity of agroclimatic zones as the foundation to enable the transportability of field study data by encouraging the comparison of physical characteristics of the field study environment to the region where the data could be used. Identification of analogous agronomic climates in a given country could then allow for easy acceptance of data generated in the same agronomic climate in another country. This approach is intended to provide very explicit evidence to justify a regulatory agency's decision to accept data generated in another location.

In recent years, however, more studies examining field data from different environments have revealed that agroclimatic similarity is in fact not necessary for DT to be employed as part of the ERA of GM plants. Horak et al. [11] demonstrated that data collected to evaluate the weediness potential of soybean is transportable between cultivation countries. In this example, comparative studies were conducted in diverse locations across the U.S. and Argentina over three years, evaluating two GM soybean products and their conventional control. Data collected from distinct geographic and environmental conditions yielded similar results and conclusions regarding a lack of environmental risk. Where statistically significant differences were observed, no consistent trends across years and regions for these weediness characteristics were observed, and these differences were within the range of natural variability for soybean, thus providing additional evidence that these differences were not associated with the genetic modification process or the locations where the field study data were generated.

Nakai et al. [23] demonstrated that confined field trial data for GM plants are also transportable between cultivation and import countries. While GM plants are not cultivated in Japan and China, these countries require that in-country (local) confined field trials be performed for GM grain imported as food/feed or for processing. Currently, Japanese authorities will accept data derived in a cultivation country for GM maize with familiar traits (e.g., already registered). By examining the parameters under which the confined field trials are conducted, demonstrating that the endpoints assessed are relevant for the protection goals in import countries, and highlighting the low exposure scenario inherent in import scenarios, Nakai et al. [23] concluded that field study data, regardless of the characteristics of the inserted gene(s), are transportable from cultivation countries to importing countries (e.g., from the U.S. to Japan). Japan has accepted confined field trial data from other countries for ERA of GM maize for which the inserted gene(s) had already been assessed in other GM maize events to grant cultivation and import approval since December, 2014 [23]. As of March, 2018, confined field data collected in the U.S. for three GM maize products (MON87416, MZHG0JG, MZIR098) have already been accepted for implementing ERA in Japan.

In Mexico and other countries, cultivation approval requires in-country field assessment of the potential effects of the GM plants on NTAs. Corrales Madrid et al. [6] demonstrated that NTA data is transportable within diverse ecoregions in Mexico. Relevant NTA data from three types of GM maize were shown to be transportable across four ecoregions in Mexico. Importantly, the sites of the field studies represented high geographic and environmental diversity. No statistically significant differences in NTA taxa abundance between tests and controls were observed, and likewise, no adverse effects on NTAs were reported. As reported elsewhere [1], within the maize agroecosystem, a high conservation of taxa exists that link to core ecological functions (e.g., herbivores, predators, parasitoids, etc.). These conserved ecosystem services are present irrespective of the regional biodiversity and across temperate and tropical agroclimatic zones. This repetition of taxa facilitates their use as representative taxa for maize systems, thus enabling the transportability of data collected from one region to another [1]. The breadth of sites and high conservation of taxa shown in Corrales Madrid et al. [6], further demonstrates that NTA data and the associated conclusions regarding risk are transportable even in mega-diverse countries.

As described in Corrales Madrid et al. [6], the above studies provide empirical support that data from well-designed, comparative assessments and the associated conclusions on potential environmental risk are independent of the local environments and are transportable to other regions to inform the risk assessment.

5. Transportability of ERA Conclusions

This paper has focused on transporting data from one region to another to form the basis of an ERA in the recipient one. This principle can often be extended so that not just the data, but also the ERA conclusions, can be transported across regions based on problem formulation. Countries tend to have broadly similar protection goals for their agricultural environments, such as protecting sustainable food production and biodiversity, and therefore, similar risk hypotheses for the same crop. The risk assessments conducted based on those risk hypotheses are, therefore, similar and the conclusions are the same.

There are a few cases where ERA conclusions may differ in one region from another. First, if the agronomic data show meaningful differences between a GM plant and its conventional counterparts under certain environmental conditions, and those conditions are more prevalent in one region than another, the risk assessments may reach different conclusions. If there is a plausible hypothesis for how that agronomic difference could lead to environmental harm, additional assessment

may be warranted. Second, if there are sexually compatible wild relatives in one country that are absent in another country, the risk assessment conclusions may differ. Third, if there are specific (usually protected due to being endangered) NTOs in one country that may be affected by an insecticidal trait, the conclusion of the NTO risk assessment may differ. However, even in these situations where the risk assessment conclusions cannot be transported, the risk assessment data upon which they are based can still be transported.

6. Discussion and Conclusions

The transportability and acceptance of ERA data and/or conclusions from well-designed laboratory and field studies can facilitate the efficiency of regulatory approvals of GM plants across countries and regions. Acceptance of such data leads to more rapid access to benefits for farmers, reduces duplicative requirements, and ensures consistent science-based testing, data, and conclusions. This approach is similar to the standard practice of mutual acceptance of data that has broad acceptance within the chemical industry and is supported by international organizations such as the Organisation for Economic Cooperation and Development (OECD). The controlled nature of laboratory studies and comparative nature of field studies conducted across diverse environmental conditions allow for data to be viewed and conclusions to be made independent of an agroclimate or region, unless a specific risk hypothesis exists to oppose that consideration. Numerous peer-reviewed publications have demonstrated the scientific rationale for DT, and both cultivation and import countries are beginning to adopt and benefit from this practice.

7. Declaration of Conflicting Interest

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

8. 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.

9. Article Information

This article was received November 25, 2019, in revised form March 27, 2020, and made available online January 5, 2021.

10. References

[1] Ahmad, A., Negri, I., Oliveira, W., Brown, C., Asiimwe, P., Sammons, B., Horak, M., Jiang, C., & Carson, D. (2016). Transportable data from non-target arthropod field studies for the environmental risk assessment of genetically modified maize expressing an insecticidal double-stranded RNA. *Transgenic Research, 25*(1), 1-17. doi: 10.1007/s11248-015-9907-3

[2] Anderson, J. A., Bachman, P., Burns, A., Chakravarthy, S., Goodwin, L., Privalle, L., Song, S., & Storer, N. P. (2021). Streamlining data requirements for the environmental risk assessment of genetically modified (GM) crops for cultivation approvals. *Journal of Regulatory Science, 9*(1), 26-37. doi: 10.21423/jrs-v09i1anderson

[3] Carstens, K., Anderson, J., Bachman, P., De Schrijver, A., Dively, G., Federici, B., Hamer, M., Gielkens, M., Jensen, P., Lamp, W., Rauschen, S., Ridley, G., Romeis, J., & Waggoner, A. (2012). Genetically modified crops and aquatic ecosystems: considerations for environmental risk assessment and non-target organism testing. *Transgenic Research, 21*(4), 813-842. doi: 10.1007/s11248-011-9569-8

[4] Carstens, K., Cayabyab, B., De Schrijver, A., Gadaleta, P. G., Hellmich, R. L., Romeis, J., Storer, N., Valicente, F. H., & Wach, M. (2014). Surrogate species selection for assessing potential adverse environmental impacts of genetically engineered insect-resistant plants on non-target organisms. *GM Crops & Food, 5*(1), 11-15. doi: 10.4161/gmcr.26560

[5] Chandler, S., & Dunwell, J. M. (2008). Gene flow, risk assessment and the environmental release of transgenic plants. *Critical Reviews in Plant Sciences, 27*(1), 25-49. doi: 10.1080/07352680802053916

[6] Corrales Madrid, J. L., Martínez Carrillo, J. L., Osuna Martínez, M. B., Durán Pompa, H. A., Alonso Escobedo, J., Javier Quiñones, F., Garzón Tiznado, J. A., Castro Espinoza, L., Zavala García, F., Espinoza Banda, A., González García, J., Jiang, C., Brown, C. R., de la F. Martínez, J. M., Heredia Díaz, O., Whitsel, J. E., Asiimwe, P., Baltazar, B. M., & Ahmad, A. (2018). Transportability of non-target arthropod field data for the use in environmental risk assessment of genetically modified maize in Northern Mexico. *Journal of Applied Entomology, 142*(5), 525-538. doi: 10.1111/jen.12499

[7] EFSA Panel on Genetically Modified Organisms. (2015). Guidance on the agronomic and phenotypic characterisation of genetically modified plants. *EFSA Journal, 13*(6). doi: 10.2903/j.efsa.2015.4128

[8] Garcia-Alonso, M., Hendley, P., Bigler, F., Mayeregger, E., Parker, R., Rubinstein, C., Satorre, E., Solari, F., & McLean, M. A. (2014). Transportability of confined field trial data for environmental risk assessment of genetically engineered plants: a conceptual framework. *Transgenic Research, 23*(6), 1025-1041. doi: 10.1007/s11248-014-9785-0

[9] Goto, H., McPherson, M. A., Comstock, B. A., Stojšin, D., & Ohsawa, R. (2017). Likelihood assessment for gene flow of transgenes from imported genetically modified soybean (*Glycine max* (L.) Merr.) to wild soybean (*Glycine soja* Seib. et Zucc.) in Japan as a component of environmental risk assessment. *Breeding Science, 67*(4), 348-356. doi: 10.1270/jsbbs.16134

[10] Goto, H., Shimada, H., Horak, M. J., Ahmad, A., Baltazar, B. M., Perez, T., McPherson, M. A., Stojšin, D., & Ohsawa, R. (2016). Characterization of natural and simulated herbivory on wild soybean (*Glycine soja* Seib. et Zucc.) for use in ecological risk assessment of insect protected soybean. *PloS one, 11*(3), e0151237. doi: 10.1371/journal.pone.0151237

[11] Horak, M. J., Rosenbaum, E. W., Kendrick, D. L., Sammons, B., Phillips, S. L., Nickson, T. E., Dobert, R. C., & Perez, T. (2015). Plant characterization of Roundup Ready 2 Yield® soybean, MON 89788, for use in ecological risk assessment. *Transgenic Research, 24*(2), 213-225. doi: 10.1007/s11248-014-9839-3

[12] Japan Biosafety Clearing House. (2014). *Biosafety regulations in Japan. Assessment of effects on biological diversity*. Retrieved November 2019 from https://www.biodic.go.jp/bch/english/cartagena/s_05.html

[13] Koëter, H. B. W. M. (2003). Mutual acceptance of data: Harmonised test methods and quality assurance of data - The process explained. *Toxicology Letters, 140*, 11-20. doi: 10.1016/S0378-4274(02)00491-5

[14] Lu, B-R. (2008). Transgene escape from GM crops and potential biosafety consequences: An environmental perspective. *Collection of Biosafety Reviews, 4*, 66-141.

[15] Ministry of Agriculture, Forestry and Fisheries. (2011). *Survey on GM plants in 2009* (in Japanese). Retrieved from http://www.maff.go.jp/j/syouan/nouan/carta/c_data/pdf/21kekka.pdf

[16] Ministry of Agriculture, Forestry and Fisheries. (2011). *Survey on GM plants in 2010* (in Japanese). Retrieved from http://www.maff.go.jp/j/syouan/nouan/carta/c_data/pdf/22_natane.pdf

[17] Ministry of Agriculture, Forestry and Fisheries. (2012). *Survey on GM plants in 2011* (in Japanese). Retrieved from http://www.maff.go.jp/j/press/syouan/nouan/pdf/120912-02.pdf

[18] Ministry of Agriculture, Forestry and Fisheries. (2013). *Sur-*

vey on GM plants in 2012 (in Japanese). Retrieved from http://www.maff.go.jp/j/syouan/nouan/carta/c_data/pdf/24_kekka.pdf

[19] Ministry of Agriculture, Forestry and Fisheries. (2014). *Survey on GM plants in 2013* (in Japanese). Retrieved from http://www.maff.go.jp/j/syouan/nouan/carta/torikumi/pdf/h25_kekka.pdf

[20] Ministry of Agriculture, Forestry and Fisheries. (2015). *Survey on GM plants in 2014* (in Japanese). Retrieved from http://www.maff.go.jp/j/syouan/nouan/carta/torikumi/pdf/h26_houkoku.pdf

[21] Ministry of Agriculture, Forestry and Fisheries. (2017). *Survey on GM plants in 2015* (in Japanese). Retrieved from http://www.maff.go.jp/j/press/syouan/nouan/attach/pdf/170110-1.pdf

[22] Ministry of Agriculture, Forestry and Fisheries. (2018). *Survey on GM plants in 2016* (in Japanese). Retrieved from http://www.maff.go.jp/j/syouan/nouan/carta/torikumi/attach/pdf/index-134.pdf

[23] Nakai, S., Hoshikawa, K., Shimono, A., & Ohsawa, R. (2015). Transportability of confined field trial data from cultivation to import countries for environmental risk assessment of genetically modified crops. *Transgenic Research, 24*(6), 929-944. doi: 10.1007/s11248-015-9892-6

[24] Organisation for Economic Co-operation and Development. (2016). Low-level presence of transgenic plants in seed and grain commodities: Environmental risk/safety assessment and availability and use of information. In *Safety Assessment of Transgenic Organisms in the Environment, Volume 6: OECD Consensus Documents*. OECD Publishing. Retrieved from https://www.oecd-ilibrary.org/docserver/9789264253421-4-en.pdf?expires=1603915225&id=id&accname=ocid177419&checksum=682F6AB550E8B0CA8B3968A8625A706D

[25] Organisation for Economic Co-operation and Development. (2019). *Saving Costs in Chemicals Management: How the OECD Ensures Benefits to Society*. OECD Publishing. Retrieved from doi: 10.1787/9789264311718-en

[26] Raybould, A. (2007). Ecological versus ecotoxicological methods for assessing the environmental risks of transgenic crops. *Plant Science, 173*(6), 589-602. doi: 10.1016/j.plantsci.2007.09.003

[27] Romeis, J., Hellmich, R. L., Candolfi, M. P., Carstens, K., De Schrijver, A., Gatehouse, A. M. R., Herman, R. A., Huesing, J. E., McLean, M. A., Raybould, A., Shelton, A. M., & Waggoner, A. (2011). Recommendations for the design of laboratory studies on non-target arthropods for risk assessment of genetically engineered plants. *Transgenic Research, 20*(1), 1-22. doi: 10.1007/s11248-010-9446-x

[28] Romeis, J., Raybould, A., Bigler, F., Candolfi, M. P., Hellmich, R. L., Huesing, J. E., & Shelton, A. M. (2013). Deriving criteria to select arthropod species for laboratory tests to assess the ecological risks from cultivating arthropod-resistant genetically engineered crops. *Chemosphere, 90*(3), 901-909. doi: 10.1016/j.chemosphere.2012.09.035

[29] Rose, R. I. (2006). Tier-based testing for effects of proteinaceous insecticidal plant-incorporated protectants on non-target arthropods in the context of regulatory risk assessments. *IOBC WPRS Bulletin, 29*(5), 143-149.

[30] 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