USDA United States Department of Agriculture
Foreign Agricultural Service

GAIN Global Agricultural Information Network

Voluntary Report – Voluntary - Public Distribution **Date:** November 27,2019

Report Number: JA2019-0196

Report Name: MAFF Guidance for the Handling of Genome Edited Organisms under the Cartagena Act

Country: Japan

Post: Tokyo

Report Category: Biotechnology and Other New Production Technologies, Biotechnology and Other New Production Technologies, Biotechnology - Plants and Animals

Prepared By: Suguru Sato

Approved By: Zeke Spears

Report Highlights:

On October 9, 2019, Japan's Ministry of Agriculture, Forestry, and Fisheries released procedures for providing information on the effects of organisms obtained by using genome editing technology on biological diversity. This procedure applies to plant and animal organisms used in agriculture, forestry, and fisheries.

On October 9, 2019, Japan's Ministry of Agriculture, Forestry, and Fisheries (MAFF) released final procedures for providing information on the effects on biological diversity of organisms obtained by using genome editing technology. These procedures were developed following the Ministry of Environment (MOE)'s regulation of genome editing technology released on February 8, 2019 that assigned MAFF as the competent authority for genome edited agricultural products (JA9024). The procedures address MAFF's notification requirements for the development and commercialization of genome edited plant and animal products in Japan.

The procedures are in alignment with MOE's determination that "If an extracellularly processed nucleic acid is not transferred into the host" or "if, after the transfer of an extracellularly processed nucleic acid into the host, it has been confirmed that no nucleic acid or a replicated product thereof remains in the finally obtained organism," the product is not considered a "living modified organisms" and is therefore not considered genetically engineered.

However, if non-genetically-engineered genome edited organism are used without "containment measures" (i.e., open field cultivation, exposure to open environment through transportation, etc.), MAFF requires in-advance consultation to confirm the organism is not a living modified organism.

For more details, please see the following provisional translation of MAFF's procedures. The provisional translation includes a translation of Form 1, but excludes:

- Annex 2: Specific contents of information to describe in case where the specie is fish
- Form 2: Pre-consultation request
- Form 3: Provision of product information
- Form 4: Report of commercial use
- Form 5: Confirmation of containment measures for the use of organisms obtained by using genome editing technology
- Annex 1 (for Form 5): Specific contents of information to describe in case where the specie is microorganism
- Annex 2 (for Form 5): Specific contents of information to describe in case where the specie is animal
- Annex 3 (for Form 5): Specific contents of information to describe in case where the specie is plant

MAFF is expected to release an official translation.

Point of contact for consultation:

- Plant Product Safety Division, Food Safety and Consumer Affairs Bureau, the Ministry of Agriculture, Forestry and Fisheries
- Tel: +81-3-6744-2102 (Capacity of communication in English might be limited)
- Fax: +81-3-3580-8592
- Email: nbt_tetsuzuki@maff.go.jp

MAFF's website:

- Handling of organisms developed by new breeding techniques (in Japanese)
  http://www.maff.go.jp/j/syouan/nouan/carta/tetuduki/nbt.html

(Provisional Translation)

Specific Procedures for Providing Information on the Adverse Effects on Biological Diversity of Organisms Obtained by Using Genome Editing Technology in the Field of Agriculture, Forestry, and Fisheries

Notification No. 2743 issued by the Director of Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries, dated October 9, 2019

1 Objective

The handling of organisms obtained by the use of genome editing technology, under the "Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms" (Act No. 97 of 2003, hereinafter referred to as the "Cartagena Act") was reviewed by the Central Environment Council, and based on the results of the review, "Handling of organisms that are obtained through the use of genome editing technology and do not fall under 'living modified organisms' as stipulated in the Cartagena Act" (Notification No. 1902081 issued by the Director of Nature Conservation Bureau, Ministry of the Environment, dated February 8, 2019, hereinafter referred to as the "Ministry of the Environment Notification") was issued this February by the Director of the Nature Conservation Bureau, Ministry of the Environment.

This notification is to stipulate specific procedures for providing information regarding adverse effects on biological diversity, based on the Ministry of the Environment Notification, of the organisms over which the Minister of Agriculture, Forestry and Fisheries has jurisdiction with respect to production or distribution [including those used by persons whose businesses are under the jurisdiction of the Minister of Agriculture, Forestry and Fisheries, if they are used by taking containment measures; excluding those which fall under the living modified organisms in Article 2, paragraph 2 of the Cartagena Act, as well as those that are in the research and development stage (those related to research and development, if they are used by taking containment measures); hereinafter referred to as "subject organisms"], among organisms obtained through the use of genome editing technology.

Note that the particulars stipulated in this notification shall be reviewed as necessary, based on international trends regarding the enhancement or management of future scientific knowledge regarding adverse effects on biological diversity that could arise from the use of organisms obtained through the use of genome editing technology (refers to using, cultivating and growing, processing, storing, transporting and disposing of living modified organisms, and other related actions, to provide food, animal feed, or for other related purposes; the same shall apply, hereinafter).

2 Outline of the Arrangement in the Ministry of the Environment Notification

1. In the Ministry of the Environment Notification, "the scope subject to regulations in the Cartagena Act with respect to organisms obtained through the use of genome editing technology" shall be handled as follows.

(1) If an extracellularly processed nucleic acid is not transferred into the host, it does not fall under “living modified organisms” in the Cartagena Act.

(2) If, after the transfer of an extracellularly processed nucleic acid into the host, the finally obtained organism contains the nucleic acid or a replicated product thereof, or if it has not been confirmed that no said nucleic acid or replicated product thereof remains in the obtained organism, it falls under “living modified organisms” in the Cartagena Act, and it is thus necessary to take appropriate measures based on this Act.

(3) If, after the transfer of an extracellularly processed nucleic acid into the host, it has been confirmed that no nucleic acid or a replicated product thereof remains in the finally obtained organism, it does not fall under “living modified organisms” in the Cartagena Act.

2. In addition, in the Ministry of the Environment Notification, among organisms obtained by genome editing technology, those organisms that do not fall under “living modified organisms” in the Cartagena Act shall be handled as follows.

(1) Prior to the use of such said organism, a person who intends to use this organism shall provide information to the competent ministry regarding the characteristics of the organism and the results of a review regarding the possibility of an adverse effect on biological diversity. However, this does not apply to use in an environment in which the containment measures stipulated by the Order of the competent ministry under Article 12 of the Cartagena Act, or containment measures approved by the competent minister are being taken.

(2) If it is determined that there is a risk of an adverse effect arising from the said organism on biological diversity after the start of use, necessary measures shall be taken immediately to prevent the said impact, and at the same time, this fact shall be reported promptly to the competent ministry.

3 Procedures for Using Subject Organisms

Based on the Ministry of the Environment Notification, the procedures for using subject organisms are as follows.

1. In the case of general use (use for a so-called open system)

If a subject organism is to be used without taking the containment measures described in 2 above, a consultation is required in advance based on (1), and after confirming that this organism does not fall under living modified organisms, an information provision form shall be submitted based on (2); the organism may then be used.

However, if the subject organisms published on the website of the Ministry of Agriculture, Forestry and Fisheries based on the provisions of (ii) in (2) are used in accordance with the contents of the said published information [excluding the addresses in (1) in 3], there is no need to provide such information.

(1) Pre-consultation

(i) Prior to the use of a subject organism, a draft of an information provision form containing information regarding the following items, from (a) to (j) shall be prepared using Form 1, and this form shall be submitted to the Director of the Plant Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries (hereinafter referred to as "the Director of the Plant Products Safety Division") using Form 2.

(a) Name and summary of the organism obtained by genome editing technology

(b) Application of the corresponding organism

(c) Summary of the use-facility

(d) A fact that no extracellularly processed nucleic acid or any replicated product thereof specified in Article 2, paragraph 2, item 1 of the Cartagena Act, remains in the organism

(e) Taxonomic species of the modified organism

(f) Method of genome editing used for the modification

(g) Modified gene and the function of the corresponding gene

(h) Trait changes caused by the corresponding modification

(i) Presence or absence of other trait changes except 8 above (if present, the content)

(j) Discussion regarding the possibility of causing an adverse effect on biodiversity (referring to effects caused by use of a living modified organism that poses an unacceptable risk of impairing biological diversity; the same shall apply hereinafter) through use of the organism. (A review shall be conducted for each item listed in Appendix 1, while a comprehensive review shall be conducted based on these items.)

When submitting a draft of the information provision form, a copy of this form shall be attached. Furthermore, if the contents of this form are recorded in an electromagnetic record, such record shall also be submitted.

Note that, when it is difficult to determine whether or not an organism falls under the living modified organisms stipulated in the Cartagena Act, or otherwise when particulars are involved that require confirmation through the provision of information, consultation shall be undertaken with the Plant Products Safety Division, Food Safety and Consumer Affairs Bureau, Ministry of Agriculture, Forestry and Fisheries (hereinafter referred to as the "Plant Products Safety Division").

(ii) When (i) is submitted, the Plant Products Safety Division shall, without delay, send a copy of the submitted draft of the information provision form to the Wildlife Division, Nature Conservation Bureau, Ministry of the Environment (hereinafter referred to as the "Wildlife Division of the Ministry of the Environment"), and at the same time, shall confirm that the said organism does not fall under living modified organisms, and that the draft of the information provision form has been completed appropriately, from the perspective of adverse effects on biological diversity.

In the process of said confirmation, the advice of persons with specialized academic experience regarding adverse effects on biological diversity shall be sought, as necessary. Moreover, in case of any doubt, the provision of additional information shall be requested.

(iii) As a result of the confirmation in (ii), if the Plant Products Safety Division confirms that the organism does not fall under living modified organisms and that the draft of the information provision form has been completed appropriately from the perspective of adverse effects on biological diversity, the person who submitted (i) shall be notified.

(2) Submission of an information provision form

(i) The person who engaged in the pre-consultation in (1) shall submit an information provision form regarding the completion of said pre-consultation, to the Director of the Plant Products Safety Division using Form 3. In doing so, a copy of the information provision form shall be attached, and if the contents of this form are recorded in an electromagnetic record, this record shall also be submitted. In addition, when it has been determined when use of the said organism will begin, the start date of use shall be reported to the Director of the Plant Products Safety Division using Form 4.

(ii) The Plant Products Safety Division shall, without delay, send a copy of the submitted information provision form to the Wildlife Division of the Ministry of the Environment when (i) is submitted. In addition, if (i) is submitted or reported, the submitted or reported information (excluding information that may create an unreasonable advantage or disadvantage to specific persons, if published) shall be published on the website of the Ministry of Agriculture, Forestry and Fisheries.

(3) Handling of crossbred progeny

(i) A person who intends to use an organism that has been bred and raised by breeding subject organisms published on the website of the Ministry of Agriculture, Forestry and Fisheries based on the provisions of (ii) in (2) shall, for the time being, contact the Plant Products Safety Division for each individual case.

(ii) The Plant Products Safety Division shall request for the provision of information if there is a possibility that changes could arise in either the characteristics of the organism used for breeding or its adverse effects on biological diversity.

3 Others

(1) Report of changes in name, etc.

(i) The person who submitted an information provision form based on the provisions of (2) of 1, or the person who submitted a confirmation form based on the provisions of (1) of 2 shall promptly report to the Director of Plant Products Safety Division, using Form 6 when there is any change in the name, address, or phone number (hereinafter referred to as “name, etc.”) written on the said information provision form or confirmation form.

(ii) The Plant Products Safety Division shall send a copy of the submitted report to the Wildlife Division of the Ministry of the Environment, without delay, when (i) is reported pertaining to a change in the name, etc. written on the information provision form.

(2) Response when there is a risk of effects that impair biological diversity

(i) If a person who uses or has used subject organisms determines that there is a risk of adverse effects on biological diversity, the person shall immediately take necessary measures to prevent such effects, while promptly reporting the measures taken to the Director of the Plant Products Safety Division.

(ii) If (i) is reported, the Plant Products Safety Division shall contact the Wildlife Division of the Ministry of the Environment without delay regarding the contents of the said report.

(iii) If (i) is reported, or if it is otherwise deemed necessary from the perspective of adverse effects on biological diversity, the Director of the Plant Products Safety Division shall take necessary measures.

(3) Response when procedures based on this notification are not taken

If the Director of the Plant Products Safety Division confirms that the following procedures have not been taken, the Director shall request for those who have not taken the said procedures to take these procedures.

(i) Submission of an information provision form in (2) of 1

(ii) Confirmation of the containment measures in 2 (including cases where confirmation has been received, and no containment measures for which the said confirmation was received have been taken)

(4) Handling of self-cloning and natural occurrence

(i) Procedures of 1 and 2 are not required from a person who intends to use a subject organism, if the said organism falls under the provisions of each item of Article 2 (so-called self-cloning and natural occurrence) under the “Regulations related to the Enforcement of the Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms” (Ministerial Ordinance No. 1 of 2003 from the Ministry of Finance; the Ministry of Education, Culture, Sports, Science and Technology; the Ministry of Health, Labour and Welfare; the Ministry of Agriculture, Forestry and Fisheries; the Ministry of Economy, Trade and Industry; and the Ministry of the Environment; hereinafter referred to as “Enforcement Regulations”); however, since a clear scientific basis is required to determine whether or not the said organism falls under the provisions, the Plant Products Safety Division shall be contacted for each individual case, as before.

(ii) If there is an inquiry regarding (i) the Plant Products Safety Division shall determine whether the said organism falls under the provisions of each item of Article 2 of the Enforcement Regulations, after seeking the advice of persons with specialized academic experience, when necessary.

(5) Handling of technologies to be newly developed in the future

Since the provisions of this notification shall apply, where necessary, mutatis mutandis to organisms obtained by using new breeding technologies other than genome editing technology, including technologies

that are newly developed in the future, a person who intends to use said organisms shall contact the Plant Products Safety Division, in advance regarding whether or not information needs to be provided.

(Form 1)

Information providing form for usage of organisms obtained by genome editing technology

In order to use organisms obtained through the use of genome editing technology and so on, information of the corresponding organism is provided as follows.

Items		Entry field
1 Name and summary of the organism obtained by genome editing technology		
2 Application of the corresponding organism		
3 Summary of the use-facility		
4 A fact that no extracellularly processed nucleic acid or any replicated product thereof specified in Article 2, paragraph 2, item 1 of the Cartagena Act, remains in the organism.	(1) Whether extracellularly processed nucleic acids were transferred or not (if transferred, information about the transferred nucleic acids must be provided.)	
	(2) Whether residues of transferred nucleic acids exist or not (including information about the process of selection/breeding and the method of confirming the presence or absence of the corresponding transferred nucleic acid.)	
5 Taxonomic species of the modified organism	(1) Name of the species based on the taxonomic classification and the variety or lineage of the host	

	(2) Naturally growing area in the natural environment and cultivating area and physiological / ecological characteristics	
6 Method of genome editing used for the modification	(1) Information about artificial nuclease	
	(2) Method of introducing the corresponding artificial nuclease	
7 Modified gene and the function of the corresponding gene	(1) Target cleavage site on the host genome and variation that has occurred at the cleavage corresponding site	
	(2) Information about the gene with target cleavage site and the theoretically likely trait changes caused by the modification	
8 Trait changes caused by the corresponding modification		
9 Presence or absence of other trait changes except 8 above (if present, the content)	(1) Information about the possibility of other modifications than that at the target site	
	(2) Other trait changes than that mentioned in 8 above that were caused in the created organism compared with the host	
10 Discussion regarding the possibility of	(1) Competitive advantage	
	(2) Predacity or Parasitism	

causing an adverse effect on biodiversity through use of the organism	(3) Production of harmful substances	
	(4) Crossability	
	(5) Other characteristics	
	(6) Comprehensive discussion	

[Remarks]

In cases where an applicant is a corporation, regarding the name, describe the name of the corporation and the name of the representative and append the enterprise identification number. Regarding the address, in case of a corporation, describe the location of the main office. Regarding the phone number, describe the phone number of the relevant department that can be contacted when the content of information providing form is needed to be confirmed.

Regarding the content of the information in each item of the table, describe it according to Annex 1 in case where the corresponding specie is agricultural crop, according to Annex 2 in case where the corresponding specie is fish. In case where the corresponding specie is other than agricultural crop or fish, describe according to Annex 1 or Annex 2 depending on the physiological and ecological characteristics of the corresponding specie. In addition, in case where the corresponding specie is microorganism, replace "Competitive advantage" in 10 (1) to "Property to reduce other organisms," "Predacity or Parasitism" in (2) to "Pathogenicity," "Crossability" in (4) to "Property to horizontally transfer nucleic acids" when describing.

In Annex 1 and Annex 2, regarding the references to be stored by the information provider, attach a list of the references to this information providing form. The information provider has to store the references as such so that they can be submitted promptly to the Ministry of Agriculture, Forestry and Fisheries or the Ministry of the Environment, if required. The said materials shall be retained for a minimum of five years after the submission of an information provision form and the publication of the said information on the website of the Ministry of Agriculture, Forestry and Fisheries.

Annex 1 Specific contents of information to describe in case where the specie is agricultural crop

1 Clearly distinguish the name from that of other organisms by including information about the species name based on the taxonomic classification to which the host or original organism of the corresponding organism belongs, and the characteristics of the corresponding organism, and so on.

Regarding the summary, describe a summary of the characteristics obtained by using genome-editing technology, etc.

2 Regarding the application of the corresponding organism, list any of the following applications that are applicable; "Food," "Feed," "Ornamental purposes," "Cultivation" and "Others." In case where the application falls under "Others," briefly describe the content in brackets.

In case where the scope of the use of the corresponding organism is limited within a facility managed so as to prevent release of the corresponding organism outside such as an isolated field, describe "Cultivation in an isolated field" and describe specifications of the equipment and production methods in the corresponding facility in 3.

3 In case where the scope of the use of the corresponding organism is limited within a facility managed so as to prevent release of the corresponding organism outside such as an isolated field, describe the outlines of specifications of the equipment and production methods of a facility where the corresponding organism is cultivated.

The information provider shall store references describing the name and location of the corresponding facility, as well as references describing details of specifications of the equipment and production methods, and add them to the list of stored references.

In addition, in case where the scope of use, etc., of the corresponding organism is not limited within a facility, describe "-" in the entry field.

4 (1)In case extracellularly processed nucleic acids were transferred, provide a summary of the genetic elements and transfer method of the nucleic acids (for example, direct transfer of artificial nuclease of which the site involved in binding to the target DNA is RNA, transfer of the mRNA of artificial nuclease, transfer of the vector carrying the gene of the artificial nuclease, or plasmid transfer, etc.). The information provider shall store substantiating references and add them to the list of stored references.

4(2) Regarding the process of selection/breeding, provide a summary of the process from the creation of individual in which extracellularly processed nucleic acids were transferred to the selection of the finally obtained individual (objective of this provided information).

Regarding the method of confirmation of the presence or absence of residues of transferred nucleic acid, describe the analytical method used for confirmation and the results of analysis. The information provider shall store substantiating references and add them to the list of stored references.

5(1) Regarding the name of the species based on the taxonomic classification, describe the Japanese name, English name and scientific name.

5(2) Regarding the naturally growing area in the natural environment, describe the presence or absence of a natural growing area in the natural environment of Japan and outside of Japan, and if any, also describe the regional name.

For histories and current status of the use, etc., describe the regional name, country name, etc., where the corresponding organism is mainly cultivated.

For physiological and ecological characteristics, describe the characteristics of each of the following items.

a Basic characteristics (distinction of annual, biennial or perennial)

b Environmental conditions that allow habitation and growth (the temperature range, moisture conditions and soil conditions necessary for habitation)

c Reproduction or proliferation system (presence or absence of shedding of the seeds, seed dispersal, presence or absence of seed dormancy, seed longevity under natural conditions, presence or absence of vegetative propagation [if vegetative propagation occurs, the property of budding from the tissue or organs of the plant that can regenerate the plant body under natural conditions], levels of autogamy/allogamy, presence or absence of self-incompatibility, presence or absence of closely related wild species [if any, kinds of closely related wild species, crossing rate, etc.], methods of pollination)

d Production of harmful substances (whether or not the species is known to produce substances that affect the habitation or growth of wild animals and plants or microorganisms [hereinafter referred to as "wildlife"] found in close vicinity under natural conditions. If it is known, the type of the corresponding substance, toxicity, produced amount, pathways of exposure and other related information)

6(1) Describe a summary of the type (ZFN, TALEN, CRISPR/Cas9, etc.) and composed elements of the artificial nuclease. The information provider shall store the references including designs of the artificial nuclease and add to the list of stored references.

6(2) Describe a summary of the introducing method, for example, transfer of the artificial nuclease itself into the host cell, transfer of the vector carrying the gene of the artificial nuclease into the host cell, integration of the gene of the artificial nuclease into the host genome. In addition, in case the gene of the artificial nuclease is integrated into the host genome, describe the method used (using Agrobacterium, particle gun method, etc.).

7(1) Provide a summary of the cleavage site and the change in the DNA sequence (addition, replacement and/or deletion of bases) caused at the cleavage site targeted by the artificial nuclease. The information provider shall store the references including figures about these changes and add to the list of stored references.

7(2) Regarding the gene with target cleavage site, describe the name, function of the corresponding gene, function of the protein produced with the expression of the corresponding gene, as well as providing a summary of theoretically likely functional changes caused by modification of the corresponding gene. The information provider shall store references intended to confirm the detailed contents and add to the list of stored references.

8 Describe characteristically important points regarding the physiological and ecological changes actually caused by modification of the target gene, compared with the host. The information provider shall store references intended to confirm the detailed contents and add to the list of stored references.

9(1) The presence or absence of a sequence that is similar to the target sequence shall be investigated in the genomic base sequence that has been determined for the host or the taxonomic species, breed, or strain to which the host belongs, and the results shall be recorded. If any sequence is found that is similar to the target sequence, an analysis shall be conducted to determine whether there is a sequence difference at the said site, and the results shall be recorded.

In either case, the information provider shall store the references to confirm the adequacy of the corresponding method and add to the list of stored references.

9(2) Describe other traits than those described in 8 above, such as morphological and growth characteristics, wintering ability/summering ability, seed production, seed shedding, dormancy and viability of the seeds, possibility of having differences between the host and the organism obtained by genome-editing technology. The information provider shall store substantiating references and add them to the list of stored references.(If necessary, this examination shall be undertaken based on the following matters: the progress of selection/growth, as specified separately; the functions of the target gene and the characteristics actually imparted by modification of said gene; and, the presence or absence of sequence differences in the sequence that is similar to the target sequence.)

10 In case where the organism is used as described in 2 above, describe the possibility of causing adverse effects on biological diversity.

This should be discussed one by one for each item a to d listed below, and then further discussed comprehensively based on the content of each discussion. In addition, describe "-" in the entry field of 10 (2), "Predacity or Parasitism."

a Competitive advantage (a trait that competes with wild plants for resources such as nutrients, sunlight and space for growth to affect their growth)

b Production of harmful substances (a trait of producing substances that affect habitation or growth of wildlife)

c Crossability (a trait of being able to hybridize with closely related wild plants and to transfer nucleic acids modified by genome-editing technology to them)

d Other characteristics (for example, other traits than those listed from a to c that could indirectly affect wildlife by altering the basic ecosystem. Traits that are thought to be appropriate to consider for discussion of the possibility of causing adverse effects on biological diversity)

The information provider shall store substantiating references of the corresponding discussion and add them to the list of stored references.

Attachments:

No Attachments.