USDA Foreign Agricultural Service
GAIN Report
Global Agricultural Information Network

Voluntary - Public

Date: 7/19/2019
GAIN Report Number: JA9101

Japan

Post: Tokyo

Japan 224th Food Safety Group

Report Categories:
Sanitary/Phytosanitary/Food Safety
Biotechnology and Other New Production Technologies
Biotechnology - GE Plants and Animals

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Report Highlights:
On July 18, 2019, Japan's Ministry of Health, Labor and Welfare (MHLW) announced revisions to Japan's Maximum Residue Levels (MRLs) for the following agricultural chemicals and a veterinary drug/feed additive: Afidopyropen, Oxpoconazole fumarate, Flubendiamide, and Salinomyvin. In addition, MHLW shared a draft of regulatory and handling procedures for foods and additives using genome editing technology. The Embassy comment period for these proposals is open until August 1, 2019. MHLW will then notify these revisions to the World Trade Organization (WTO), which will provide another opportunity for interested parties to comment.

Keyword: JA9101, Afidopyropen, Oxpoconazole fumarate, Flubendiamide, Salinomyvin, Genome editing

General Information:

(The following is taken information distributed by MHLW at 224th Food Safety Group)

<The manner of submitting comments>

The Ministry of Health, Labour and Welfare (MHLW) will amend the existing standards and specifications for food as shown in this document. Please provide comments in writing by **Thursday, August 1, 2019**. After the given date, comments should be directed to the enquiry point in accordance with the WTO/SPS Agreement.

If you wish to request Japan to adopt the same limits as your country's MRLs, you are requested to submit data supporting your country's MRLs, such as risk assessment and residue data.

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Item 1. Establishment of the Maximum Residue Limits for Agricultural and Veterinary Chemicals in Foods

The Food Sanitation Act authorizes the Ministry of Health, Labour and Welfare (MHLW) to establish residue standards (maximum residue limits, "MRLs") for pesticides, feed additives, and veterinary drugs (hereafter referred to as "agricultural and veterinary chemicals") that may remain in foods. Any food for which standards are established pursuant to the provisions in Article 11, Paragraph 1 of the act is not permitted to be marketed in Japan unless it complies with the established standards.

On May 29, 2006, Japan introduced the Positive List System[1] for agricultural and veterinary chemicals in food. All foods distributed in the Japanese marketplace are subject to regulation of the system.

The MHLW is going to modify or newly set MRLs in some commodities for the following substances:

Pesticides : Afidopyropen, Oxpoconazole fumarate, Flubendiamide

Veterinary drugs and Feed additives : Salinomycin

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[1] The aim of the positive list system is to prohibit the distribution of any foods which contain agricultural chemicals at amounts exceeding a certain level (0.01 ppm) in the Japanese marketplace unless specific maximum residue limits (MRLs) have been set.

Summary

Afidopyropen (pesticide: insecticide): Not permitted for use in Japan. The MHLW is going to establish MRLs in some commodities in response to a request for setting import tolerances based on the Guideline for Application for Establishment and Revision of Maximum Residue Limits for Agricultural Chemicals Used outside Japan (Shokuan No. 0205001, 5 February 2004).

Oxpoconazole fumarate (pesticide: fungicide): Permitted for use in Japan. The MHLW is going to modify MRL in one commodity in response to a request for setting MRL by the Ministry of Agriculture, Forestry and Fisheries (MAFF) with the intention to expand its use pattern. In addition, the MHLW is going to modify MRLs in some commodities that were provisionally set at the introduction of the Positive List System.

Flubendiamide (pesticide: insecticide)): Permitted for use in Japan. The MHLW is going to establish MRLs in some commodities in response to a request for setting MRL by the MAFF with the intention to expand its use pattern and to establish them in also animal products. This action will not strengthen the current regulation for any commodities.

Salinomycin (veterinary drug and feed additive: antibiotic, coccidiostat): Permitted for use in Japan as a feed additive. The MHLW is going to modify MRLs in some commodities that were provisionally set at the introduction of the Positive List System.

Afidopyropen

Commodity		MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
					Codex ppm	National ppm	
Soybeans, dry	○	0.01		IT		0.01	USA
Potato	○	0.01		IT		0.01	USA
Taro	○	0.01		IT		0.01	USA
Sweet potato	○	0.01		IT		0.01	USA
Japanese yam (including Chinese yam)	○	0.01		IT		0.01	USA
Other potatoes	○	0.01		IT		0.01	USA
Japanese radish, leaves (including radish)	○	5		IT		5.0	USA
Turnip, leaves (including rutabaga)	○	5		IT		5.0	USA
Watercress	○	5		IT		5.0	USA
Chinese cabbage	○	0.5		IT		0.50	USA
Cabbage	○	0.5		IT		0.50	USA
Brussels sprouts	○	0.5		IT		0.50	USA
Kale	○	5		IT		5.0	USA
Kyona	○	5		IT		5.0	USA
Qing-geng-cai	○	5		IT		5.0	USA
Cauliflower	○	0.5		IT		0.50	USA
Broccoli	○	0.5		IT		0.50	USA
Other cruciferous vegetables	○	5		IT		5.0	USA
Endive	○	2		IT		2.0	USA
Shungiku	○	2		IT		2.0	USA
Lettuce (including cos lettuce and leaf lettuce)	○	2		IT		2.0	USA
Other composite vegetables	○	3		IT		3.0	USA
Parsley	○	2		IT		2.0	USA
Celery	○	3		IT		3.0	USA
Other umbelliferous vegetables	○	3		IT		3.0	USA
Tomato	○	0.2		IT		0.20	USA
Pimiento (sweet pepper)	○	0.2		IT		0.20	USA
Egg plant	○	0.2		IT		0.20	USA
Other solanaceous vegetables	○	0.2		IT		0.20	USA
Cucumber (including gherkin)	○	0.7		IT		0.70	USA
Pumpkin (including squash)	○	0.7		IT		0.70	USA
Oriental pickling melon (vegetable)	○	0.7		IT		0.70	USA
Water melon(whole commodity after removal of stems.)	○	0.7		IT		0.70	USA
Melons(whole commodity after removal of stems.)	○	0.7		IT		0.70	USA
Makuwauri melon(whole commodity after removal of stems.)	○	0.7		IT		0.70	USA
Other cucurbitaceous vegetables	○	0.7		IT		0.70	USA
Spinach	○	2		IT		2.0	USA
Okra	○	0.2		IT		0.20	USA
Ginger	○	0.01		IT		0.01	USA
Other vegetables	○	3		IT		3.0	USA
Unshu orange(whole commodity.)	○	0.2		IT		0.15	USA
Citrus natsudaidai, whole	○	0.2		IT		0.15	USA
Lemon	○	0.2		IT		0.15	USA
Orange (including navel orange)	○	0.2		IT		0.15	USA
Grapefruit	○	0.2		IT		0.15	USA
Lime	○	0.2		IT		0.15	USA
Other citrus fruits	○	0.2		IT		0.15	USA
Apple	○	0.02		IT		0.02	USA
Japanese pear	○	0.02		IT		0.02	USA
Pear	○	0.02		IT		0.02	USA
Quince	○	0.02		IT		0.02	USA

Commodity		MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
					Codex ppm	National ppm	
Loquat(whole commodity after removal of stems.)	○	0.02		IT		0.02	USA
Peach (whole commodity after removal of stems and stones but the residue calculated and expressed on the whole commodity without stems.)	○	0.03		IT		0.03	USA
Nectarine	○	0.03		IT		0.03	USA
Apricot	○	0.03		IT		0.03	USA
Japanese plum (including prune)	○	0.03		IT		0.03	USA
Cherry	○	0.03		IT		0.03	USA
Other fruits	○	0.2		IT		0.20	USA
Cotton seeds	○	0.08		IT		0.08	USA
Chestnut	○	0.01		IT		0.01	USA
Pecan	○	0.01		IT		0.01	USA
Almond	○	0.01		IT		0.01	USA
Walnut	○	0.01		IT		0.01	USA
Other nuts	○	0.01		IT		0.01	USA
Other spices (limited to roots or rhizome)	○	0.01		IT		0.01	USA
Other herbs	○	5		IT		5.0	USA

The residue definition is Afidopyropen only.

* The uniform limit 0.01 ppm will be applied to commodities for which draft MRLs are not given in this table and to commodities not listed above.

* In the Commodity column, for the food categories to which the word other is added, refer to the Notes given in the last two pages of the Attachment.

○：Commodities for which MRLs are to be maintained, increased or newly set.

IT：Import tolerance

Oxpoconazole fumarate

Commodity	MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
				Codex ppm	National ppm	
Water melon	●	2				
Melons	●	2				
Makuwauri melon	●	2				
Unshu orange, pulp		0.5	§			
Unshu orange(whole commodity.)	○ 2		§			
Citrus natsudaidai, whole	● 2	5	§			
Lemon	● 2	5	§			
Orange (including navel orange)	● 2	5	§			
Grapefruit	● 2	5	§			
Lime	● 2	5	§			
Other citrus fruits	● 2	5	§			
Apple	● 1	2	§			
Japanese pear	○ 2	2	§			
Pear	○ 2	2	§			
Quince	●	2				
Loquat	●	2				
Peach		2	§			
Peach (whole commodity after removal of stems and stones but the residue calculated and expressed on the whole commodity without stems.)	○ 3		§			
Nectarine	○ 2	2	§			
Apricot	● 1	5	§			
Japanese plum (including prune)	● 0.7	5	§			
Mume plum	● 1	5	§			
Cherry	● 2	5	§			
Strawberry	●	5				
Raspberry	●	5				
Blackberry	●	5				
Blueberry	●	5				
Cranberry	●	5				
Huckleberry	●	5				
Other berries	●	5				
Grape	○ 5	5	§			
Japanese persimmon	●	2				
Banana	●	2				
Kiwifruit	●	2				
Papaya	●	2				
Avocado	●	2				
Pineapple	●	2				
Guava	●	2				
Mango	●	2				
Passion fruit	●	2				
Date	●	5				
Other fruits	●	5				
Other spices	○ 10	5	Request			

The residue definition is sum of Oxpoconazole fumarate, Oxpoconazole expressed as Oxpoconazole fumarate and metabolite U【4,4-Dimethyl-1,3-oxazolidine-2-on】expressed as Oxpoconazole fumarate.

* The uniform limit 0.01 ppm will be applied to commodities for which draft MRLs are not given in this table and to commodities not listed above.

* Shaded figures indicate provisional MRLs.

* In the Commodity column, for the food categories to which the word other is added, refer to the Notes given in the last two pages of the Attachment.

●：Commodities for which MRLs are to be lowered or deleted.

○：Commodities for which MRLs are to be maintained, increased or newly set. (*It should be noted that the residue definition for agricultural will be changed.)

§：Permitted for use in Japan.

Request：Request for setting/revising MRL was made by the MAFF.

Flubendiamide

Commodity		MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
					Codex ppm	National ppm	
Corn (maize, including pop corn and sweet corn)	○	0.05	0.05	§	0.02		
Buckwheat	○	10	10	§			
Soybeans, dry	○	1	1	§	1		
Beans, dry	○	1	1	§	1		
Peas	○	1	1		1		
Broad beans	○	1	1		1		
Other pulses	○	1	1		1		
Potato	○	0.05	0.05	§			
Taro	○	0.05	0.05	§			
Sweet potato	○	0.05	0.05	§			
Japanese yam (including Chinese yam)	○	0.05	0.05	§			
Sugar beet	○	0.05	0.05	§			
Japanese radish, roots (including radish)	○	0.1	0.1	§			
Japanese radish, leaves (including radish)	○	10	10	§			
Turnip, roots (including rutabaga)	○	0.3	0.3	§			
Turnip, leaves (including rutabaga)	○	25	25	§			
Horseradish	○	0.3	0.3	§			
Chinese cabbage	○	5	5	§			
Cabbage	○	4	4	§	4		
Brussels sprouts	○	4	4	§	4		
Kale	○	20	20	§			
Komatsuna (Japanese mustard spinach)	○	20	20	§			
Kyona	○	20	20	§			
Qing-geng-cai	○	5	5	§			
Cauliflower	○	4	4	§	4		
Broccoli	○	5	5	§	4		
Other cruciferous vegetables	○	20	20	§	4		
Burdock	○	0.05	0.05	§			
Lettuce (including cos lettuce and leaf lettuce)	○	15	15	§	7		
Other composite vegetables	○	3		Request			
Welsh (including leek)	○	3	3	§			
Asparagus	○	1	1	§			
Carrot	○	0.3	0.3	§			
Celery	○	10	10	§	5		
Tomato	○	2	2	§	2		
Pimiento (sweet pepper)	○	3	3	§	0.7		
Egg plant	○	1	1	§			
Other solanaceous vegetables	○	5	5	§	0.7		
Cucumber (including gherkin)	○	0.7	0.7	§	0.2		
Pumpkin (including squash)	○	0.5	0.5	§	0.2		
Water melon			0.05	§			
Water melon(whole commodity after removal of stems.)	○	0.5			0.2		
Melons			0.05	§			
Melons(whole commodity after removal of stems.)	○	1			0.2		
Other cucurbitaceous vegetables	○	2	2	§	0.2		
Okra	○	2	2	§			
Ginger	○	0.05	0.05	§			
Peas, immature (with pods)	○	2	2	§	2		
Kidney beans, immature (with pods)	○	3	3	§	2		
Green soybeans	○	5	5	§	2		
Other vegetables	○	5	5	§	2		

Commodity		MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
					Codex ppm	National ppm	
Unshu orange, pulp			0.2	§			
Unshu orange(whole commodity.)	○	2		§			
Citrus natsudaidai, whole	○	3	3	§			
Lemon	○	3	3	§			
Orange (including navel orange)	○	3	3	§			
Grapefruit	○	3	3	§			
Lime	○	3	3	§			
Other citrus fruits	○	3	3	§			
Apple	○	1	1	§	0.8		
Japanese pear	○	0.8	0.8	§	0.8		
Pear	○	0.8	0.8	§	0.8		
Quince	○	0.8	0.8		0.8		
Loquat(whole commodity after removal of stems.)	○	2		Request	0.8		
Peach			0.05	§			
Peach (whole commodity after removal of stems and stones but the residue calculated and expressed on the whole commodity without stems.)	○	1		§			
Nectarine	○	2	2	§	2		
Apricot	○	2	2	§	2		
Japanese plum (including prune)	○	2	2	§	2		
Mume plum	○	2	2	§	2		
Cherry	○	2	2	§	2		
Strawberry	○	2	2	§			
Blueberry	○	2	2	§			
Grape	○	2	2	§	2		
Japanese persimmon	○	0.8	0.7	§	0.8		
Kiwifruit			0.05	§			
Kiwifruit(whole commodity.)	○	2					
Other fruits	○	0.1	0.1		0.1		
Cotton seeds	○	2	2		1.5		
Ginkgo nut	○	0.1	0.1		0.1		
Chestnut	○	0.1	0.1	§	0.1		
Pecan	○	0.1	0.1		0.1		
Almond	○	0.1	0.1		0.1		
Walnut	○	0.1	0.1		0.1		
Other nuts	○	0.1	0.1		0.1		
Tea	○	50	50	§	50		
Other spices	○	10	10	§			
Other herbs	○	25	25	§			
Cattle, muscle	○	2	2		2		
Pig, muscle	○	2	2		2		
Other terrestrial mammals, muscle	○	2	2		2		
Cattle, fat	○	2	2		2		
Pig, fat	○	2	2		2		
Other terrestrial mammals, fat	○	2	2		2		
Cattle, liver	○	1	1		1		
Pig, liver	○	1	1		1		
Other terrestrial mammals, liver	○	1	1		1		
Cattle, kidney	○	1	1		1		
Pig, kidney	○	1	1		1		
Other terrestrial mammals, kidney	○	1	1		1		
Cattle, edible offal	○	1	1		1		
Pig, edible offal	○	1	1		1		

Commodity	MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
				Codex ppm	National ppm	
Other terrestrial mammals, edible offal	○ 1	1		1		
Milk	○ 0.1	0.1		0.1		
Chicken, muscle	○ 0.01		Request			
Other poultry, muscle	○ 0.01		Request			
Chicken, fat	○ 0.05		Request			
Other poultry, fat	○ 0.05		Request			
Chicken, liver	○ 0.02		Request			
Other poultry, liver	○ 0.02		Request			
Chicken, kidney	○ 0.02		Request			
Other poultry, kidney	○ 0.02		Request			
Chicken, edible offal	○ 0.02		Request			
Other poultry, edible offal	○ 0.02		Request			
Chicken eggs	○ 0.01		Request			
Other poultry, eggs	○ 0.01		Request			
Pepper,dried				7		

The residue definition is Flubendiamide only.

* The uniform limit 0.01 ppm will be applied to commodities for which draft MRLs are not given in this table and to commodities not listed above.

* In the Commodity column, for the food categories to which the word other is added, refer to the Notes given in the last two pages of the Attachment.

●：Commodities for which MRLs are to be lowered or deleted.

○：Commodities for which MRLs are to be maintained, increased or newly set.

§：Permitted for use in Japan.

Request：Request for setting/revising MRL was made by the MAFF.

※Food category ”Pepper,dried" will be deleted,and hereafter, MRLs in its raw commodity (peppers) will also apply to such processed commodity, taking into account its processing factors. For this substance, JMPR estimated processing factors of 10 for Pepper,dried.

Salinomycin

Commodity		MRL (draft) ppm	MRL (current) ppm	Registration	Reference MRL		
					Codex ppm	National ppm	
Cattle, muscle	○	0.02	0.02	§			
Pig, muscle	○	0.1	0.1			0.1	Australia
Cattle, fat	○	0.02	0.02	§			
Pig, fat	○	0.1	0.1			0.1	Australia
Cattle, liver	●	0.1	0.4	§			
Pig, liver	●	0.1	0.2			0.1	Australia
Cattle, kidney	●	0.02	0.5	§			
Pig, kidney	○	0.1	0.1			0.1	Australia
Cattle, edible offal	●	0.2	0.5	§			
Pig, edible offal	○	0.1	0.1			0.1	Australia
Chicken, muscle	●	0.02	0.1	§		0.015	EU
Other poultry, muscle	●	0.02	0.1	§			
Chicken, fat	●	0.2	0.4	§		0.15	EU
Other poultry, fat	○	0.2	0.1	§			
Chicken, liver	●	0.2	0.5	§		0.15	EU
Other poultry, liver	●	0.2	0.5	§			
Chicken, kidney	●	0.04	0.5	§		0.04	EU
Other poultry, kidney	●	0.04	0.5	§			
Chicken, edible offal	●	0.2	0.5	§			
Other poultry, edible offal	●	0.2	0.5	§			
Chicken eggs	●		0.02				
Other poultry, eggs	●		0.02				

The residue definition is salinomycin only.

* The compound shall not be included in any commodity for which MRL is not given in the above table and in any commodity not listed above.

* Shaded figures indicate provisional MRLs.

* In the Commodity column, for the food categories to which the word other is added, refer to the Notes given in the last two pages of the Attachment.

●: Commodities for which MRLs are to be lowered or deleted.

○: Commodities for which MRLs are to be maintained, increased or newly set.

§: Permitted for use in Japan.

Notes:

“Other cereal grains” refers to all cereal grains, except rice (brown rice), wheat, barley, rye, corn (maize), and buckwheat.

“Beans, dry” includes butter beans, cowbeans (red beans), lentil, lima beans, pegia, sultani, sultapya and white beans.

“Other legumes/pulses” refers to all legumes/pulses, except soybeans (dry), beans (dry), peas, broad beans, peanuts (dry), and spices.

“Other potatoes” refers to all potatoes, except potato, taro, sweet potato, yam, and konjac.

“Other cruciferous vegetables” refers to all cruciferous vegetables, except Japanese radish roots and leaves (including radish), turnip roots and leaves, horseradish, watercress, Chinese cabbage, cabbage, brussels sprouts, kale, *komatsuna* (Japanese mustard spinach), *kyona*, qing-geng-cai, cauliflower, broccoli, and herbs.

“Other composite vegetables” refers to all composite vegetables, except burdock, salsify, artichoke, chicory, endive, *shungiku*, lettuce (including cos lettuce and leaf lettuce), and herbs.

“Other liliaceous vegetables” refers to all liliaceous vegetables, except onion, welsh (including leek), garlic, *nira*, asparagus, multiplying onion, and herbs.

“Other umbelliferous vegetables” refers to all umbelliferous vegetables, except carrot, parsnip, parsley, celery, *mitsuba*, spices, and herbs.

“Other solanaceous vegetables” refers to all solanaceous vegetables, except tomato, pimiento (sweet pepper), and egg plant.

“Other cucurbitaceous vegetables” refers to all cucurbitaceous vegetables, except cucumber (including gherkin), pumpkin (including squash), oriental pickling melon (vegetable), watermelon, melons, and *makuwauri* melon.

“Other mushrooms” refers to all mushrooms, except button mushroom, and
shiitake mushroom.

“Other vegetables” refers to all vegetables, except potatoes, sugar beet, sugarcane, cruciferous vegetables, composite vegetables, liliaceous vegetables, umbelliferous vegetables, solanaceous vegetables,

cucurbitaceous vegetables, spinach, bamboo shoots, okra, ginger, peas (with pods, immature), kidney beans (with pods, immature), green soybeans, mushrooms, spices, and herbs.

“Other citrus fruits” refers to all citrus fruits, except *unshu* orange (pulp), citrus *natsudaidai* (pulp), citrus *natsudaidai* (peel), citrus *natsudaidai* (whole), lemon, orange (including navel orange), grapefruit, lime, and spices.

“Other berries” refers to all berries, except strawberry, raspberry, blackberry, blueberry, cranberry, and huckleberry.

“Other fruits” refers to all fruits, except citrus fruits, apple, Japanese pear, pear, quince, loquat, peach, nectarine, apricot, Japanese plum (including prune), mume plum, cherry, berries, grape, Japanese persimmon, banana, kiwifruit, papaya, avocado, pineapple, guava, mango, passion fruit, date and spices.

“Other oil seeds” refers to all oil seeds, except sunflower seeds, sesame seeds, safflower seeds, cotton seeds, rapeseeds and spices.

“Other nuts” refers to all nuts, except ginkgo nut, chestnut, pecan, almond and walnut.

“Other spices” refers to all spices, except horseradish, *wasabi* (Japanese horseradish) rhizomes, garlic, peppers chili, paprika, ginger, lemon peels, orange peels (including navel orange), *yuzu* (Chinese citron) peels and sesame seeds.

”Other spices (limited to roots and rhizome)” includes asafoetida roots, turmeric root, galangal rhizome and licorice root.

“Other herbs” refers to all herbs, except watercress, *nira*, parsley stems and leaves, celery stems and leaves.

“Edible offal” refers to all edible parts, except muscle, fat, liver, and kidney.

“Other terrestrial mammals” refers to all terrestrial mammals, except cattle and pig.

“Other poultry animals” refers to all poultry, except chicken.

“Other fish” refers to all fish, except salmoniformes, anguilliformes, and perciformes.

“Other aquatic animals” refers to all aquatic animal, except fish, shelled molluscs and crustaceans.

Food hygiene handling procedures for foods and additives derived from genome editing technology (draft)

1. Definition

(1) Genome editing technology

Genome editing technology is defined as a technology to modify a specific site of a specific base sequence on a chromosome using an enzyme recognizing the base sequence in order to provide specific functions. Moreover, the technology which brings the final product including foreign genes and their parts falls under recombinant DNA technology.

(2) Foods derived from genome editing technology

Foods derived from genome editing technology are items which fall under any of the following:

1) An entire organism or its parts obtained by genome editing technology.
2) An item including the entire organism or its parts.
3) An item manufactured using microorganisms obtained by genome editing technology or an item containing such item.

(3) Additives derived from genome editing technology

Additives derived from genome editing technology are defined as additives manufactured using organisms obtained by genome editing technology or items containing such items.

Moreover, additives derived from genome editing technology, when their final products are highly purified to be non-proteinous (such as amino acids) and meet both the following conditions 1) and 2), are handled as highly purified nonprotein additives. The additives derived from recombinant DNA technology are already handled as highly purified nonprotein additives.

1) Purity of the product is high. For example, more than or equal to that of amino acids, nucleotides, vitamins, and monosaccharides, which are notified as designated additives.

2) As compared with conventional additives, the contents of existing inactive ingredients in such additive do not significantly increase up to around the levels with safety concerns and such additive does not contain new inactive ingredients suggesting adverse effects.

2. Foods derived from genome editing technology for which notification is required

Notification is required for a food derived from genome editing technology,

- when the food is an entire organism or its parts obtained by genome editing technology, or
- when the food is an item manufactured using a microorganism obtained by genome editing technology, and the results brought from the technology show that the gene status of the organism or microorganism indicates no remaining foreign gene or its parts, and that deletion of bases, substitution and insertion of several bases, resulting insertion of one to several mutations by cleavage with an enzyme recognizing the specific base sequence, etc. occur.

Therefore, foods manufactured and processed using notified foods derived from genome editing technology do not require notification.

When the results indicating that the gene status is beyond the above description finally shows that foreign gene and its parts remain, the technology used for the item falls under recombinant DNA technology and such item is subject to safety assessment according to the Procedures for safety inspection of foods and additives derived from recombinant DNA technology (Ministry of Health and Welfare Notification No. 233 of 2000, hereinafter referred to as “Procedures for safety assessment”). Notification and the necessity or unnecessity of safety assessment of any other foods are determined on a specific case-by-case basis by the Ministry of Health, Labour and Welfare (MHLW).

3. Additives derived from genome editing technology for which notification is required

(1) Additives derived from genome editing technology using microorganisms

Basically, it is assumed that additives comply with the compositional standards specified in the specifications and standards for food and food additives, etc. (Ministry of Health and Welfare Notification No. 370 of 1959, hereinafter referred to as "Notification for specifications and standards").

Notification is required for additives derived from genome editing technology, when for microorganisms used in manufacturing of such additives,

- the gene status obtained by genome editing technology indicates no remaining foreign gene or its parts
- deletion of bases, substitution and insertion of several bases, resulting insertion of one to several mutations by cleavage with an enzyme recognizing the specific base sequence, etc. occur.

However, notification is not required for items that fall under the following 1) and 2).

1) It is clear that such additive is manufactured using a microorganism obtained by genome editing technology and the gene constitution is equal to that of organisms belonging to the identical species or naturally occurring microorganisms.
2) Such additive is manufactured using a microorganism obtained by genome editing technology and is a highly purified nonprotein additive.

When the results indicating that the gene status is beyond the above description finally shows that foreign gene and its parts remain, the technology used for the item falls under recombinant DNA technology and such item is subject to safety assessment according to the Procedures for safety assessment. Notification and the

necessity or unnecessity of safety inspection of any other foods are determined on a specific case-by-case basis by the MHLW.

(2) Additives derived from genome editing technology using materials other than microorganisms

Follow the handling in section 2.

4. Procedure for notification, etc. (see Appendix)

(1) As for foods and additives derived from genome editing technology for which notification is required mentioned in the above sections 2 and 3, the developer of such items, its representative, or a person/institute that can submit appropriate data (hereinafter referred to as "developer, etc.") submits certain information prior to marketing in principle. A part of the information submitted is published by the MHLW.

(2) As for foods, etc. derived from genome editing technology, in order to confirm whether such foods, etc. fall under a target of notification or safety assessment, the developer, etc. request a prior consultation with the Office of Health Policy on Newly Developed Food, Food Safety Standards and Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, the MHLW using Attachments 1-1 and 1-2 for foods and additives, respectively, before notification.

Foods, etc. to be subject to a prior consultation are limited to those which have been developed for commercialization. For consultation, the information mentioned in section 5. (1) or (2) is provided as much as possible.

(3) The MHLW gives the developer, etc. the results about whether foods, etc. that have undergone a prior consultation fall under a target of notification or safety assessment using Attachment 2, as appropriate, confirming with Subcommittee

on Genetically Modified Foods, Newly Developed Food Committee of the Food Sanitation Council established under the Pharmaceutical Affairs and Food Sanitation Council (hereinafter referred to as “the Subcommittee”).

During the confirmation, when the Subcommittee determines to request for advice from the Food Safety Commission, Cabinet Office (hereinafter referred to as “Food Safety Commission”), the Minister of Health, Labour and Welfare consults with the Food Safety Commission, and then based on the advice, determines how to proceed, and gives the results to the developer, etc.

(4) For foods, etc. derived from genome editing technology, which have been confirmed to be subject to notification in a prior consultation, the developer, etc. notify the MHLW of the information mentioned in section 5 (1) or (2) about the foods, etc. using Attachment 3 (Notification and Publication Form) with necessary supporting data prior to marketing. However, the year and month of marketing are reported using Attachment 4 at a future date when such foods, etc. are marketed.

(5) After receiving the notification, the MHLW posts and publishes the information mentioned in section 5. (3) or (4) on the MHLW website promptly. However, the year and month of marketing are published after receiving a report of Attachment 4 by the developer, etc.

(6) The same procedures are followed for imported products. Importers, etc. may perform the procedures instead of the developer, etc. when feasible.

(7) Out of additives derived from genome editing technology subject to notification, those which are determined to fall under the following 1) or 2) by the developer, etc. are subject to a prior consultation with the reasons of determination and the materials as necessary. Items which fall under 1) or 2) based on the results of

prior consultation are considered to have been notified by such prior consultation and do not require the procedures in the above sections (4) and (5).

1) Such additive is manufactured using a microorganism obtained by genome editing technology and the gene constitution is equal to that of organisms belonging to the identical species or naturally occurring microorganisms.

2) Such additive is manufactured using a microorganism obtained by genome editing technology and is a highly purified nonprotein additive.

5. Information to be notified and published

(1) For foods derived from genome editing technology subject to notification, developer, etc. notify the MHLW of the following information.

1) Names of item and breed and summary (usage and intended use) of the developed food
2) Method of genome editing technology used and details of modification
3) Information on confirmation that there are no remaining foreign genes or their parts
4) Information on confirmation that confirmed changes in DNA do not cause production of new allergens having adverse effects on human health or increase of known toxic substances contained
5) Information on changes in major components (nutrient components only) related to the target metabolic system for items which modification affecting the metabolic system was performed in order to increase or decrease specific components
6) Year and month of marketing (*Notify the MHLW of it after marketing)

(2) For additives derived from genome editing technology, developer, etc. notify the MHLW of the following information.

1) Name of item and summary (usage and intended use) of the developed additive
2) Method of genome editing technology used and details of modification
3) Information on confirmation that there are no remaining foreign genes or their parts
4) The fact that the additive complies with the compositional standards specified in the Specifications and standards

5) Year and month of marketing (*Notify the MHLW of it after marketing)

(3) For foods derived from genome editing technology, the MHLW publishes the following information.

1) Names of notifier and developer, and date (year/month/day) of notification
2) Names of item and breed and summary (usage and intended use)
3) Summary of genome editing technology and gene modification used
4) The fact that it is conformed that confirmed changes in DNA do not cause production of new allergens having adverse effects on human health or increase of known toxic substances contained
5) Summary of changes in major components (nutrient components only) related to the target metabolic system
6) Year and month of marketing (*Publish it after receipt of notification mentioned in section 5. (1), 6))

(4) For additives derived from genome editing technology, the MHLW publishes the following information.

1) Names of notifier and developer, and date (year/month/day) of notification
2) Names of item
3) Summary of genome editing technology and gene modification used
4) The fact that the additive complies with the compositional standards specified in the Specifications and standards
5) Year and month of marketing (*Publish it after receipt of notification mentioned in section 5. (2), 5))

6. Handling of crossbred progeny

(1) The following foods derived from genome editing technology do not require notification.

1) Crossbred progeny between breeds whose notification to the MHLW was published or between such breed and a traditional breed.
2) Crossbred progeny of a breed whose notification to the MHLW was published and an organism obtained using recombinant DNA technology which has underwent safety assessment.

(2) Out of foods derived from genome editing technology, crossbred progeny between breeds for which safety assessment are required or between such breed and an organism obtained using recombinant DNA technology require a prior consultation with the MHLW.

7. Others

The items specified in this procedures are reviewed, when necessary, based on usage record, future substantial scientific knowledge, or international trends, etc. for foods, etc. derived from genome editing technology.

It should be noted that when any fact not complying with this notice is found, the background, etc. are confirmed and such fact may be published with the information about such developer, etc.

Appendix: Flow to the distribution of genome-edited foods, etc.

Attachment 1-1: Prior Consultation Form: Food

Attachment 1-2: Prior Consultation Form: Additive

Attachment 2: Response Form

Attachment 3-1: Notification and Publication Form: Food

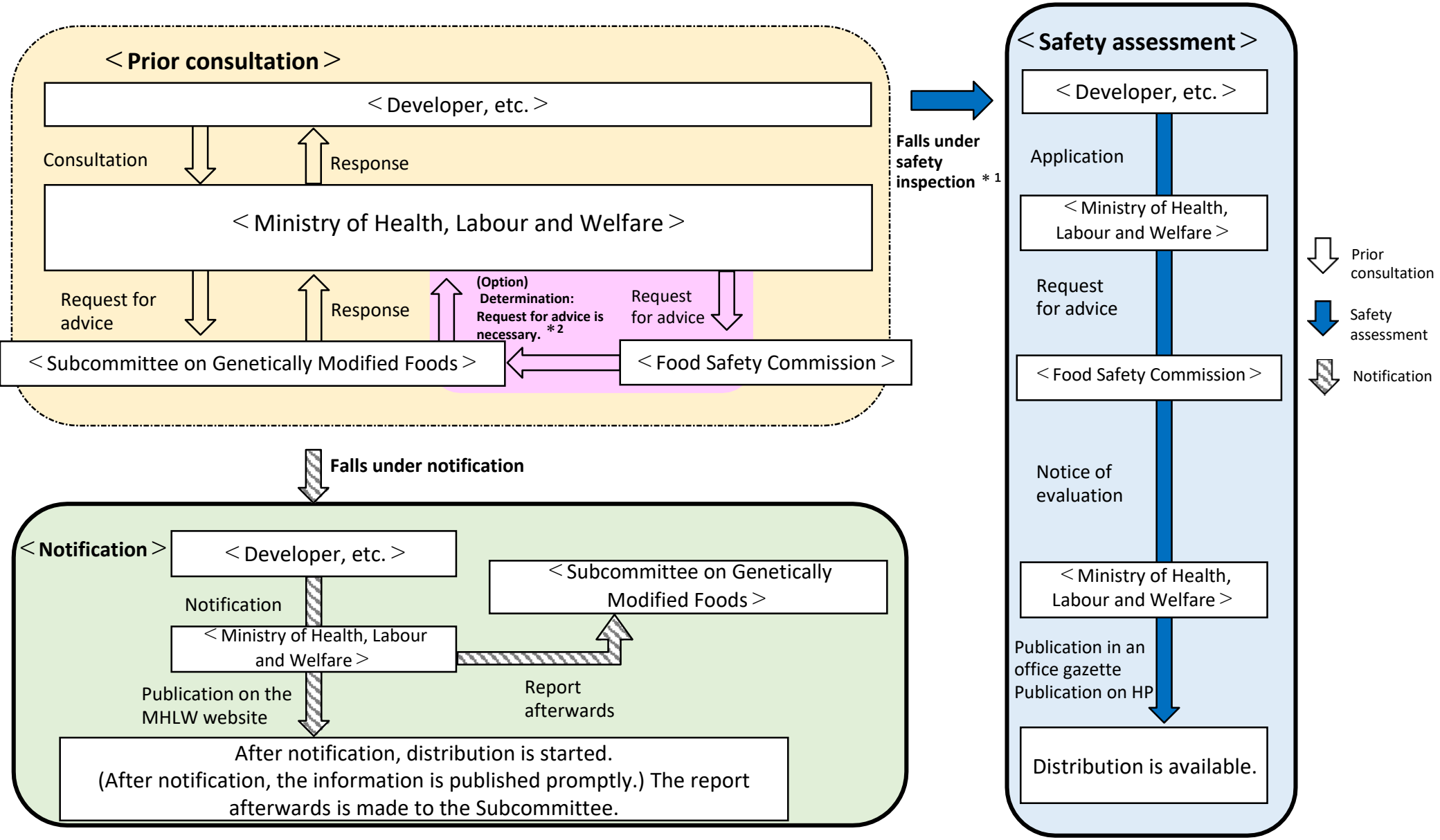
Attachment 3-2: Notification and Publication Form: Additive

Attachment 4: Notification Form for Commercialization

(Omitted)

Flow diagram of handling of foods derived from genome editing technology

Appendix (draft)



*1 As foods derived from recombinant DNA technology, for foods, etc. which are determined to "fall under safety assessment," Ministry of Health and Welfare Notification No. 233 of 2000 is applied mutatis mutandis.

*2 For new foods and new technology, advice is requested for the Food Safety Commission as necessary and their handling, etc. are determined by the Subcommittee on Genetically Modified Foods

Points to be noted regarding the notification (draft)

I. Points to be noted regarding entry methods for notification forms, etc.

The points to be noted regarding entry methods for Notification Forms, Attachments 3-1 and 3-2 in the notice of handling are as follows:

1. The submission of the Forms and the Notifications should be in Japanese.

The name and contact (address, telephone number, e-mail address, etc.) of the person in charge of inquiry concerning notification forms are added in the remarks column.

2. The name of notified item is written to clearly describe characteristics of the notified food and additive.
(ex.) ***-enhanced *** strain (name of food), anti-*** *** (name of food)
(ex.) *** produced using *Escherichia coli* *** strain (name of additive)

3. Notification forms are submitted with necessary materials attached. It should be noted that the entries in the Publication Form are published on the website of the Ministry of Health, Labour and Welfare (MHLW).

4. For foods derived from genome editing technology, the following should be noted.

1) Names of item and breed and summary (usage and intended use) of the developed food

○ The names of item and breed indicate the information and strain name which can identify the item. Also, the strain name alone is acceptable.
○ When the intended use and usage are different from those of the existing food, their summaries are described.

2) Method of genome editing technology used and details of modification

○ The type of genome editing technology used and the operation which was actually performed are described.
○ The name of target gene and its function is specified.
○ The fact that the breeding process, including passage and selection, was underwent to establish a breed shall be described.

○ It is confirmed and described that intended changes in the target gene and the resulting transformation have been achieved in an appropriate stage of the breed selection process. The intended changes in the target gene are confirmed using a sequencer, etc. The transformation is confirmed by the method selected by developer, etc. on a specific case-by-case basis.

○ When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.

3) Information on confirmation that there are no remaining foreign genes or their parts

○ When a foreign gene is transferred in the use of genome editing technology and subsequently removed, it is confirmed that no foreign gene or its parts remain using appropriate methods, including Southern blot, next-generation sequencer, and PCR.

○ When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.

○ When a foreign gene is present or valid data to determine that the foreign gene has been removed are not submitted, the technology is regarded as recombinant DNA technology and the process of safety assessment has to be gone through based on the Procedures for safety assessment of foods and additives derived from recombinant DNA technology. (Ministry of Health and Welfare Notification No. 233 of 2000, hereinafter referred to as "Procedures for safety assessment")

4) Information on confirmation that confirmed changes in DNA do not cause production of new allergens having adverse effects on human health or increase of known toxic substances contained.

○ Sequences which are presumed to have a high probability of off-target effect occurring are confirmed, as appropriate, by a combination of several appropriate search tools, such as CRISPRdirect, and then checked by searching homology with allergens and existing toxic substances and the results are submitted. The names and versions of search tools used, etc. are specified.

○ The fact of confirmation results showing no corresponding substances is mentioned.

5) Information on changes in major components (nutrient components only) related to the target metabolic system for items which modification affecting the metabolic system was performed in order to increase or decrease specific components.

○ Information on increase or decrease of other substances associated with modification of the metabolic system (list of substances related to the target metabolic system (ex. Table of fatty acid composition, metabolic pathway map, etc.)) is submitted.

○ When specific substances accumulate due to modification of the metabolic system, the toxicity and the accumulation of such substances are estimated and then the information indicating that they do not affect human health (ex. Data on risk of excessive intake a developer, etc. collected based on the literature) is submitted. When the toxicity of the substances cannot be confirmed, further information is not required.

○ In a food analysis, multiple samples are analyzed and the name of analysis method used, instruments used, testing conditions, detection limits, etc. are specified.

6) Year and month of marketing (*Notify the MHLW of it after marketing)

○ The year and month when the food which was first commercialized out of the notified foods derived from genome editing technology or foods obtained using such foods was marketed are reported.

5. For additives derived from genome editing technology, the following should be noted.

1) Name of item and summary (usage and intended use) of the developed additive

○ The name of item indicates the information which can identify the item.

○ When the intended use and usage are different from those of the existing food, the details are described.

2) Details of method of genome editing technology and modification used

○ The type of genome editing technology used and the operation which was actually performed are described.

○ The name of target gene and its function are specified.

○ It is confirmed and described that intended changes in the target gene and the transformation have been achieved by microorganisms used in manufacturing. The intended changes in the target gene are confirmed using a sequencer, etc. The transformation is confirmed by the method selected by a developer, etc. on a specific case-by-case basis.

○ When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.

○ The safety of microorganisms used in manufacturing and the summary of manufacturing process are specified.

○ The summary to be published includes major genome editing technology used and clear description of effects of modification of the target gene on the metabolic system.

3) Information on confirmation that there are no remaining foreign genes or their parts

○ When a foreign gene is transferred in the use of genome editing technology, it is confirmed that the foreign gene and its parts does not remain using appropriate methods, including Southern blot, next-generation sequencer analysis, and PCR.

○ When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are be recorded.

○ When a foreign gene is present or valid data to determine that the foreign gene has been removed are not submitted, the technology is regarded as recombinant DNA technology and the process of safety assessment has to be gone through based on the Procedures for safety assessment.

4) The fact that the additive complies with the compositional standards specified in the Specifications and standards.

○ It is confirmed that additives obtained comply with the compositional standards specified in the specifications and standards for food and food additives, etc. (Ministry of Health and Welfare Notification No. 370 of 1959, hereinafter referred to as "Notification for specifications and standards"). Submission of the information confirmed is not required.

○ When analytical instruments, etc. are used, the name of analysis method used, instruments used, testing conditions, detection limits, etc. are recorded.

○ It should be noted that non-compliance with the compositional standards specified in the Notification for specifications and standards is subject to the penalty based on the Food Sanitation Act.

5) Scheduled year and month of marketing (*Notify the MHLW of it after marketing)

○ The year and month when the additive which was first commercialized out of the notified additives derived from genome editing technology was marketed, are reported.

II Others

- For notification, a prior consultation with the Office of Health Policy on Newly Developed Food, Food Safety Standards and Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau, the MHLW is performed.