

Current status of New & Emerging GM Technologies in Japan and Consumer Reactions

By Consumers Union of Japan

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This is a brief report on the current status of new and emerging GM technologies, including genome editing, in Japan. We also want to highlight the debate and protests that are ongoing regarding such technologies. Consumers Union of Japan has concluded that we do not want to be unknowingly exposed to food artificially created in this way, and that we do not need such genome-edited food.

2016

The first meeting of the Japanese Society for Genome Editing was held on 6 and 7 September 2016. As Professor Takashi Yamamoto of the Hiroshima University, Graduate School of Science has led this field in Japan, the meeting was held at Hiroshima University and reports were given on the outcomes of developments such as an alkaloid-reduced potato. On 26 August 2016, a symposium on functional development of agricultural products using advanced technology was organized by the International Union of Food Science and Technology - Japan. The central theme of the symposium was crop development using genome editing technology.

2017

On 20 April 2017, the National Agriculture and Food Research Organization (NARO), under the jurisdiction of MAFF, and Hirosaki University (Aomori Prefecture) held a joint press conference announcing the start of outdoor cultivation trials of an epigenetically modified potato developed by the Faculty of Agriculture and Life Science, Hirosaki University. The purpose of the trials is an assessment of impacts on biodiversity. This potato was formerly known as an epigenome edited potato and blocks the working of genes by methylation (deactivation) of DNA using the RNA interference method.

In the Hirosaki University potatoes, the workings of the DNA and RNA remain as they are, but by working on the epigenetics the invertase gene and the CBSSI gene have been invalidated. It is reported that invalidating the invertase gene, it becomes possible to suppress scorching when manufacturing potato chips, and by invalidating the CBSSI gene it becomes possible to reduce amylose starch. It is reported that reducing amylose starch

increases the stickiness of the potato, making it more chewy and gooey when eaten.

(On 20 July 2017, MHLW assessed as safe the new GM crop "RNA interference potato" and approved it as food for distribution. Since a biodiversity impact assessment according to the Cartagena laws has not been carried out, the intention is not to cultivate the potato in Japan. The approval is thus for import and there is a strong possibility that it will be used to make fried potatoes in fast food stores.)

The National Agriculture and Food Research Organization (NARO), under the jurisdiction of MAFF, has applied for trial cultivation in isolated fields of a "sink-ability altered rice," the first GM rice to be produced by gene editing.

According to the Cartagena law, in the case of the cultivation of crops produced using GM technology without preventative methods for the spread of genetic material to other fields or to the environment must receive prior approval from MEXT.

The "sink" of "sink-ability altered rice" refers to storage ability. This rice variety was produced by splicing the DNA to insert a CRISPR/Cas9 gene to prevent the function of a particular gene, this being expressed throughout the plant anatomy. It is said that by preventing the function of a degradative enzyme gene for a plant hormone, the plant hormone is increased, leading to more floral buds and resulting in an increased number of grains. To insert the gene, the agrobacterium method is used with an antibiotic hygromycin resistant gene as a marker gene. The trial cultivation is due to be carried out for five years from April this year at the Kannondai Facility (Tsukuba City, Ibaraki Prefecture) high-performance isolated fields.

On 31 October 2017, the National Agriculture and Food Research Organization, NARO, in Tsukuba City, Ibaraki Prefecture, harvested rice that it had developed using genome editing. This year, six varieties of rice were planted in 10 ares (1/10 hectare) of paddy field. This rice has been named "sink function modified rice" and was developed to raise yields beyond conventional rice varieties. By destroying the gene of the enzyme that breaks down the plant hormone promoting the division of flower buds, the plant hormone is increased, the number of flower buds rises, which causes the number of seeds to increase, leading to a higher yield. The aim of the cultivation this time was to see if the yield would actually increase or not.

2018

On 28 May 2018 the Japanese Ministry of the Environment set up an investigative panel on genome editing technology and the Cartagena laws

under the Central Environment Council's Natural Environment Subcommittee, Specialist Panel on GMOs to determine whether genome editing should be subject to the Cartagena laws. Japan has yet to clarify its stance on living organisms developed through the use of genome editing. A conclusion is to be reached by the autumn, after several meetings of the investigative panel.

On 11 July 2018, the Natural Environment Subcommittee of the Central Environment Council under the Ministry of the Environment (MoE), held a meeting of its GMO, etc. specialist panel, at which it was decided to establish an "investigative panel on genome editing technology, etc. and the Cartagena laws" thus setting the direction for deliberations. The most important task is to organize the concepts that will help to make a decision on whether or not genome editing will be subject to restrictions under the Cartagena laws.

Under the concepts indicated by the MoE, genome editing is divided into three types, known as SDN1 to SDN3. SDN1 is the editing technology in greatest use at present, in which DNA is simply cleaved. This case does not fall under restrictions regardless of whether nucleic acid (e.g. guide RNA) is included in the artificial nuclease (DNA-cleaving enzyme). SDN2 inserts several bases at the location of the cleavage, and while nucleic acid is not included in the artificial nuclease this is subject to restrictions. SDN3 is the case in which genes are inserted at the location of the cleavage, and since nucleic acid is included, this is also subject to restrictions. Therefore, deliberations are to be conducted on the basis that no restrictions are imposed in the case that nothing is inserted, and imposed in the case that something is inserted.

Self-cloning and "natural occurrence," which are not covered by GM technology restrictions, have also been exempted for genome technology. Self-cloning is where genetic modification is carried out using only genes from the same species of organism, and natural occurrence refers to genetic modification that could also occur in the natural world. The issues of off-target and mosaics, etc. that have become a problem with genome editing have been left up to the deliberations of the investigative panel.

The panel members were decided on at the same time as the establishment of the panel. Professor Ryo Ohsawa of Tsukuba University was selected as chairperson and all the remaining members consist of researchers in the same field, including Professor Takashi Yamamoto of Hiroshima University Graduate School of Science and Chairperson of the Japanese Society for Genome Editing, and exclude right from the outset anyone who might possibly recommend restrictions, such as specialists in environmental issues, scholars of social sciences, legal scholars, etc. It is not hard to imagine, therefore, that deliberations will move in the direction of evading restrictions on genome editing.

In June, the government gave cabinet approval to the Integrated Innovation Strategy, in which clarification on the relationship of organisms produced using genome editing and the Cartagena laws as well as restrictions under the Food Sanitation Act are called for by the end of this fiscal year. Because of this, in parallel with the deliberations on the Cartagena laws by the MoE, an investigative panel on the safety of such organisms when consumed as food is about to be set up by the Ministry of Health, Labour and Welfare. It is certain that this will be strongly influenced by the deliberations in the MoE.

Based on the result of the investigative panel on genome editing technology, etc. and the Cartagena laws held on 7 and 20 August 2018, a meeting of the specialist panel on genome editing technology (under the Ministry of the Environment's Central Environment Council) was held and approved the original policy leaving outside the scope of regulation by the Cartagena laws cases in which DNA is cleaved but no gene is inserted. This means that at the present stage the greater part of genome editing technology will not be subject to any MoE restrictions.

It has become clear that the Cabinet Office has requested budget for coordinating regulations for foods developed using "new plant breeding techniques (NPBT)." Based on the Integrated Innovation Strategy approved by the cabinet in June, coordination and improvement of regulations of the Cartagena laws and Food Sanitation Act relating to organisms produced by genome editing and so on, to be completed during this fiscal year, and testing technologies related to these, are being pushed forward at a rapid pace.

As things stand, many of the new plant breeding technologies that will become subject to EU regulations due to the decision handed down by the Court of Justice of the European Union will not be subject to regulations in Japan and are very likely to be left outside regulations for labelling.

2019

The GM Food, etc. Investigative Panel of the Pharmaceutical Affairs and Food Sanitation Council, MHLW, which was examining the handling of food modified by genome editing to secure safety ended its deliberations on December 5, 2018. Having reached a conclusion, deliberations began in the superior organization, Investigative Panel on Newly-Developed Foods, on December 12. This panel also held a hearing with related organizations and ended on January 17, 2019. In this rush schedule of just over a month, the conclusion that "genome-edited foods basically do not require regulation" was reached in the wink of an eye.

The Integrated Innovation Plan approved by cabinet resolution in June 2018

urged that the legal regulation problem of genome-edited foods be settled within the fiscal year (by March 2019), and this schedule has been faithfully kept to. The GM Food, etc. Investigative Panel mentioned above concluded that, firstly, for the Food Sanitation Act, since there are only cases of the cleaving of DNA in genome editing technology, and, secondly, for the Cartagena laws, since there are no cases of the insertion of one to several bases, which would be subject to regulation, “this does not amount to recombination of DNA and is therefore outside the scope of safety screening.”

The reasons given for this relaxation of restrictions were:

- 1) Cases in which DNA is simply cleaved and one to several bases are inserted, replaced or deleted also occur in nature and are indistinguishable from the same occurrences in nature.
- 2) No difference can be found between off-targets occurring in the use of mutation and off-targets occurring in genome editing.
- 3) It is not possible to completely sequence off-targets.
- 4) Research by the Karolinska Institute in Sweden and by Novartis does not indicate that carcinogenicity is promoted.
- 5) Adverse impacts that occur at first are eliminated by selective breeding. All of the above are theories that have been negated by scientific knowledge and experience with genome editing technology.

Based on the conclusion of the panel, the final conclusion of the Investigative Panel on Newly-Developed Foods, submitted on January 17, was that neither notification nor punishments were required. This can be said to completely ignore the spirit of the Food Sanitation Act, which is supposed to protect the safety of food. This conclusion is scheduled to be finalized by the end of March, following the solicitation of public comments.

The Consumer Agency is to consider food labelling at sometime in the future, but as notifications have become voluntary it is impossible to distinguish genome-edited foods and there is a great possibility that the implementation of labelling will face difficulties.

It is now certain that the first genome-edited crop product to be imported from the US to Japan will be the Calyxt high oleic acid soybean, and Falco is expected to follow on from this. As appeals are being made for high oleic acid soybeans as a "healthy" food, they are likely to be separated, but since herbicide-resistant rapeseed will be mixed with the general rapeseed crop, separation will be impossible.

Calyxt, which is developing genome-edited crops one after another, has already received notification from US FDA that the white mildew resistant

wheat (2016) and the high-amylose wheat (2018) will not be subject to regulations or safety evaluations. Planting will begin in 2020. After soybeans and rapeseed, it is likely to be wheat that will be the next to be imported into Japan.

The Institute of Fruit Tree and Tea Science of the National Agriculture and Food Research Organization (NARO) is working on the remodeling of grape varieties using genome editing. Research has now begun on the Kyoho variety after working on Shine Muscat. The remodeling involves the elimination of a retrotransposon gene in an attempt to alter and improve the coloration of the fruit skin, according to Nikkei Biotech (13 September 2019).

Reflecting moves to use genome editing technology to promote US organic farming, Japan's Food and Agriculture Agricultural Materials Inspection Center (FAMIC) has held meetings to consider how to handle organic certification for genome editing since September 30. On November 8, FAMIC formally indicated its policy not to grant organic certification for genome-edited crops and initiated a call for opinions from the general public. However, the meetings are still continuing and since a formal decision has not yet been reached, there is a possibility that exceptions will be approved.

On 19 December 2019, at a Diet study meeting organized by the citizens' organizations the Japan Organic Agriculture Association and the NO! GMO Food Campaign and held in the House of Representatives Diet Members Office Building, Director Mayu Nishikawa of the Standards Certification Office of the Food Industry Agency of MAFF, who attended the meeting, stated, "No crops that have been genetically modified, including genome-edited crops, will be certified as organic."

(At a meeting of the Council for the Japanese Agricultural Standards held on 31 January 2020, a draft amendment of the organic Japanese Agricultural Standards (JAS) that incorporated a clause on crops, etc. that use genome-editing technology was submitted. With this, the MAFF policy not to approve crops applying genome editing technology as organic was confirmed.)

2020

A plan to use genome-edited fish to eliminate exotic fish species is being pushed forward at the National Research Institute of Aquaculture in Tamaki Town, Mie Prefecture. The plan involves the release of male fish in which the gene for producing eggs is destroyed to cause infertility in females. Female fish born from breeding with these genome-edited fish will then be unable to produce eggs. After repetition of this cycle, female fish able to produce eggs will disappear, and the species will become extinct. Even without the use of

gene drive technology, it will be possible to bring about the extinction of a species, resulting in a serious impact on the ecology. As this use of genome editing is outside the scope of the Biodiversity Convention Cartagena laws, and thus there are no legal restrictions. If the plan is implemented, it need not therefore be publicized, and there is the possibility that anyone will simply be allowed to do it whenever they want.

On 1 September 2020, Tokyo Institute of Technology announced the launch of a "Bacteria Genome Architecture Project" (BGAP) to produce an artificial microorganism genome. Assistant Professor Yasunori Aizawa and his research team at the Tokyo Institute of Technology School of Life Science and Technology, Department of Life Science and Technology, are proceeding with the research jointly with the venture company Logomix, established by Tokyo Institute of Technology. The research team will start by attempting to compile a synthetic genome of *E. coli*. According to Nikkei Biotech (15 September 2020)

Consumer Reactions in Japan

“Consumers Union of Japan started the No! GMO Campaign in 1996, ” says Koketsu Michiyo, CUJ. “There is no commercial farming of GMOs in Japan, but a lot of soy, corn and canola is being imported. We think the labelling should be better so consumers can avoid GMO food.”

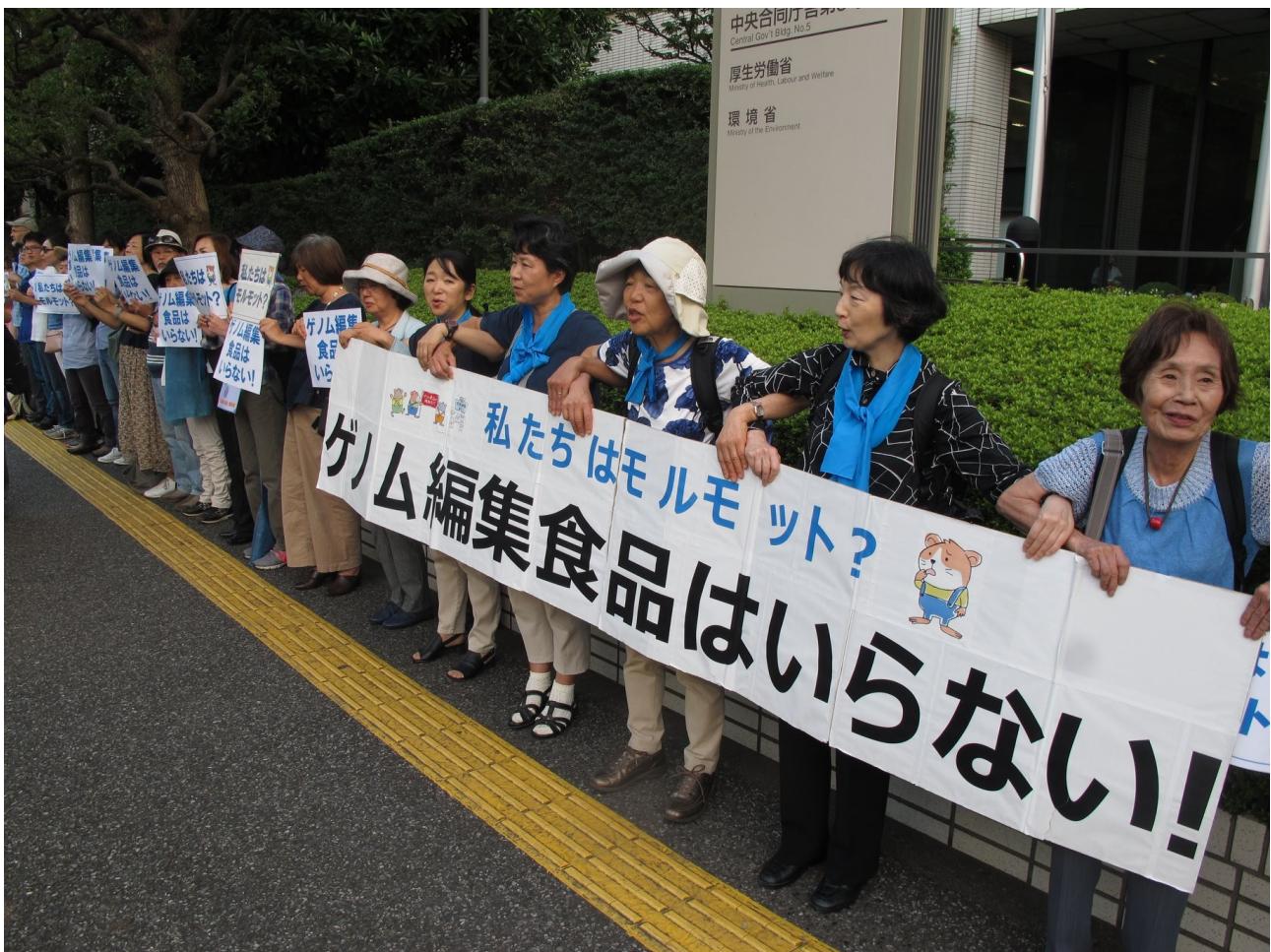
CUJ, Japan Citizens’ Network for Sustainable Food and Agriculture and other organizations have been investigating GM canola contamination since 2004 at many locations around Japan. The participants have seen the effect of the unintentional transboundary movement of living modified organisms, such as hybridization of indigenous rapeseed as well as the advent of wild growing GM broccoli. These GM crops pose a real risk to local biological diversity as a number of related food crops that are popular in Japan may be contaminated with GMOs.

Consumers Union of Japan participated together with other Japanese NGOs at the large Planet Diversity Conference in Bonn, Germany on 12-16 May 2008. It was a global congress on the future of food and agriculture, with a demonstration to celebrate biodiversity.

By 2018, some 43% of respondents to a University of Tokyo internet survey said they would not want to eat agricultural products developed with genome editing technology, according to The Mainichi Newspaper. The figure topped 53% when people were asked about whether they would eat genome-edited animal products. The poll results were unveiled at a June 5 meeting of the

Japanese Society for Genome Editing in Tokyo. The survey team led by Masato Uchiyama, a guest researcher at the University of Tokyo's Institute of Medical Science, queried some 38,000 men and women aged 20-69 in May and June 2018, receiving around 10,700 valid responses.

On 18 May 2019, Japanese, South Korean and Taiwanese citizens' organizations taking action against GMOs announced a joint statement protesting against the potato using RNA interference. South Korea is very close to approving this potato and there is a possibility that Taiwan will also approve it. In Japan, the potato is already approved for distribution as human food, but as it has yet to receive approval under the Cartagena laws, it cannot yet be cultivated. There is a strong possibility that the potato will be imported as fried potatoes or potato chips. Because of this, Consumers Union of Japan and other organizations are calling on fast food chains and family restaurant chains not to use the potato.



Consumers Union of Japan held a protest action outside the Ministry of Health in Tokyo today on Wednesday, 25 September 2019 to protest against the lack of rules to deal with genome edited foods. Gene editing or genome editing may soon appear in food stores as the novel technology appears to

gain ground among crops abroad. The lack of labelling in Japan is a serious problem. Meanwhile, Koketsu Michiyo, secretary general of Consumers Union of Japan, was invited to share our views at the NHK TV program Closeup Gendai on 24 September 2019 about the lack of regulations.

The Conference to Consider the Genome Issue (representative Susumu Shimazono, Honorary Professor of the Graduate School of the University of Tokyo and currently professor at Sophia University, Tokyo), consisting of experts and citizens, submitted to the government and academic associations a "Request concerning the establishment of a forum to discuss genome editing of the human embryo with the participation of a wide range of researchers and citizens," holding a press conference in the Lower House Diet Members' Office Building No. 2 on 13 July 2020. Representative Shimazono stated that there is a huge ethical problem in the application of genome editing to human embryos, and, moreover, since the building of a social consensus is as yet insufficient, a forum for discussion in which citizens can also participate should be established. There is currently no forum for citizens to speak out on this issue in Japan.

A total of 447,725 signatures were submitted at the House Study Session they held in September 2019 and January 2020 calling for the regulation and labeling of genome-edited foods were gathered in anticipation of the "unsettling situation" that there will be no labelling for these foods: "At the House Study Session in January, we heard from your ministry's officials that they have already received a number of consultations on how to report on the issue, but despite the fact that more than six months have passed since then, the government is still showing a lack of interest in the issue," according to Consumers Union of Japan.

Many consumers in Japan are deeply unhappy with this state of affairs. Consumers are saying, "We do not want to eat food which is the result of genome editing and genetically modified organisms which have been created by the use of such technologies." And consumers are demanding both safety assessment and mandatory labelling of such foods.
