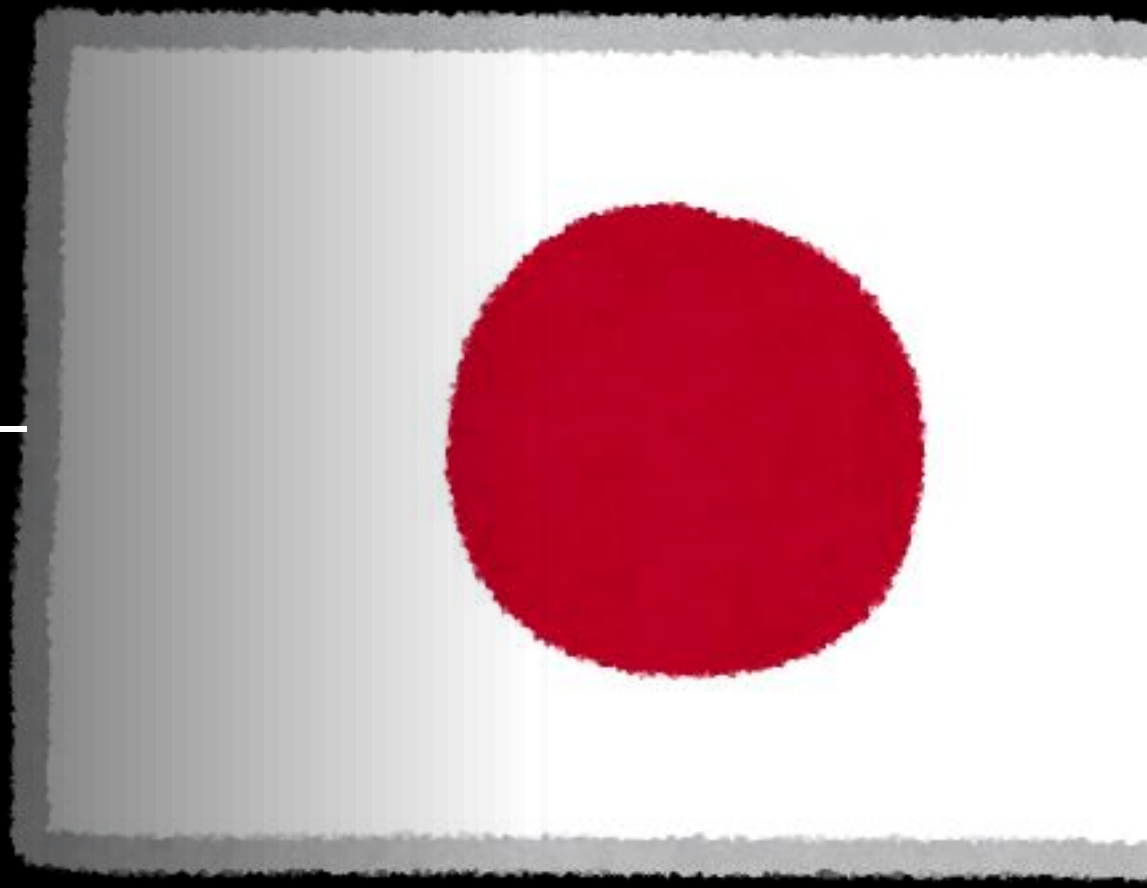
Regulatory Status of Genome-Edited Organisms Under the Japanese Cartagena Act



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Regulatory Status of Genome-Edited Organisms Under the Japanese Cartagena Act

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The Japanese government recognizes the substantial values of genome-edited agricultural organisms and has defined in which cases these are covered by the existing regulatory framework to handle this technology. Genome-editing technologies could revolutionize and accelerate plant breeding owing to the simplicity of the methods and precision of genome modifications. These technologies have spread rapidly and widely, and various genome-edited crops have been developed recently. The regulatory status of genome-edited end products is a subject of controversy worldwide. In February 2019, the Japanese government defined genome-edited end products derived by modifications of SDN-1 type (directed mutation without using a DNA sequence template) as not representing "living modified organisms" according to the Japanese Cartagena Act. Here, we describe the classification and regulatory status of genome-edited end products in this decision. We hope that reporting the progress in Japan toward the implementation of this regulatory approach will provide insight for scientific and regulatory communities worldwide.

Keywords: genome editing, regulatory status, Japan, Cartagena Protocol, LMOs

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Regulatory Framework of LMOs in Japan

Safety Categories	Legislations
Environment	Cartagena Act
Food	Food Sanitation Act
Feed	Feed Safety Law

Japanese law
to ensure
the Cartagena Protocol

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The Cartagena Act states that **LMOs** are regulated in terms of **the final products** as "*living organisms* ***having nucleic acids obtained by utilizing a technique for processing nucleic acids outside the cell*** *for the purpose of transferring or replicating the nucleic acids by transferring them into a cell, virus, or viroid*" (Chapter I, Article 2, item 2)

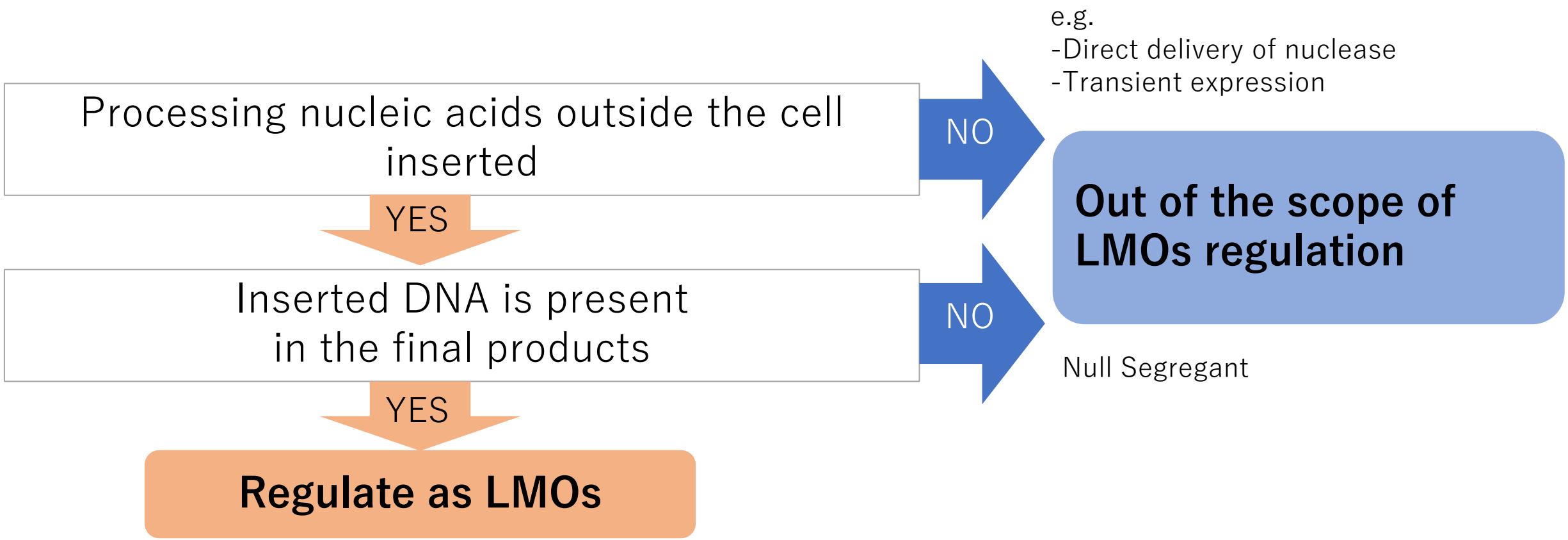
Environmental Safety of Genome-Edited organisms under the Cartagena Act

In February 2019,

the Japanese government defined **genome-edited final products** derived by modifications of SDN-1 type (**directed mutation without using a DNA sequence template**) **as not representing "living modified organisms"**

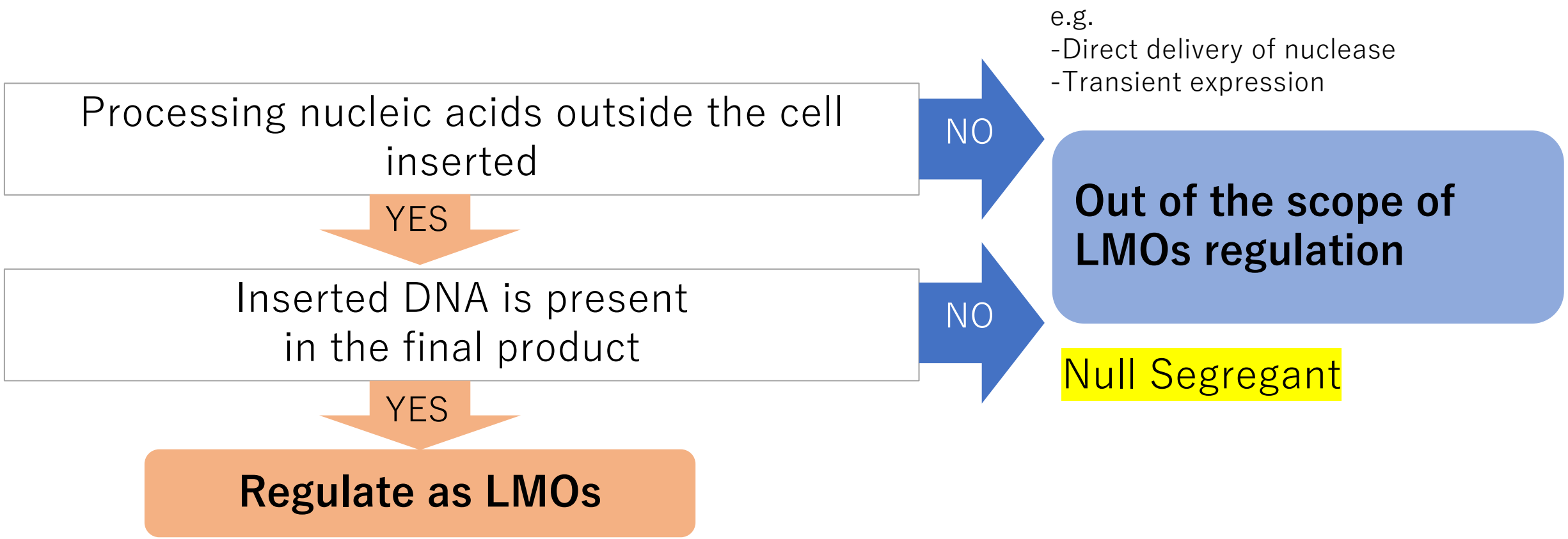
according to the Japanese Cartagena Act.

Handling flow of Genome-Edited Organisms under Cartagena Act



Reference: J-BCH, To Genome Editing Technologies Users
https://www.biodic.go.jp/bch/download/genome/genome_chirashi_english.pdf

Handling flow of Genome-Edited Organisms under Cartagena Act



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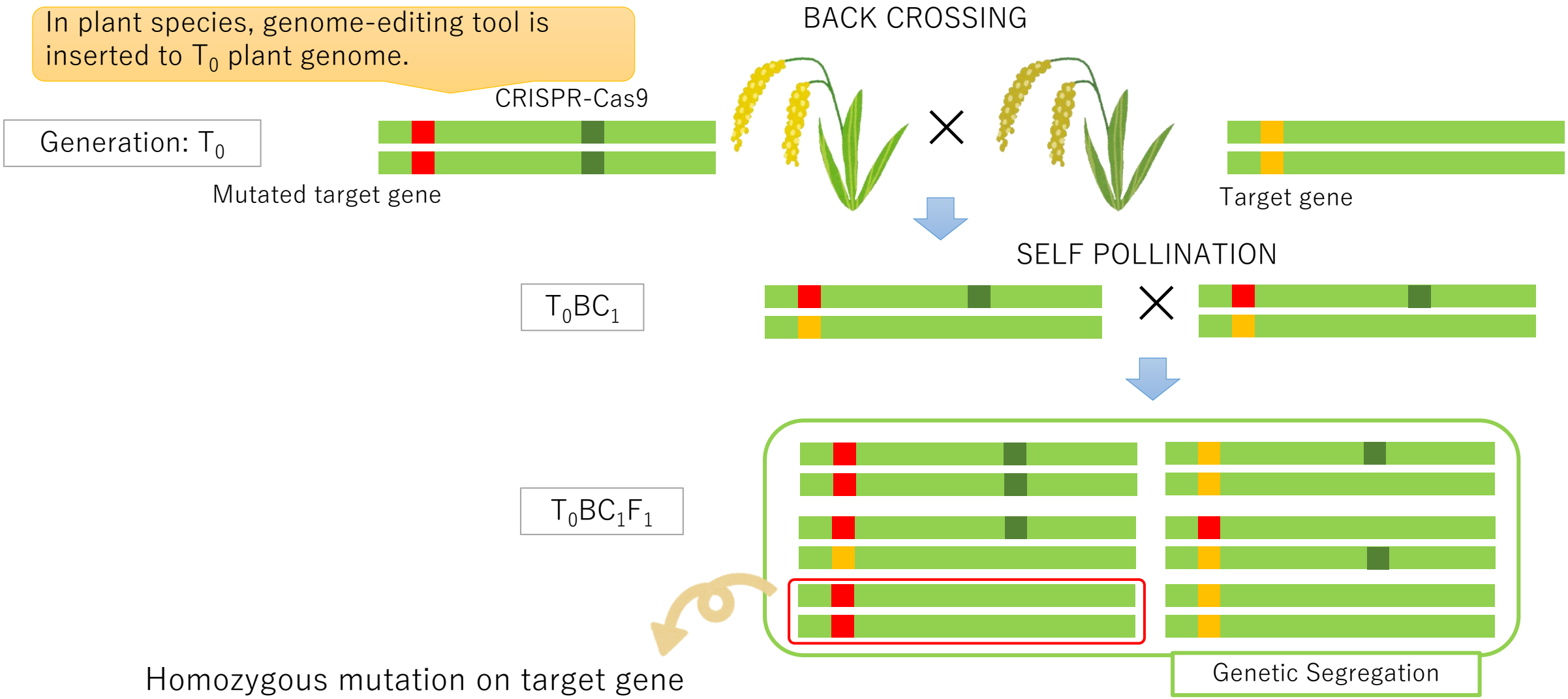
What is the Null Segregant?

In plant species, genome-editing tool is inserted to T_0 plant genome.



Homozygous mutation on target gene
, and not present Cas9 vector
= **Null segregant**

When Handling of Genome-Edited Organisms is out of the Scope of LMOs Regulation,

Japanese government:

-**requests developers to provide notification** that includes the information such as development processes, for the purpose of accumulating knowledge related to genome editing organisms.

-**publish a part of the notified information on the website** of Japan Biosafety Clearing House.

Food Safety of Genome-edited organisms under the Food Sanitation Act

Article 2 (excerpt)

LM Food is defined as "*the food including the organism which was obtained by recombinant DNA technique;*

the technique to generate recombinant DNA by cleavage/ligation,

insert the DNA into living cell and multiply"

Handling flow of Genome-Edited Organisms under Food Sanitation Law

Foreign DNA is absent from the final products

NO

Regulated as LMOs

YES

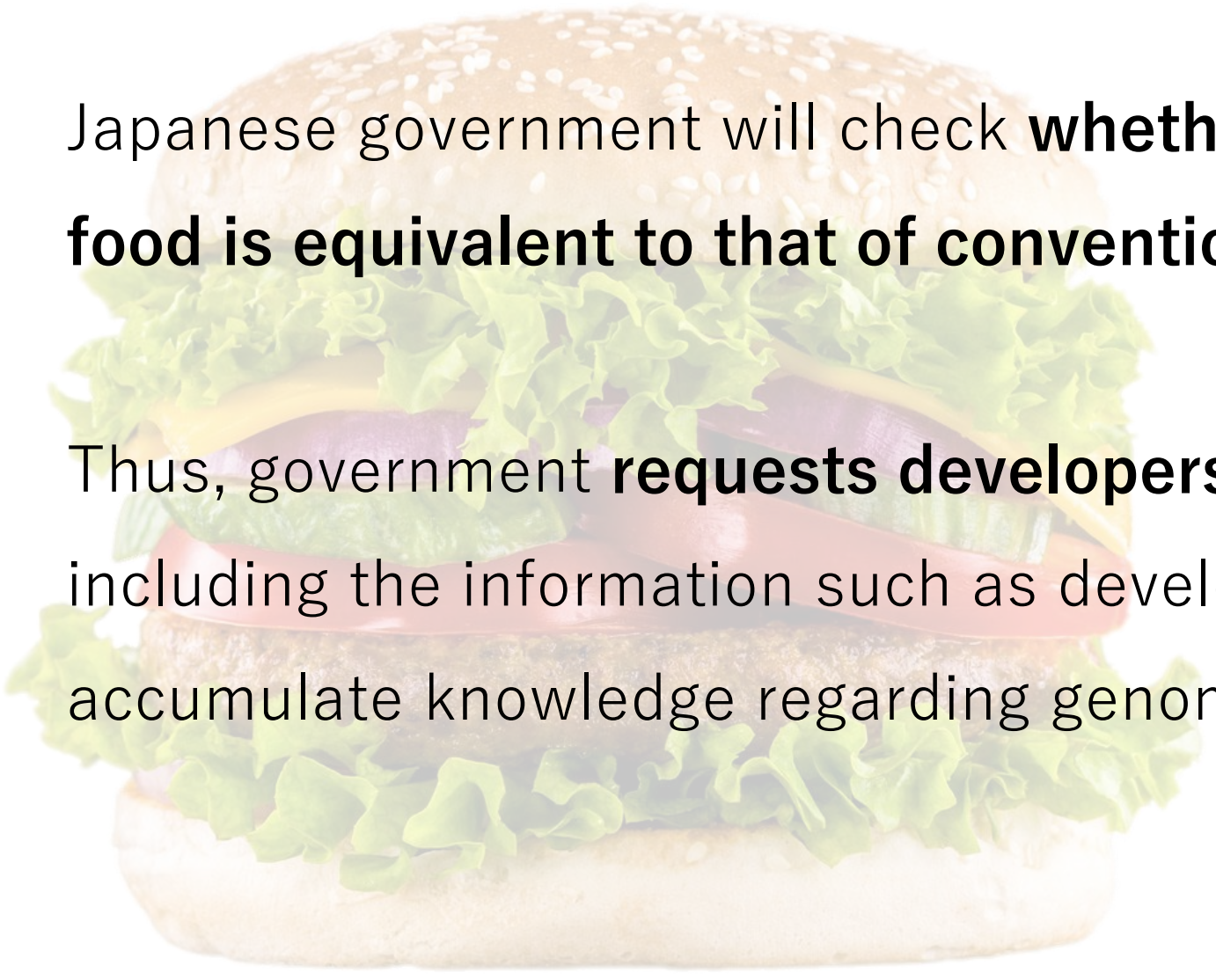
The change induced by genome editing is within the range of naturally occurring sequence repair (nucleotide deletion /replacement, naturally occurring gene deletion, and one to several bases insertion).

NO

YES

Out of the Scope of LMO Regulation

When Handling of Genome Edited Food is out of the scope of LMO regulation,



Japanese government will check **whether safety of genome editing food is equivalent to that of conventional food**.

Thus, government **requests developers to provide notification** including the information such as development processes, in order to accumulate knowledge regarding genome editing food.

Summary: Handling of Genome Editing in Japan in terms of SDN classes (by Lusser et al. 2011, 2012)

Class	Environment (Ministry of Environment : MOE)	Food (Ministry of Health, Labour and Welfare: MHLW)
SDN-1	Non-LMO	Non-LMO
SDN-2	LMO*	Non-LMO/LMO
SDN-3	LMO*	LMO

* In case nucleotides are from same species (self cloning) or cross compatible species (natural occurrence), the product is considered as non-LMO.

Handling of SDN-2 by MHLW and MOE

MHLW,

✓Product-based judgment

✓As a product-based evaluation, same regulation of genetically modified foods under the Food Sanitation Act will not be applied to genome editing foods that modified DNA sequences indistinguishable from natural mutation or conventional artificial mutagenesis.

MOE,

Definition: Process-based

✓LMO is defined as “the organism containing extracellularly processed nucleic acid or its replicate” according to Cartagena Act.

✓Although the product by SDN-2 can not be distinguished as the product from SDN-1 or the product by mutation, it is legally difficult to define that the product is “Non-LMO” because the template is used externally.

Information Requested for Notification

	MHLW (Food)	MOE (Environment)
Absence of foreign DNA	✓	✓
Taxonomic species of host organisms	✓	✓
Purpose of use of the product	✓	✓
Method of genome editing	✓	✓
Name and function of targeted genes	✓	✓
Detail of modification and resulting traits	✓	✓
Unintended change if any	✓	✓
Confirmation of no adverse effects on biological diversity		✓
Confirmation of no adverse effects on human health; the identified changes in DNA (including those that are off-target) do not produce allergens or enhance known inherent toxic substances	✓	

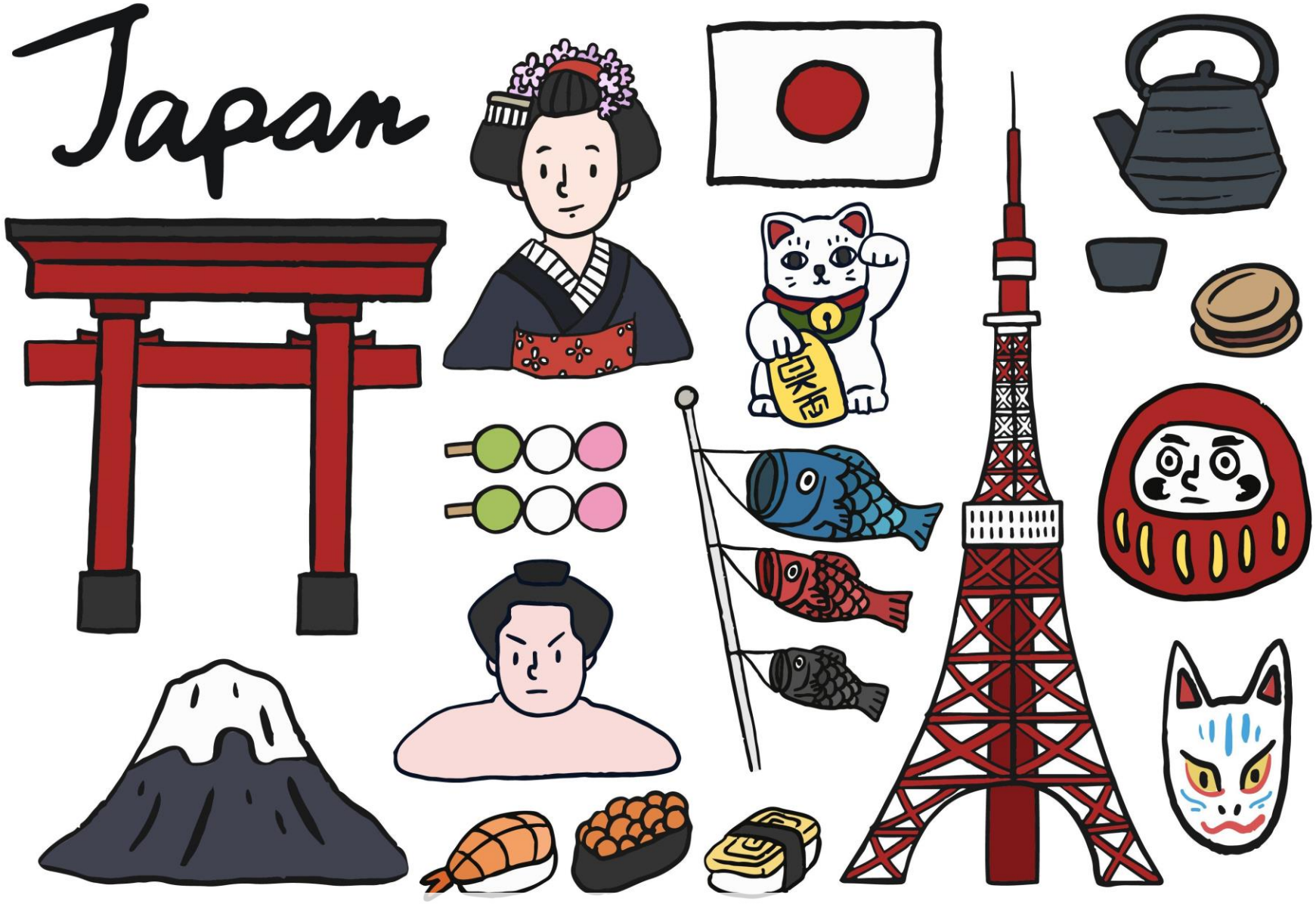
Development of Genome-edited Organisms in Japan

Wider Body FISHES

SEA BREAM

High yield
RICE

Easy-aquafarming TUNA



Thank you !ありがとうございました！