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CONSULTATION ON REGULATORY FRAMEWORK FOR THE USE OF GENOME EDITED CROPS FOR FOOD AND ANIMAL FEED

Posted on: *20 December 2023* | ***Closing Date:*** *19 February 2024*

Aim

1. The Singapore Food Agency (SFA) is seeking feedback from the food and animal feed industry, as well as interested parties, on a proposed regulatory framework for the use of genome edited (GEd) crops[1] in food for human consumption and animal feed. This applies to both imported, as well as locally developed, cultivated, and processed crops.

Background

2. Modern biotechnology has accelerated the breeding of new crop varieties with desirable agronomic traits, such as disease resistance, drought tolerance, and improved nutrition, for use as food and animal feed. These traits can bring benefits for the farmer and the consumer.

3. Genome editing represents a set of modern biotechnological tools that allow crop developers to make precise changes within an organism's genome.[2] Examples of genome editing tools that have been used to generate new food crop varieties include zinc finger nucleases (ZFN), transcription activator-like effector nucleases (TALENs), and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) nucleases.

4. Genome editing has been employed to expedite the breeding of new crop varieties that could have been generated via conventional breeding[3]. This is because genome editing can be used to generate precise changes in an organism's genome that are equivalent to the changes that naturally arise during conventional crop breeding. SFA considers such GEd crops to be equivalent to conventionally bred crops. For example, genome editing tools can be used to breed a new tomato variety

[1] A crop is a plant, a macroscopic fungus (e.g., mushroom), or a macroscopic alga (e.g., seaweed), that is grown for subsistence.
[2] The genome of an organism includes its entire hereditary material content, which is made from deoxyribonucleic acid (DNA). The genome includes, but is not limited to, the chromosomal DNA, mitochondrial DNA, chloroplast DNA and plasmid DNA.
[3] Conventional crop breeding techniques include selective breeding, cross breeding, somatic hybridization and mutagenesis via ionizing radiation or chemical mutagens, but excludes molecular biotechnology techniques such as genome editing and genetic modification (GM).

that could have been bred using via cross breeding between two other tomato varieties.

5. Genome editing can also be employed to generate new crop varieties that could not have been plausibly generated via conventional breeding techniques. For example, corn DNA could not be inserted into a tomato via conventional breeding techniques. SFA considers such GEd crops to be equivalent to genetically modified organisms (GMOs). GMO crops and genome edited (GEd) crops equivalent to GMOs are subject to SFA's GMO pre-market safety assessment and approval. Please refer to the Conditions related to Genetically Modified Crops on SFA's website for further information on the GMO pre-market safety assessment and approval process: https://www.sfa.gov.sg/food-import-export/commercial-food-imports

6. Presently, there are no explicit regulatory pathways for GEd crops to be used in food and/or animal feed in Singapore. Crop developers may choose to submit their GEd crop under the existing GMO pre-market safety assessment and approval process. However, this process would likely not be fit for purpose for GEd crops that are equivalent to conventionally bred crops.

7. SFA has taken note of updated regulations or regulatory guidance in Canada, Japan, the United Kingdom, and the United States to exempt GEd crops that are equivalent to conventionally bred crops from GMO pre-market safety assessment. These updated regulations or regulatory guidance provide clarity to crop developers on whether their GEd crop would be subject to the GMO pre-market safety assessment and approval process.

8. SFA has therefore developed a science-based, risk-proportionate regulatory framework to provide regulatory clarity to crop developers seeking to use GEd crops in food and animal feed.

Regulatory framework for the use of GEd crops in food and animal feed

9. A crop developer intending to sell a GEd crop in Singapore for use as food and/or animal feed must first determine whether said crop contains foreign DNA.[4] If the crop does not contain foreign DNA, SFA encourages the developer to notify SFA on the crop (**Pathway A**). A non-exhaustive list of examples of GEd crops that are considered to not contain foreign DNA include:

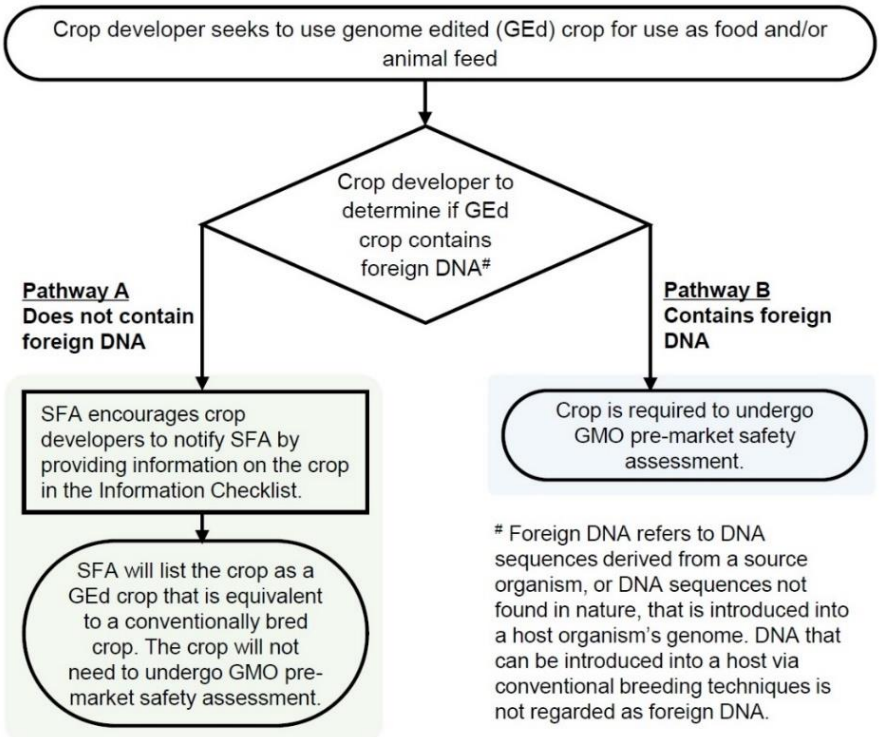
[4] Foreign DNA refers to DNA sequences derived from a source organism, or DNA sequences not found in nature, that is introduced into a host organism's genome. DNA that can be introduced into a host via conventional breeding techniques is not regarded as foreign DNA.

a. A crop with a non-functional gene arising from cellular repair of a targeted DNA strand break (i.e., gene knock-out).
b. A crop containing a targeted single base pair substitution in any part of the genome.
c. A crop (host) where an endogenous gene has been substituted with a homologous gene variant (i.e., allele) originating from another crop that can reproduce with said host via conventional breeding (e.g., breeding between two tomato varieties).

10. If the crop contains foreign DNA, said crop will need to undergo SFA's pre-market safety assessment (**Pathway B**). A non-exhaustive list of examples of GEd crops that are considered to contain foreign DNA include:

a. A crop containing DNA from a bacterial, animal, viral sources, or containing DNA sequences not found in nature.
b. A crop containing DNA from another crop that cannot undergo conventional breeding with the GEd crop (e.g., insertion of corn DNA into tomato).

11. **Pathways A** and **B** are depicted in the flowchart below:



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12. SFA encourages developers seeking to use GEd crops that fall under **Pathway A** for food and/or animal feed to notify SFA by providing information on such crops to SFA via an Information Checklist (see **Annex I**). Upon submission of complete information requested in the Information Checklist for a GEd crop, SFA will determine if SFA agrees with the developer that said GEd crop does not contain foreign DNA and is therefore equivalent to conventionally bred crops. If SFA agrees with the developer that said GEd crop is equivalent to conventionally bred crops, SFA will inform the developer that the crop would not need to undergo GMO pre-market assessment.

13. To promote transparency towards consumer acceptance, a List of GEd crops that have completed notification will be made publicly available on SFA's website. Only the common / scientific name of the crop, commercial / proprietary name, marketed traits, and intended use (as food and/or feed) will be made publicly known. Business confidential information submitted by developers will not be disclosed outside of SFA without the developer's explicit consent.[5]

14. Crop developer intending to use GEd crops that fall under **Pathway B** for food and/or feed are required to seek GMO pre-market safety assessment and approval for such crops. SFA expects that the GMO pre-market safety assessment and approval process to take 12 – 18 months upon receipt of complete information as required by GMAC.

FAQs

15. SFA understands that genome editing is a new technology and anticipates that there will be questions on various aspects of the regulatory framework for the use of GEd crops in food and animal feed. SFA has prepared a list of FAQs and replies in **Annex II**.

Request for Comments

16. SFA invites feedback and comments on the regulatory framework on the use of GEd crops in food and animal feed detailed in paragraphs 9 to 14. All submissions should be clearly and concisely written and should provide a reasoned explanation for

[5] Please note that SFA does not sign non-disclosure agreements (NDA) with companies for the purposes of evaluating the information submitted, as SFA employees are bound to the preservation of secrecy under Section 34 of the Singapore Food Agency Act 2019.

any proposed revisions. Please submit your feedback and comments in the form of the table provided in **Annex III**.

17. Submissions should reach SFA no later than 6:00 p.m. (Singapore time; UTC+8), 19 February 2024, through email to the following address: tan_yong_quan@sfa.gov.sg (Dr Tan Yong Quan, Scientist, Risk Assessment and Communication Department, National Centre of Food Science).

18. Feedback and comments on the regulatory framework will be consolidated and a summary will be published, together with SFA's responses, on the SFA website after the close of the consultation exercise.

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Annex I

Information Checklist to notify SFA of GEd crop for use as food and/or feed

Q1. Developer information (a) Company name (b) Unique Entity Number (applicable for entities based in Singapore) (c) Address (d) Name and designation of contact person (e) Contact information
Q2. Basic information on GEd crop Note: SFA will include only the company name and information provided in Q2 in the List of GEd crops that have completed notification that is published on SFA's website. (a) Scientific / common name of the crop from which the GEd crop was bred (b) Commercial / proprietary name of the GEd crop (c) Marketed traits (e.g., pest resistance, increased vitamin production, longer shelf life) (d) Intended use of GEd crop (i.e., as human food and/or animal feed)
Q3. Further information on GEd crop (a) Provide information on complete and ongoing international regulatory approvals / registrations / notifications in other countries and jurisdictions. (b) Indicate if the GEd crop has any food safety hazards that are new or at increased levels compared to the conventional counterpart.
Q4. Information on genome edited process and verification (a) Provide the name(s) of genome editing technique(s) used, along with a summary of the genome editing process.

(b) Provide name(s) and genomic location(s) of the genetic sequence(s) in the organism's genome that has/have been edited, along with known function(s) of the edited sequence(s).

(c) Provide a description of the intended effect(s) resulting from the genome editing process on the crop.

(d) Provide a summary of how the sequence alterations in the organism were verified. Verification should be performed using standard molecular biology techniques, such as targeted sequencing, or Next Generation Sequencing (NGS).

(e) Provide a summary of the measures taken to minimise the probability of off-target genetic alterations during the genome editing process.

(f) Indicate if off-target alterations in the genome were detected. If off-target genomic alterations were detected, state the observed or predicted effects of said alterations on the organism.

(g) For the final GEd crop, provide evidence verifying the complete removal of foreign nucleotides (e.g., plasmids, guide RNA, oligonucleotides, carrier DNA) and/or proteins, but which were transiently present in the organism at some point during the genome editing process. Evidence provided should be based on standard molecular biology methodologies such as whole genome sequencing or genomic Southern blotting. Provide a summary of the removal process, including details of the number of generations of segregation or backcrossing where applicable.

(h) Provide a summary of how the intended phenotypic trait(s) in the final GEd crop was/were verified.

(i) Provide evidence that the genome alterations resulting from genome editing, as well as the phenotypic traits resulting from said alterations, are stably inherited through several generations and are consistent with applicable laws of inheritance.

(j) Indicate if the GEd crop could have plausibly been generated using conventional breeding methods. Provide substantiating scientific evidence or reasoning where relevant.

(k) Indicate if the genetic alterations in the GEd crop could potentially be transferred to another organism that is unable to reproduce with said food crop via conventional breeding techniques.

Q5. Other information

(a) Please provide information on the GEd crop that the developer thinks may be relevant but was not requested above.

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Annex II

FAQs

Q1. Why is genome editing being used to generate new crop varieties?

Genome editing enables scientists to make small alterations in the existing DNA of a crop to impart useful properties for agriculture and food. All organisms naturally experience such small variations in their DNA when a new generation is bred from their parents. For thousands of years, farmers have been selecting crops with useful properties based on these naturally occurring DNA variations. However, this traditional selection process is imprecise and requires decades of continual breeding. Genome editing is able to expedite the breeding of desirable crops that could have been achieved using traditional methods, allowing such crops to be obtained in approximately 1 – 5 years.

Useful crop properties that have been obtained using genome editing so far include resistance to disease, faster maturation time, longer shelf life and improved nutritional content. These crops provide consumers with more choices in the food products that are available on the market. Genome edited crops can also bring benefits for farmers. Certain genome edited crops that are resistant to plant pests allow farmers to reduce the use of pesticides.

Q2. Is genome editing the same as gene editing? What are other terms that refer to genome editing?

Genome editing is used interchangeably with gene editing by scientific researchers and by various food agencies all over the world. Both terms have the same meaning, and genome editing is the term used by SFA for consistency.

Genome editing can fall under terms used by other food safety agencies. These terms include but are not limited to:

- New Genomic Techniques (NGT)
- New Breeding Techniques (NBT)
- Precision breeding

Q3. Is genome editing the same as genetic modification?

From SFA's perspective, genome editing is not the same as genetic modification. While both genome editing and genetic modification refer to the use of modern biotechnology tools to alter an organism's genome, genome editing represents a

more recent set of tools that allow researchers to make precise changes to an organism's genome. Many of these changes could have been made via conventional breeding techniques, though genome editing can speed up the process of making these desired changes relative to conventional breeding.

In contrast, genetic modification generally involves insertion of foreign DNA, generating organisms that could not have been produced via conventional breeding. SFA has in place a GMO pre-market safety assessment and approval process: https://www.sfa.gov.sg/food-import-export/commercial-food-imports

Q4. How might more recently developed genome editing techniques, such as base editing, prime editing or retron editing, be regulated under this framework?

SFA focuses on the product when looking at the food safety of GEd crops. Products generated using very recent or other genome editing techniques not developed at the point of writing can still be eligible for notification (**Pathway A**) as long as the final crop is equivalent to a conventionally bred crop and does not contain foreign DNA, nucleotides, and/or proteins.

Q5. Foreign DNA, nucleotides, and/or proteins were introduced into the host crop during genome editing. Does this disqualify the host crop from notification?

SFA is aware that transient introduction of foreign DNA, nucleotides, and/or proteins is often used during the genome editing process to make the necessary genomic alterations. If said DNA, nucleotides and/or proteins remain in the GEd final crop, the crop would be subject to the GMO pre-market safety assessment. If said DNA, nucleotides and/or proteins are completely removed from the final crop, and removal was verified using standard molecular biology methodologies, the product would be eligible for notification (**Pathway A**).

Q6. Does SFA require raw chemical and biological analysis data for the information requested?

For first submission of the Information Checklist, summary figures or tables of the characterisation data would be preferred. Nonetheless, if further information is needed to clarify if the crop contains foreign DNA, SFA may request for companies to provide further data, including raw data from chemical and biological analysis.

Q7. Will SFA implement a similar framework for the use of GEd animals for use in food and feed?

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SFA notes that GEd animals for use in food and feed are a more recent scientific development compared to crops. SFA is monitoring international developments in regulations concerning GEd animals for use in food and feed and will conduct a public consultation in due time.

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Annex III

Table to provide feedback and comments

Questions	Comments
1. Are the two regulatory pathways (**Pathway A** and **Pathway B**, detailed in paragraphs 9 – 11) suitable for categorising all current GEd crops and those that are under development or will be developed in the future?	Yes / No If "No", please suggest an alternative way of categorisation and provide an explanation.
2. Is the Information Checklist (paragraph 12 and **Annex I**) suitable for determining if a GEd crop is equivalent to a conventionally bred crop?	Yes / No If "No", please suggest amendments to the Information Checklist and provide explanations for the suggested amendments.
3. Do crop developers have concerns over the information to be made public in the List of GEd crops that have completed notification (detailed in paragraph 13 and Q2 in **Annex I**)?	Yes / No / Not applicable (if not a crop developer) If "No", please explain why.
4. Any other comments?	