

RESPONSES TO COMMENTS RECEIVED FROM THE PUBLIC CONSULTATION ON REGULATORY FRAMEWORK FOR THE USE OF GENOME EDITED CROPS FOR FOOD AND ANIMAL FEED

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The Singapore Food Agency (SFA) initiated a public consultation on the regulatory framework for the use of genome edited (GE_d) crops for food and animal feed from 20 December 2023 to 19 February 2024. Contemporaneously, trading partners and interested parties were notified via World Trade Organization (WTO) SPS notification G/SPS/N/SGP/84.

At the close of the public consultation exercise and WTO notification period, SFA received comments from 11 respondents. SFA's responses are tabulated in Table 1.

SFA appreciates the time taken by stakeholders to submit feedback and comments which would contribute to the decision-making process. The amendments are targeted to come into effect in the third quarter of 2024. We would like to encourage all parties to actively participate in future consultations.

TABLE 1

<p>A. Comments on whether Pathway A and Pathway B (detailed in paragraphs 9 – 11 of the public consultation document) are suitable for categorising all current GEd crops and those that are under development or will be developed in the future</p>	<p>SFA’s response</p>
<p>1. Four respondents expressed support for Pathway A and B in categorising current and future GEd crops. Respondents agreed with the regulatory approach that GEd crops that are equivalent to conventionally bred crops are exempted for pre-market safety assessment for genetically modified organisms (i.e., Pathway A). Respondents also agreed that GEd crops that contain foreign DNA should undergo pre-market safety assessment for genetically modified organisms (i.e., Pathway B).</p>	<p>SFA notes the support expressed for SFA’s categorisation method for GEd crops and the regulatory pathways to be taken, i.e., voluntary notification for GEd crops that are equivalent to conventionally bred crops versus pre-market safety assessment for GEd crops that contain foreign DNA.</p>
<p>2. One respondent expressed concerns on the absence of a numerical threshold for DNA base-pair changes made to categorise a GEd crop into either Pathway A or B.</p>	<p>SFA understands that conventional breeding methods can result in significant DNA base-pair changes in an organism. SFA is also aware that for countries/regions that have implemented updated regulatory guidance for GEd similar to SFA’s categorisation, none have set an explicit numerical threshold for DNA base-pair changes to determine whether a GEd crop is equivalent to conventional varieties or equivalent to GM crops.</p> <p>Given that GEd crops are a recent innovation and international regulatory</p>

	<p>approaches for their use in food are nascent, GEd crop developers may request to discuss with SFA on the most appropriate Pathway for their specific GEd crop if they are unsure on which pathway is applicable.</p>
<p>3. Three respondents commented that the examples of crops that would fall under Pathway A or B (denoted in paragraphs 9 and 10) are limited. Nonetheless, two respondents appreciated that SFA indicated the lists of examples as non-exhaustive.</p>	<p>With increasing familiarity gained through discussions with developers and completed Notifications, SFA will update the lists with further examples in SFA's Guidance Document on GEd Crops to provide greater clarity to developers. Nonetheless, the lists will still be indicated as non-exhaustive so as not to exclude crops that could be conceivably bred using genome editing but have yet to be bred.</p>
<p>4. Four respondents commented that SFA's current definition for foreign DNA (<i>Foreign DNA refers to DNA sequences derived from a source organism, or DNA sequences not found in nature, that are 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.</i>) may lead to some confusion as it can be difficult to prove if a DNA sequence can be introduced via conventional breeding.</p>	<p>SFA notes that it can be difficult in certain situations to prove that a DNA sequence can be introduced via conventional breeding techniques, given that the extent of DNA alterations that can be made via conventional breeding is not known and there may not be a defined limit. In line with SFA's key consideration that GEd crops that could not have been plausibly generated via conventional breeding are equivalent to GM crops, SFA has amended the definition of foreign DNA as follows (changes in bold):</p> <p><i>Foreign DNA refers to DNA sequences derived from a source organism, or DNA sequences not found in nature, that are introduced into a host organism's genome and could not have been inserted naturally or been introduced into said organism using conventional breeding techniques.</i></p>

<p>5. One respondent suggested for a separate regulatory approach for crops containing DNA from other food crops, even if the inserted DNA could not have been inserted using conventional breeding. For example, corn with tomato DNA should be subject to a different regulatory approach from corn containing DNA from a bacterial species.</p>	<p>SFA notes that any insertion of foreign DNA in a crop has the potential to introduce new allergens or other food safety hazards not expected from crops derived via conventional breeding. For example, insertion of genes from soybean into corn may introduce new allergens into said corn. Therefore, SFA will continue to request that all crops containing foreign DNA be subject to pre-market safety assessment.</p>
<p>B. Comments on whether the Information Checklist (paragraph 12 and Annex I of the public consultation document) is suitable for determining if a GEd crop is equivalent to a conventionally bred crop</p>	<p>SFA's response</p>
<p>1. On Question 3(b) (<i>Indicate if the GEd crop has any food safety hazards that are new or at increased levels compared to the conventional counterpart.</i>), two respondents stated that it is a safety assessment question and suggested to remove it.</p>	<p>SFA would like to highlight that all food businesses have a continuing responsibility to ensure the safety of their food products sold or offered to the public. This includes developers of new crop varieties that have been obtained through genome editing. Therefore, for GEd crops where there is a scientific basis to investigate if new food safety hazards could be introduced or existing hazards could be produced at increased levels, SFA expects developers to have already analysed these hazards as part of their product development process. For example, a tomato variety that has undergone genome editing to increase its plant sterol levels should also be analysed for potentially increased levels of toxic glycoalkaloids, such as tomatine. This is because plant sterols and glycoalkaloids share a similar biosynthesis pathway.</p>

	<p>On the other hand, for GEd crops where there is no scientific basis to identify and conduct analysis on hazards that are new or at increased levels, there will not be a need to conduct hazard analysis. For example, a GEd tomato variety that has a disease susceptibility gene inactivated is unlikely to produce new or increased levels of food safety hazards if the gene is not involved in biosynthesis of components that are food safety hazards.</p> <p>Due to the complexities of plant biology, SFA understands that for some GEd crop varieties, developers may have uncertainties on whether these varieties could have new food safety hazards or increased production of existing hazards. In such cases, developers may consider discussing further with SFA on their specific products.</p> <p>SFA will amend Question 3(b) as follows: <i>Is there a scientific basis to identify and analyse any food safety hazard(s) that is/are new or at increased levels in the GEd crop compared to the conventional counterpart? If so, please provide results of analysis.</i></p>
<p>2. On Question 4(c) (<i>Provide a description of the intended effect(s) resulting from the genome editing process on the crop</i>), one respondent suggested to amend to “<i>Provide a description of the obtained changes (trait or phenotype) resulting from the genome editing process on the crop</i>”</p>	<p>SFA agrees that the description of the obtained effect is a more relevant question as it can be demonstrated. SFA will amend Question 4(c) to:</p> <p><i>Provide a description of the obtained phenotypic traits resulting from the genome editing process on the crop.</i></p> <p>By the same reasoning, SFA will also update Question 4(h) to:</p>

	<p><i>Provide a summary of how the [removed: intended] phenotypic trait(s) in the final GEd crop was/were verified.</i></p>
<p>3. On Questions 4(e) and 4(f) (<i>Provide a summary of the measures taken to minimise the probability of off-target genetic alterations during the genome editing process and 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</i>), two respondents suggested to remove both questions, with the reason stated being that off-target mutations can also occur in conventional breeding.</p>	<p>SFA has reviewed the comment and notes that conventional crop breeding routinely introduces off-target DNA alterations. SFA also notes that while there are existing scientific tools and genome editing protocols to reduce the probability of off-target alterations, it is not possible for current genome editing tools to have zero probability of off-target DNA alterations.</p> <p>Off-target DNA alterations can either have no impact or negatively impact the resulting crop's characteristics. For conventional breeding, SFA is aware that developers routinely identify crops with undesirable characteristics and eliminate them from further development. Therefore, SFA anticipates that developers who utilise genome editing will likewise identify and eliminate crops with undesirable characteristics as part of the crop development process.</p> <p>Based on the above considerations, SFA will remove Questions 4(e) and 4(f). In the guidance document to the industry, SFA will include references to scientific tools and protocols that help to minimise off-target edits.</p>
<p>4. On Question 4(g) (<i>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</i></p>	<p>SFA notes that genomic Southern blotting is routinely used to demonstrate the presence / stability / absence of target DNA in plants. SFA is aware that whole genome sequencing is increasingly being used to analyse genomic DNA in GM and GEd crop development. However, smaller crop</p>

<p><i>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), one respondent stated that genomic Southern blotting may be too insensitive and suggested that SFA require whole genome sequencing data for this question.</i></p>	<p>developers may not be able to utilise this technology. Furthermore, the use of whole genome sequencing for genomic DNA analysis for a crop first requires a reference genome, which may not always be publicly available. Therefore, as long as the evidence provided is based on prevailing standard molecular biology methodologies, SFA will not prescribe a specific methodology.</p>
<p>5. On Question 4(i) (<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</i>), two respondents stated that this is not asked for conventionally bred crops and suggested to remove it.</p>	<p>SFA expects crop developers to have already conducted studies to ascertain that desired phenotypic traits are stably inherited as part of their crop development process, as this helps to ensure that food and feed products sold are consistent in terms of their characteristics. Therefore, SFA will retain Question 4(i).</p>
<p>6. On Question 4(j) (<i>Indicate if the GEd crop could have plausibly been generated using conventional breeding methods. Provide substantiating scientific evidence or reasoning where relevant</i>), one respondent stated that this question is unnecessary as the achievability of a given GEd crop through conventional breeding is already embedded in the definition of “foreign DNA”</p>	<p>SFA has reviewed the comment and agrees that Question 4(j) is not necessary in view of the revised definition of “foreign DNA” and will remove it.</p>
<p>7. On Question 4(k), (<i>Indicate if the genetic alterations in the GEd crop</i></p>	<p>SFA has reviewed the comment and notes that if a GEd crop does not have foreign DNA, it would not be possible for</p>

<p><i>could potentially be transferred to another organism that is unable to reproduce with said food crop via conventional breeding techniques)</i> four respondents stated that the question is not relevant as it is not asked for conventionally bred crops.</p>	<p>said crop to transfer foreign DNA to other organisms. SFA also notes that Questions 4(a) – (d), as well as Questions 4(g) – (i), already serve to verify if the GEd crop contains foreign DNA. Therefore, SFA will remove Question 4(k).</p>
<p>C. Comments on whether 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)</p>	<p>SFA’s response</p>
<p>1. All crop developers / associations representing crop developers who responded stated that they do not have concerns.</p>	<p>SFA appreciates the commitment to transparency from the industry. Upon implementation of the Regulatory Framework for the Use of GEd crops for Food and Animal Feed, SFA will publish GEd crops that have completed either Pathway A or B on SFA’s website.</p> <p><i>Note: SFA already publishes the List of Approved GM Crops for Use as Food / Feed on SFA’s website.</i></p>
<p>D. Other comments</p>	<p>SFA’s response</p>
<p>1. Two respondents asked for a prescribed timeline and process for Notifications under Pathway A.</p>	<p>SFA will make known the timeline and detailed process for Notifications under Pathway A in SFA’s Guidance Document on GEd crops, which will be published on SFA’s website.</p>
<p>2. Two respondents asked for establishment of regulatory guidelines on GEd crops with Plant Incorporated Protectants (PIPs).</p> <p><i>Background info:</i> PIPs are substances produced by plants that confer pesticide or herbicide resistant traits. PIPs could be naturally</p>	<p>SFA notes the call for regulatory guidelines on GEd crops with PIPs. However, regulatory guidelines on PIPs relate to their potential impact on biodiversity from their cultivation, which is outside of the scope of the Regulatory Framework for the Use of GEd crops for Food and Animal Feed. Nonetheless, should there be a need, SFA will work</p>

<p>produced by plants or introduced via genetic engineering.</p>	<p>with Singapore’s Genetic Modification Advisory Committee (GMAC) and relevant regulatory agencies to develop such guidelines.</p>
<p>3. One respondent sought clarification on whether mutagenesis using cosmic rays and proton beams will be considered as mutagenesis via ionising radiation, which is a conventional breeding technique.</p>	<p>SFA will consider new modalities in mutagenesis via ionising radiation, such as using cosmic rays (also termed “space breeding”) and proton beams to be conventional breeding techniques. This is because the nature of mutagenesis (using high energy particles / radiation to induce DNA mutations) is the same.</p>