Health Canada Santé Canada

Canada

Consultation Document:

Proposed Health Canada Guidance on the pre-market assessment of foods derived from Retransformants under of Division 28 of Part B of the *Food and Drug Regulations* (the *Novel Food Regulations*)

March 2021

The goal of this public consultation is to obtain the views/perspectives of those for whom the new guidance is intended, including plant developers and the general public at large.

The final guidance will be published by the end of August 2021.

YOUR HEALTH AND SAFETY... OUR PRIORITY.

1. Introduction

Since the *Novel Food Regulations* were enacted in 1999, Health Canada has evaluated the safety of foods derived from over 140 genetically modified[1] (GM) plant varieties. In all cases, foods derived from these GM plant varieties were found to be safe for food use. As a result, there are some characteristics that Health Canada has assessed multiple times and have continually been determined not to pose a food safety concern. This extensive experience has allowed regulators to develop a substantial degree of familiarity with these characteristics.

In addition, Canadian regulators have reviewed the scientific literature regarding the types of genetic changes that can occur as a result of inserting DNA into a plant's genome (collectively referred to as insertional effects) (Schnell et al., 2015). This review concluded that the unintended genetic changes that may result from the insertion of DNA into a plant's genome are no different from those that can occur through conventional plant breeding or as a result of plant-environment interactions. These unintended effects are accounted for in the practices used by plant developers[2]. Developers produce thousands of plants containing the same inserted DNA and, through analysis, select the ideal plant (i.e., no unintended effects observed).

Furthermore, developers often then breed multiple generations of the ideal plant to ensure that, with the exception of the inserted DNA, the plant's genome is as similar to its unmodified counterpart as possible. Consequently, the potential for unintended effects of interest are those related to what is encoded and expressed from the inserted DNA itself. In cases where a new plant variety has been developed through the insertion of a DNA sequence identical to another previously assessed GM plant, the potential unintended effects that could occur are either controlled through breeding practices or have been considered as part of the assessment of the previous GM plant for which the DNA insert is identical.

On this basis, Health Canada has developed a tiered approach to the information requirements novel foods derived from GM plants that are identical to previously assessed GM plants. These products are commonly referred to as 'retransformants' as the plants have been transformed with the identical sequence of DNA to introduce the same characteristic(s) in the new plant variety. The information requirements are tiered in a way that is commensurate with the level of risk associated with these plant-derived food products while maintaining the safety of Canadians. Furthermore, the pre-market safety assessment of eligible retransformants will be conducted under an expedited service standard. The following sections explain the tiers and associated criteria, the information requirements and the service standard for the pre-market safety assessment of retransformants.

Health Canada will continue to conduct pre-market safety assessments with a regular service standard (i.e., 410 calendar days) for those products that are novel and unlike any previously assessed novel food.

[1] As defined in Section B.28.001 of the *FDRs*, "genetically modify" means to change the heritable traits of a plant, animal or microorganism by means of intentional manipulation.
[2] For the purpose of this document, the term 'developer' is used as an umbrella term that represents all parties involved in the development of a new plant variety from concept to commercialisation.

2. Assessment Tiers and Criteria

The following tiers of products will be used to determine the pre-market assessment requirements for retransformants identical to previously assessed GM plants:

Tier 1 products are those with identical genetic modifications using the same modification methods in a plant species that results in the same characteristics including the mode of action as a previously assessed GM plant of the same species or closely related species (e.g., *Brassica napus* and *Brassica juncea*).

An example of a Tier 1 product would be a new canola variety that is herbicide tolerant due to the expression of a phosphinothricin acetyltransferase (PAT) protein which is encoded by a bacterial gene inserted into the plant genome using agrobacterium-mediated transformation. In this case, Health Canada has previously assessed a canola variety that contains the identical bacterial gene that was also introduced using agrobacterium-mediated transformation.

Tier 2 products are those with identical genetic modification using different modification methods in a plant species that results in the same characteristics including mode of action as a previously assessed GM plant of the same or closely related species.

An example of a Tier 2 product would be new canola variety that is herbicide tolerant due to the expression of a phosphinothricin acetyltransferase (PAT) protein which is encoded by a bacterial gene inserted into the plant genome using a gene editing technology (e.g., CRISPR Cas9). In this case, Health Canada has previously assessed a canola variety that contains the identical bacterial gene that was introduced using agrobacterium-mediated transformation.

For Tier 1 and 2 products, the following criteria must be met in order to be eligible for a pre-market safety assessment with an expedited service standard:

- There is more than one entry for the specific plant (species) with the specific characteristic found on *Health Canada's List of Completed Assessments for Novel Foods*; and
- The characteristic was achieved through the identical (Tier 1) or through a different (Tier 2) method, functions with the same mode of action, and it results in the same measurable phenotype.

Developers can demonstrate that a product meets the Tier 1 or Tier 2 criteria by presenting a scientific rationale, and supplying a comparison between their new product and a previously assessed GM plant in relation to the above criteria, as well as providing information that establishes that the introduced modification(s) is/are functioning as intended and identical to the previously assessed GM plant.

Health Canada will confirm that the criteria are met as part of the initial screening phase of the pre-market safety assessment. The petitioner will be notified in writing of any product that

Health Canada deems ineligible for the pre-market safety assessment process with an expedited service standard.

To conduct the pre-market safety assessment in the allotted time, incomplete submission packages and/or ineligible products will not be accepted. In these cases, petitioners will be informed of the reason why their submission package is incomplete and/or their plant is ineligible (and requires a pre-market assessment with a regular service standard). The submission will be closed without prejudice to resubmission.

Plants developed through the conventional breeding of previously assessed GM plants are not considered to be novel foods unless a new characteristic (i.e., a characteristic that neither GM plant already exhibits) was introduced into the new plant variety as a result of the breeding cross. These types of plants are referred to as breeding stacks and are not subject to a pre-market safety assessment.

3. Pre-market safety assessment with an expedited service standard of Food Products Derived from Retransformants of Previously Assessed GM Plants

Those products that undergo the pre-market assessment process with an expedited service standard will be published on the *List of Completed Assessments for Novel Foods* and the subject food products that were notified to Health Canada will only be permitted for sale when a written confirmation is provided by Health Canada.

3.1 Service standard for novel foods derived from retransformants

The pre-market safety assessment of products that meet the criteria above will be completed within 120 calendar days of receipt of the complete submission package by Health Canada.

During the pre-market safety assessment with an expedited service standard, if additional clarification and/or information is required by Health Canada, a request will be made to the petitioner of the submission. An additional 45 calendar days will be added to the service standard to accommodate time for the petitioner to respond to the request. Should the information provided by the petitioner be insufficient to complete the assessment, the submission will be closed without prejudice to resubmit.

Health Canada encourages petitioners to make use of the pre-submission consultation process. Pre-submission consultations can assist with seeking clarity on the information requirements and improve the predictability of the assessment process and the overall quality of a submission package. For more information regarding pre-submission consultations, please refer to *The Food Directorate's Pre-Market Submission Management Process for Food Additives, Infant Formulas and Novel Foods*.

3.2 Information Requirements for novel foods derived from retransformants

The pre-market safety assessment of Tier 1 and Tier 2 food products derived from plants identical to previously assessed GM plants will be as follows:

For Tier 1 products, the developer will be required to provide the following:

- A scientific rationale that demonstrates their product meets the criteria for tiered assessment, including a description of the characteristic regarding its mode of action and the lack of any substantial differences in the functionality of the novel substance or lack thereof to the novel substance in the previously assessed GM plant;
- Information to demonstrate that the plant in question has undergone a molecular characterisation, has the identical genetic modification, and was introduced with the identical method of modification as the previously approved plant;
- Information to demonstrate that the compositional analysis of the GM plant in question is comparable to the previously assessed GM plant;
- Information to demonstrate that the Tier 1 plants are not intended to be used in a way to produce food that differs, in terms of food safety, from the food products derived from the previously assessed GM plant; and
- The above-mentioned characterisations and analyses which support any rationale and the above-stated information should be available for review by Health Canada if needed.

For Tier 2 Products, the developer will be required to provide the following:

- A scientific rationale that demonstrates their product meets the criteria for tiered assessment, including a description of the characteristic regarding its mode of action and the lack of any substantial differences in the functionality of the novel substance or lack thereof to the novel substance in the previously assessed GM plant of the same species;
- Characterization of the Derived Line demonstrating the identical genetic modification as per section 4.1.3.1 and 4.1.3.2 of the *Guidelines for the Safety Assessment of Novel Foods*;
- Information to demonstrate the lack of substantial differences between the Tier 2 product and the previously assessed GM plant caused by the use of a different modification technique;
- Information to demonstrate that the compositional analysis of the plant in question is comparable to the previously assessed GM plant;
- Information to demonstrate that the Tier 2 plants are not intended to be used in a way to produce food that differs, in terms of food safety, from the previously approved GM plant; and
- In cases where an intentional change to the uptake of chemicals is made (e.g., a plant with improved nutrient uptake), a chemical analysis is required.

3.3 Outcome

Like all novel foods that undergo a pre-market safety assessment, the positive outcome for the pre-market safety assessment of an eligible retransformant with an expedited service standard will include the issuance of a Letter of No Objection to the petitioner. Furthermore, technical and summary documents that describe the assessed plant will be published as part of Health Canada's list of *Completed safety assessments of novel foods including genetically modified (GM) foods*.

If the proposed use of the novel food is not acceptable, the decision and its basis will be communicated to the applicant as early in the process as possible and the submission will be closed. A new submission that addresses the reason(s) the submission was closed can then be filed with the SMIU, without prejudice, at which time it will be processed as a new submission.

Reference

Schnell, J., Steele, M., Bean, J., Neuspiel, M., Girard, C., Dormann, N., ... & Macdonald, P. (2015). A comparative analysis of insertional effects in genetically engineered plants: considerations for pre-market assessments. Transgenic research, 24(1), 1-17.