Government of Canada
Canadian Food Inspection Agency

Canada

Directive 94-08 (Dir94-08)

Assessment Criteria for Determining Environmental Safety of Plants With Novel Traits

This document updates Directive 94-08 (Dir94-08), "*Assessment Criteria for Determining Environmental Safety of Plants with Novel Traits*."
The original Dir94-08 was first published December 16, 1994 and revised September 15, 2000.

(***publié aussi en français***) **October 2004**

This document is published by the Plant Biosafety Office. For further information, please contact:

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Table of Contents

1. Introduction

Directive 94-08, entitled "Assessment Criteria for Determining Environmental Safety of Plant with Novel Traits", has been prepared to provide guidance regarding the submission of an application for the authorization of the unconfined release of a plant with a novel trait (PNT) in Canada, as may be required under *Part V* of the *Seed Regulations*. Due to the broad range of PNTs that may be developed and submitted for approval in Canada , the information provided in these guidelines should not be considered as exhaustive and will be updated as appropriate to reflect current scientific knowledge and acquired field experience. For further clarification, applicants are strongly recommended to consult with the Canadian Food Inspection Agency's Plant Biosafety Office. For all purposes of interpreting and applying the law, applicants are invited to consult the official versions of the relevant Acts and Regulations.

The scope of this Directive covers all plants (excluding aquatic plants) containing a novel trait that has been intentionally selected, created, or introduced into a distinct, stable population of the cultivated plant species through a specific genetic change, including agricultural and horticultural crop plants and forest trees.

The purpose of this Directive is to (i) provide guidance on what constitutes a PNT, (ii) define the criteria and information relevant to an environmental safety assessment of a PNT under consideration for release and (iii) describe the steps leading to the unconfined release of a PNT. This includes identification of potential concerns, relevant information, and procedures to assess potential environmental effects associated with the unconfined release of PNTs. It should be noted that the definitions provided in Appendix 1 have been adapted from multiple sources to reflect the context of this Directive.

The Plant Biosafety Office (PBO) of the Canadian Food Inspection Agency (CFIA) is responsible for the administration of regulatory provisions regarding notification and authorization of the release of plants with novel traits (PNTs) into the Canadian environment.

By definition:

A PNT is a plant containing a trait not present in plants of the same species already existing as stable, cultivated populations in Canada, or is present at a level significantly outside the range of that trait in stable, cultivated populations of that plant species in Canada. All PNTs are subject to an environmental safety assessment.

Substantial equivalence is used in the comparative assessment of a PNT relative to its counterpart to assess its relative and acceptable risk:

i) A PNT that is substantially equivalent, in terms of its specific use and safety for the environment, as well as for human and animal health, to plants currently cultivated in Canada, having regards to its potential changes in weediness/invasiveness, gene flow, plant pest properties, impacts on other organisms and impact on biodiversity, should pose no greater risk to the Canadian environment compared with its counterpart. A plant that is substantially equivalent to its counterpart and is derived from seed authorized for unconfined release may be

exempted from the notification and authorization requirements under the *Seeds Regulations*.

ii) A PNT that is not substantially equivalent, in terms of its specific use and safety for the environment as well as for human and animal health, to plants currently cultivated in Canada, having regards to their potential changes in weediness/invasiveness, gene flow, plant pest properties, impacts on other organisms and impact on biodiversity, may be authorized for release into the Canadian environment with appropriate environmental risk management and risk mitigation measures.

Before a PNT can be released into the environment, a determination of the associated risk to the environment, including to human health, is required.

The PBO is responsible for the authorization of release, whether it is confined or unconfined, of PNTs into the Canadian environment. The confined release, which may be considered to be a release for research purposes, involves imposing conditions such as reproductive isolation as well as restrictions on the use of harvested material and the field plot in subsequent growing seasons. Information relevant for the purpose of submitting an application for an authorization of confined research field trials is detailed in Directive 2000-07 (Dir2000-07), entitled "Directive for the Environmental Release of Plants with Novel Traits Within Confined Research Field Trials in Canada."

An unconfined release involves the release of a PNT into the environment with no restrictions, with a view towards commercialization. In general, a PNT will proceed from the research stage in a laboratory, growth chamber or greenhouse, to a confined field trial-based environmental release, and finally, to an unconfined release. Information gathered over several years regarding the agronomic/silvicultural and environmental characteristics of the PNT during its confined release stage will generally contribute to a developer's determination as to whether or not to proceed to the next stage of development, which is the unconfined environmental release. Particular PNTs, such as those intended for the production of pharmaceutical or industrial compounds, may be required to grow under conditions that provide for physical and reproductive confinement, even during its commercialization.

2. Regulatory Scope

2.1 Determination of Novelty

Prior to the introduction of a new plant into the Canadian market, it is necessary to consider whether or not it would be classified as novel under the provisions of the *Feeds Act*, the *Food and Drugs Act*, the *Seeds Act*, as well as under the provisions of the respective regulations of these Acts.

A new variety of a species is subject to the notification and authorization requirements of the *Seeds Regulations* when it possesses trait(s) novel to that species in Canada, i.e.,

i) the new trait is not present in stable, cultivated populations of the plant species in Canada, or

ii) the trait in the plant species is present at a level significantly outside the range of that trait in stable, cultivated populations of that plant species in Canada.

Canada has a product-based regulatory system for plants with novel traits. It is the presence of a novel trait in a plant, **irrespective of the method used to introduce it**, which will trigger the notification and authorization requirements under the *Seeds Regulations*. PNTs may be developed through mutagenesis, somaclonal variation, intra-specific and inter-specific crosses, protoplast fusion, recombinant DNA technology, or other techniques.

Conventional breeding may produce a plant with a novel trait requiring notification and authorization of its release, depending on the selected trait's level of expression in comparison with similar existing traits present in stable, cultivated populations of the plant species in Canada. For example, an increase in yield in a new wheat line, similar to increases seen historically in wheat lines cultivated in Canada, may not be considered to be a PNT. However, a new sclerotinia resistant canola line exhibiting a resistance many folds higher than that currently grown in Canada would likely be considered a PNT. The introduction of a trait from wild biotypes or from germplasm originating outside of Canada, is more likely to produce a PNT than conventional breeding with germplasm already in use in the Canadian environment.

It is the responsibility of proponents (e.g., plant breeders, product developers, etc.) based both on their expertise and relevant scientific literature reviews, to determine the range of the selected trait in cultivated populations of the plant species in Canada. i.e. it is the proponent's responsibility to determine if they have produced a PNT. Thus, the PNT status of a new plant variety is determined on **a case-by-case basis**. The requirement for notification and authorization under the *Seeds Regulations* is triggered by the presence of a novel trait in a plant. Certain information detailed in this directive may be waived by the CFIA if it determines, based on valid, scientific rationale (supported by appropriate data and/or literature references) submitted by the proponent, that the information in question is not relevant to a particular PNT's environmental safety assessment, and as such, is not required for the CFIA's decision as to whether or not to authorize the environmental release of the PNT.

When a proponent contacts the PBO, CFIA, the Feed Section, CFIA, and/or the Novel Foods Section, regarding the determination of their plant's novelty status, as well as the novelty status of food and feed products derived therefrom, a meeting may be organized among all three groups to review the case to analyze the factors contributing to its status and to provide guidance to the proponent on applicable requirements.

Where a plant variety has been determined by the proponent to be a PNT, the food and feed products derived therefrom will usually be considered to be novel as well. However, in some cases, a plant variety will be determined not to be a PNT, but the food and feed products derived therefrom will be considered as novel. In other instances, a plant will be considered to be a PNT, but the food and feed products derived therefrom will not considered novel because of their history of safe use in the marketplace. In order to respond to a proponent's request for guidance on the novelty of their plant product, additional information may be required necessary in order to reach a decision.

2.2 Intra-specific Crosses

Once a PNT is authorized for unconfined release, all its progeny and sister lines which have been derived from the original transformation and their respective progenies, are also authorized for unconfined release provided that the proponent has determined that:

- no inter-specific crosses are performed;
- the intended uses are similar;
- based on characterization, these plants do not display any additional novel traits and are substantially equivalent, in terms of their specific use and safety for the environment and for human and animal health, to plants currently being cultivated; and
- the novel genes are expressed at a level similar to that of the authorized line.

The CFIA may ask the proponent to provide scientific evidence supporting these conclusions.

2.3 Inter-specific Crosses

Once a plant is authorized for unconfined release, an environmental safety assessment of the plant created from the first interspecific cross may be necessary. Subsequent to an unconfined release authorization for an interspecific cross, the proponent may not need to apply for unconfined release authorization of further lines, provided that the proponent has determined:

- there is no new transformation event;
- the intended uses are similar;
- based on characterization, these plants do not display any additional novel traits and are substantially equivalent, in terms of their specific use and safety for the environment and for human and animal health, to plants currently being cultivated; and
- the novel genes are expressed at a level similar to that of the authorized line.

The CFIA may ask the proponent to provide scientific evidence supporting these conclusions.

2.4 Intentional Trait Stacking

Proponents are asked to advise the PBO at least 60 days prior to the anticipated environmental release of plants having stacked traits and resulting from either intentional intra-specific or inter-specific crosses between PNTs already authorized for unconfined environmental release. Following notification, the PBO may issue a letter (within 60 days of notification) informing the proponent of any concerns the it may have regarding the unconfined environmental release. The PBO may request and review data to support the safe use of the modified plant in the environment. Stacking of traits with potential incompatible management requirements, possible negative synergistic effects, or where production of the plant may be extended to a new area of the country, may elicit an environmental safety assessment. Until all environmental safety concerns have been resolved, the modified plant should not be released in the environment.

2.5 Re-transformation and Re-mutation

A re-transformation/re-mutation, i.e.,

- transformation of a plant, with the identical construct(s) as a previously authorized plant of the same species
- mutation of the same gene in a plant as a previously authorized plant of the same species

which conveys the same novel trait to a plant as a transformation/mutation in a previously authorized plant may not trigger the notification and authorization requirements under the *Seed Regulations*, provided that:

- the method is identical to that used previously;
- the intended uses are similar;
- it is known based on characterization, that the plant does not display any additional novel traits and is substantially equivalent, in terms its specific use and safety for the environment and for human and animal health, to plants currently cultivated; and
- the novel genes are expressed at similar levels as that of the authorized line.

The PBO may ask the proponent to provide scientific evidence supporting these conclusions. For further guidance, consultation with the PBO, CFIA, the Feed Section, CFIA, and the Novel Food Section, Health Canada, is recommended.

3. Completion of an Application for Authorization of Environmental Release of PNTs

Proponents are encouraged to consult with the PBO in the early stages of development of their new plant variety in order to receive guidance regarding the determination of their plant variety's novelty status and, where appropriate, for clarification on what specific information is necessary for the PNT's environmental safety assessment. Applications that are complete and of acceptable quality and legibility will allow for timely assessments with a minimum of correspondence requesting further information.

3.1 Where to Apply

Please address your application for unconfined environmental release authorization of a PNT to:

Plant Biosafety Office
Plant Products Directorate
Canadian Food Inspection Agency
59 Camelot Drive
Ottawa, Ontario
K1A 0Y9

Telephone: (613) 225-2342

3.2 When to Apply

The developer of a PNT is strongly encouraged to apply for unconfined environmental release authorization well in advance of the anticipated time of commercialization. Applications for authorization will be processed on a **first-come-first-served basis**. Degree of completeness of

the application will also be a factor in the length of the review period required.

3.3 How to Apply and Number of Copies Requested

Applicants are asked to send a covering letter along with their application, summarizing their request for an unconfined environmental release authorization for their plant product and an explanation as to why their new variety is subject to regulatory oversight. A description of the plant species, the novel traits, and the potential geographic scope of the release should be included in this summary. Two copies of the application should be submitted to the PBO for review.

3.4 Information Considered to be Confidential

Information submitted to the PBO for the purposes of obtaining an authorization for the environmental release of a PNT may be protected under the federal *Access to Information Act*, Section 20.

All requests for such information are subject to the federal *Access to Information* and *Privacy Acts* . Please consult with CFIA's ATIP service, at (613) 225-2342, for further information.

3.5 Fees

The application fee should be included with the application for the review to be initiated. Please see Appendix 2 for a schedule of fees for the review of applications and authorization for the environmental release of PNTs. Once review of an application has been initiated, the application fee will not be refunded. Please make cheques payable to the Receiver General of Canada.

3.6 Submission to Feed Section and Health Canada

The Feed Section, CFIA, is responsible for the administration of regulatory provisions with respect to the authorization of the release of novel feeds. The Novel Foods Section, Health Canada, is responsible for the administration of regulatory provisions with respect to the authorization of the release of novel foods intended for human consumption. The unconfined environmental release of a PNT in Canada intended for feed and/or food use, or that could reasonably be expected to be used as feed or food, may require:

- a determination of environmental safety by the PBO (CFIA),
- a determination of product safety as a novel livestock feed by the Feed Section (CFIA), and
- a determination of product safety as a novel food by the Novel Foods Section (Health Canada).

Please note that it is **the responsibility of the applicant** to contact these offices.

Where registration of a pest control product is mandatory, it is the applicant's responsibility to

meet all the requirements of the *Pest Control Products Act*, an act which is administered by Health Canada's Pest Management Regulatory Agency (PMRA). PMRA is the federal agency responsible for conducting the appropriate risk and value assessments of pest control products in Canada. Applicants may wish to refer to the *Registration Handbook for Pest Control Products* as a detailed reference for the registration process.

3.7 Submissions to U.S. Authorities

Applicants seeking authorization for the unconfined environmental release in Canada of plants that may be regulated in the United States are encouraged to seek authorization for the environmental release of their product in the United States simultaneously. Obtaining such authorizations may minimize the movement of unauthorized material across the border of a product released in one country but whose release is not authorized in the other. It is recommended that applicants advise the CFIA of any notification to foreign governments of the intended unconfined environmental release within their respective foreign borders of a PNT under review in Canada. Where appropriate, the CFIA may try to coordinate its activities and work with foreign governments to minimize the presence of unauthorized products in each country's respective environment.

4. Legal Authorities

For the regulation of PNTs in confined research field trials and unconfined release:

The Seeds Act, R.S., c. S-8
The Seeds Regulations, C.R.C., c. 1400, Part V

For the importation of plant materials, including PNTs:

The Plant Protection Act, S.C. 1990, c.22
The Plant Protection Regulations, SOR/95-212

For the collection of fees:

Canadian Food Inspection Agency Fees Notice, Canada Gazette, Part 1 (05/13/2000)

5. Exemptions

A seed (which covers plants under the *Seeds Act*) is not subject to *Part V* of the *Seeds Regulations* if one of the following applies:

i) the seed was grown in Canada outside of containment before the coming into force of *Part V* of the *Seeds Regulations* (i.e., prior to December 1996),

ii) the seed is derived from seed referred to in paragraph i), or from seed in respect of which an unconfined release has been already authorized, or

iii) the seed is grown in containment in such manner that there is no release into the environment of any genetic materials from the plants derived from the seed.

6. Environmental Safety Assessment of Plants with Novel Traits

6.1 Environmental Safety Assessment Criteria

The PBO assesses the environmental safety of PNTs based on the five criteria:

- potential of the PNT to become a weed of agriculture or be invasive of natural habitats,
- potential for gene-flow to wild relatives whose hybrid offspring may become more weedy or more invasive,
- potential for the PNT to become a plant pest,
- potential impact of the PNT or its gene products on non-target species, including humans,
- potential impact on biodiversity.

6.2 Environmental Safety Assessment

The PBO performs environmental safety assessments of PNTs based on the five criteria listed above, primarily using two sets of information. The first set is a companion biology document, which provides baseline information for the plant species of the PNT under review (Please see Section 7.2 for details).

The second set of information is submitted by the applicant as part of a complete application for the unconfined release authorization of the PNT is question and consists of appropriate data and relevant scientific information describing the environmental risk of the PNT relative to its counterpart(s) already present in the Canadian environment (Please see Section 7, entitled "Authorization for Environmental Release of a PNT"). This data should be collected through testing and analysis, and during confined research field trials conducted either in Canada (Please refer to Dir2000-07 for further details), or in foreign environments similar to that of Canada's. Based on the information provided in the biology document, field experiments can be carefully designed to generate data demonstrating the agronomic/silvicultural and environmental characteristics of the PNT relative to its counterpart.

The PBO may also use other peer-reviewed scientific literature, as appropriate, to guide their safety assessments.

6.3 Consultation with Experts

During its evaluation of an application for the authorization of the environmental release of a PNT, the PBO may consult relevant scientific experts on specific issues with regards to the environmental safety of a PNT. For example, the PBO may solicit the scientific expertise of Health Canada' PMRA with respect to the environmental safety of a PNT expressing altered pesticidal tolerance or altered pesticidal properties. Information considered as confidential business information (CBI) will not be shared without prior written authorization from the

applicant. Solicited advice, given by either PMRA or other consulted scientific experts, will be considered by the PBO in the final evaluation of the PNT for unconfined environmental release.

7. Authorization of Environmental Release of a PNT

7.1 Specific Information

To enable the PBO to assess the environmental safety of a PNT, the applicant must address the following issues:

- **the identity and origin of the PNT;**
- **the properties of the novel gene and gene products;**
- **the relative phenotypic expression of the PNT compared to a similar counterpart, where differences are anticipated; and,**
- **anticipated or known relative effects on the environment resulting from the release.**

The specific information relevant for the purposes of conducting environmental safety assessments can be found in Appendix 3, entitled "Relevant Information Regarding the PNT", and Appendix 4, entitled " Information on the Biology and Interactions of the PNT". Specific information will vary with the species, characteristics of the novel trait, and the PNT's end use. All other supporting information and test data that are relevant to environmental and human health exposure and hazard identification, and which are in the applicant's possession or to which the applicant should reasonably have access to, must be included in the application. For further guidance, the applicant is encouraged to consult with the PBO.

In addition to data generated by the applicant through research and testing in laboratory, growth chamber, and/or greenhouse, as well as during confined research field trials, further information can also be submitted in an application based on available scientific literature and any other recent research. The PBO may also refer to data generated from CFIA's own research on specific key environmental areas.

The PBO may decide to waive the requirement for certain information if it determines, based on written scientific rationale submitted by the applicant, that the information is not relevant to a particular PNT's environmental safety assessment, and as such, is not required for the PBO's decision as to whether or not to authorize the environmental release of the PNT.

7.2 Biology Documents of the Plant Species

The biology of certain plant species is described in a series of species-specific biology documents, which are published on the PBO web site at the following address: http://www.inspection.gc.ca/english/plaveg/bio/dir/biodoce.shtml.

These documents describe the characteristics of the plant species in question, such as habitat, fertility, dispersal, and endogenous toxins, as well as include information about the plant species' major interactions with other life forms in its production range in Canada (e.g., predators, grazers, parasites, pathogens, competitors, symbionts and beneficial organisms,

including humans, where appropriate). This information will help identify potential risks associated with a PNT under review relative to its counterpart(s) of the same species already present in the Canadian environment. These documents act as references for comparative data.

Where a biology document is not available for a particular PNT's plant species, one should be provided to the PBO with a proponent's application for unconfined environmental release authorization. Once a biology document is submitted, it will be reviewed by the PBO as well as peer-reviewed. Comments received from the peer review will be incorporated into the biology document as appropriate. Based on comments received from the peer review, an applicant may need to submit further information and test data for the PNT's environmental safety assessment.

The format of the new biology document should follow that of the existing biology documents. The Organisation for Economic Cooperation and Development (OECD) Consensus Documents may be used as a reference tool to help applicants in the preparation of biology documents.

7.3 Quality of Data Submitted

The quality of information in the data package should be equivalent to that provided for peer reviewed publications. Applicants should clearly describe the test procedures followed in developing the test data, including test methods, reference products, quality control, quality assurances procedures, appropriate statistical analysis, together with bibliographic references, including numbered patents, where these are appropriate. The generation of field trial data should be produced using statistically valid experimental designs and protocols. Field trials should be conducted in a manner consistent with the proposed farming practices of the PNT's plant species. The applicant may be asked to submit details of field trial protocols, including experimental designs and sampling procedures.

A guide to the expected quality for some types of submitted analytical data can be found in the reviewer's checklist. This guide has been developed jointly with Health Canada and the United States Department of Agriculture's Animal and Plant Health Inspection Service (USDA-APHIS), and is available at http://www.inspection.gc.ca/english/plaveg/bio/usda/usda04e.shtml.

7.4 Detection and Identification Requirements

Along with all other data, relevant to the environmental safety assessment of a PNT, the following should also be submitted to the CFIA:

- appropriate test methodologies for the detection and identification of PNTs;
- written agreement to provide the CFIA with reference material suitable to support these methods.

Certain information regarding the detection and identification of a PNT, which is provided to the CFIA for the purposes of conducting an environmental safety assessment, may be protected under the provisions of the *Access to Information Act*. All requests for such information are not only subject to the *Access to Information Act* but to the *Privacy Act* as well.

CFIA's criteria regarding acceptable detection and identification methods can be found on the PBO web site at the following address:
http://www.inspection.gc.ca/english/plaveg/bio/detecte.shtml

Consultation with the CFIA is recommended prior to the submission of an application for authorization of environmental release for guidance in the determination of appropriate test methodologies and reference materials.

7.5 Stewardship Plan Requirements

As part of the PBO's assessment of a PNT's environmental safety, in particular, of its assessment of longer term environmental effects, the PBO's decision with regards to authorizing the release of a PNT expressing either a novel herbicide tolerance or a novel insect resistance will take into consideration whether or not the applicant has provided a stewardship plan addressing the need for the responsible deployment of the novel crop into the environment.

Stewardship plans should include appropriate strategies that will allow for the environmentally safe and sustainable deployment of such novel plants (Please see Sections 7.5.1 and 7.5.2 for specific information). In addition, communication to growers and an efficient mechanism allowing growers to report problems to the applicant are all integral parts of a stewardship plan.

7.5.1 Insect Resistance Management (IRM)

The CFIA strongly recommends that an IRM plan be implemented for all plants expressing novel insect resistance (including those expressing *Bacillus thuringiensis* (*Bt)* endotoxins) grown in fields of **greater than one hectare in size**. IRM strategies are intended to delay the development of resistance in the insect to the active compound(s) and thereby prolong the lifespan and usefulness of the technology. The development of resistance in insects to these active novel compounds due to the non-adoption of effective IRM plans could also have significant implications on sustainable agriculture.

The IRM plans currently in place for *Bt* corn and *Bt* potatoes consist of planting refugia, areas of non-*Bt* crops which provide a population of insects which have not been exposed to the *Bt* toxin and are available to breed with potentially resistant insects which could be emerging from the cultivation of a *Bt* crop.

The IRM plan should take into consideration the most recent available scientific evidence on, among other factors, the following:

1) the reproductive biology and behaviour of the insect pest;
2) the mobility of the larvae;
3) the ability of adults to disperse from the natal field before and after mating;
4) an estimate of resistance allele frequency in the insect population;
5) the impact of management practices such as insecticide use in the refuge;
6) the targeted life cycle stage of the insect pest, and;
7) any history of insect resistance to the active compound(s).

The IRM plan submitted in an application for unconfined environmental release authorization is specific to the target insect species and is based on field/laboratory research and computer models.

Communication to growers, the monitoring of the effectiveness of the plan, and an efficient mechanism allowing growers to report problems to the applicant, are all integral parts of an IRM stewardship plan.

7.5.2 Herbicide Tolerance Management (HTM)

The development of an HTM plan is the applicant's responsibility and should contain elements that address:

1) the control of volunteers, more specifically, any changes in usual agronomic practices that may arise from the novel herbicide tolerance and which could result in reduced sustainability or have significant impacts on soil conservation;
2) the selection of herbicide tolerance in weeds resulting from the potential continued-application of the same herbicide in subsequent rotations;
3) the introgression of novel trait into related species;
4) the management of the herbicide tolerant crop during the growing season, particularly where multiple herbicide tolerances, due to cross pollination, could arise in subsequent growing seasons;
5) communication to growers as well as an efficient mechanism allowing growers to report problems to developer;
6) the monitoring of effectiveness of the stewardship plan.

A PNT with a novel herbicide tolerance that could be introgressed to related species, resulting in hybrids that have no effective or sustainable control options, will not be authorized.

The PBO also cooperates with the PMRA on strategies for the safe and effective use of herbicides and herbicide tolerant crops in Canada. Safety issues concerning the application of herbicides on plants expressing novel herbicide tolerance(s) are assessed in collaboration with the PMRA.

7.6 Post-release Monitoring Plan

A general post-release monitoring plan to monitor for unintended or unexpected environmental effects of an authorized product should also be an integral part of a complete application and will be reviewed during the environmental safety assessment of the novel plant in question. The use of appropriate indicators to evaluate these effects should be based on the characteristics of the PNT. A stewardship plan (Please see Section 7.5) may be considered acceptable for post-release monitoring purposes.

The applicant must inform the PBO of any new information regarding the risks to the environment or to human health resulting from worker exposure to the PNT that could result from the unconfined release of the PNT (Please see Section 9 for further details).

8. Decision Process

The PBO will consider the information provided by the applicant to determine if the PNT poses risks to the environment. The PBO may authorize or refuse to authorize the release of a PNT based on its environmental safety assessment.

8.1 Regulatory Decision

Where the proposed release of a PNT poses a **minimal** apparent risk to the environment, the PBO may authorize the unconfined release of the PNT, and may, where necessary, impose conditions for the management of the apparent risk. Conditions will be imposed on an **indeterminate** basis.

Where the proposed release of a PNT has been assessed to pose unacceptable risk to the environment, the PBO may refuse to authorize the unconfined environmental release of the PNT, and will provide reasons for the refusal.

8.2 Harmonization of Approvals under Other Federal Acts and Regulations

A PNT that could reasonably be expected to be used as feed and food, will not be authorized for unconfined environmental release by the PBO, among other requirements, until:

- the Feed Section of the CFIA is ready to authorize the novel feed for livestock feed use under the authority of the *Feeds Act and Regulations*, and/or

- the Novel Foods Section, Health Canada, is ready to provide notification of no objection for human food use under the authority of the *Novel Food Regulations*.

Where products are intended for exclusive use as either food, feed or molecular farming (use of plants to produce industrial or therapeutic products), consultations among regulatory authorities will be required to assess any potential risks associated with the release of the product in an unintended commodity stream. For these products, an identity preservation system or alternative will be essential to minimize the likelihood of such an event.

Please note that once the safety assessments have been completed, the applicant is notified in writing by the CFIA and Health Canada (separate letters) on their respective decisions regarding the application.

8.3 PNTs Carrying Antibiotic Resistance Markers

While the presence of antibiotic resistance marker genes in transgenic plants may not pose a significant environmental risk, developers of transgenic plants are encouraged to consider alternative selection systems. The presence of an antibiotic resistance marker, to which no significant environmental risk has been associated, will not be considered as grounds for denying authorization for the environmental release of the PNT in question.

8.4 Web Site Summaries of PNTs authorized for unconfined release

A list of all authorized PNTs and novel feeds derived therefrom, as well as their accompanying decision documents, is available on the CFIA PBO's web site at the following address: http://www.inspection.gc.ca/english/plaveg/bio/pntvcne.shtml. The PBO will update its list of authorized PNTs and post related decision documents on its web site within 15 days after authorizing a PNT.

A list of approved novel foods in Canada derived from PNTs whose environmental release has been authorized, as well as their accompanying decision documents, is available on Health Canada's web site at the following address:
http://www.hc-sc.gc.ca/food-aliment/mh-dm/ofb-bba/nfi-ani/e_nf_dec.html

The decision documents explain the decision reached by the CFIA's PBO and the Feed Section and Health Canada's Novel Food Section following their safety assessments.

The PBO also submits information on the environmental release of PNTs to the Organization for Economic Cooperation and Development (OECD) publicly available Biotrack database at: http://www.oecd.org/ehs/service.htm and to the Canadian Node of the Biosafety Clearing-House under the Cartagena Protocol on Biosafety (http://www.bch.gc.ca). It is therefore important that CBI be clearly identified.

9. New information related to PNTs authorized for unconfined release

Where, at any time after providing notification of the proposed unconfined release or receiving authorization for the unconfined release of a particular PNT, the applicant becomes aware of any new information regarding the environmental safety of the PNT (e.g., enhanced weediness characteristics), including the risk to human health (e.g., exposure to allergens) that could result from the release, the applicant must immediately provide the PBO with the new information. On the basis of the new information, the PBO will re-evaluate the potential effect on, and risk to the environment, including the potential effect on, and risk to human health posed by the release. The PBO may maintain, change, or remove existing conditions respecting the release; impose additional conditions; or refuse or cancel the authorization and require the applicant to stop the release and take any appropriate action necessary to eliminate from, or minimize the risk to, the environment.

Appendix 1 Definitions

Biodiversity: The variety of life and its processes. Biodiversity includes all life forms, from one-celled fungi, protozoa and bacteria to complex organisms such as plants, insects, fishes and mammals. It includes processes, pathways and cycles that link living organisms into populations, ecosystems and landscapes. This variety of life is dynamic and constantly changing and evolving. It is sensitive to perturbations that may result from human activity. Biodiversity is generally recognized on three levels:

- genetic diversity - the variety of genetic building blocks found among individual representatives of a species;
- species diversity - the variety of living organisms found in a particular place; and
- ecosystem diversity - the variety of species and ecological functions and processes, both their kind and number, that occur in different physical settings.

Biology Document: A CFIA species-specific companion document that describes the biology, related species and interactions with other life forms of the plant.

Carrier DNA: DNA used to expedite the preparation or the transformation of genetic material into a plant but which is itself not part of the construct.

Coding Region: A DNA sequence which can be translated to produce a protein.

Confined Research Field Trials: A confined research field trial is the release of a PNT, for research purposes, under terms and conditions of confinement designed to minimize any impact the PNT may have on the environment. These terms and conditions include, but are not limited to, reproductive isolation, site-monitoring and post-harvest land use restriction. See Regulatory Directive 2000-07.

Construct: An engineered DNA fragment (e.g. plasmid) which contains, but is not limited to, the DNA sequences to be integrated into a target plant's genome.

Counterpart: The chosen counterpart should, if possible, be the host plant already existing as stable, cultivated populations in Canada. In the case of an F1 hybrid, the counterpart must be a similar genotype/phenotype of the same species. Consideration may also be given to the use of several counterparts. Since there will be a range of characteristics among varieties within a species, comparison with several counterparts may show that the PNT has characteristics within the normal range exhibited by that species.

Cultivate: To produce or grow in an agricultural system. For the purpose of this Directive, cultivate also means to produce or grow in a managed system, e.g., a forest plantation.

Database Citations: Publicly accessible sources of nucleotide or protein sequence information. Five commonly used databases and their website addresses are:

GenBank: An annotated collection of all publicly available DNA sequences maintained by the National Institute of Health (NIH).
http://www.ncbi.nlm.nih.gov/Genbank/GenbankOverview.html

DNA Data Bank of Japan: The officially certified DNA bank of Japan, which collects DNA sequences from researchers. http://www.ddbj.nig.ac.jp/fromddbj-e.html

EMBL Nucleotide Sequence: A database of DNA and RNA sequences collected from the scientific literature, patent applications, and directly submitted from researchers and sequencing groups. http://www.ebi.ac.uk/embl/

The SWISS-PROT Protein Sequence Data Bank: A database of protein sequences produced collaboratively by Amos Bairoch (University of Geneva) and the EBI.
http://www.ebi.ac.uk/swissprot/

The FARRP Allergen Database: A database containing a list of unique known and putative allergens that were identified by searching publicly available protein databases.
http://www.allergenonline.com

Please note: The CFIA is not responsible for the accuracy, currency or the reliability or the content of these databases. Please be aware that information from these databases may not be available in both official languages.

Environment: Components of the earth including air, land, water; all layers of the atmosphere; all organic and inorganic matter and living organisms; and all interacting natural systems that include components referred to above *(Canadian Environmental Protection Act, Section 3).* This includes the natural and managed ecosystems which includes agricultural ecosystems.

Environmental Risk: Possibility of causing harm to the environment.

Environmental Safety Assessment: The qualitative and/or quantitative estimation of the likelihood of adverse environmental impacts that may result from the release of the PNT into the environment.

Gene Flow: The transfer of genetic material by interbreeding from one population of a species to another population (same or related species), thereby changing the composition of the gene pool of the receiving population.

Genotype: The sum total of the genes of an organism, latent or expressed.

Insert: That part of a construct (see above) which is integrated into the recipient plant's genome.

Invasive Plant: Any plant that is successful in colonizing natural “un-managed” ecosystems and in the process displaces other species and disrupts those ecosystems.

Irritant: Any agent capable of eliciting an abnormally excited or sensitive condition in a body

part of a human or other animal.

Microfauna: Microscopic animals.

Microflora: Microscopic plants, bacteria and fungi.

Natural Ecosystem: A non-agricultural area not subject to significant human manipulation such as mowing, pesticide application, planting, etc.

Non-coding Region: DNA sequences which lie outside of an open reading frame and which are not translated to become part of a protein. These include scaffold attachment regions, promoters, leader sequences, enhancers, introns, terminators, and any other sequences that are used for gene expression either in the plant or other hosts, such as origins of replication, transposable elements, T-DNA borders, lox sequences, etc.

Non-target Organisms: An organism (including humans) that may be unintentionally affected due to the presence of the PNT in the environment.

OECD Consensus Documents: Reports published by the Organisation for Economic Cooperation and Development (OECD) that contain technical information for use in the regulatory assessment of products of biotechnology (http://www.oecd.org).

Outcrossing: Sexual reproduction involving other individuals of the same or related species.

Outcrossing Frequency: The percentage of total progeny produced by a plant as a result of outcrossing.

Parthenocarpy: Production of fruit without fertilization.

Phenotype: The observable characteristics of an organism (including physical, biochemical or other traits) which may result from the interaction of the organism with its environment.

Plant Pest: Any plant that is injurious or potentially injurious, whether directly or indirectly, to plants or to products or by-products of plants.

Seed: Any plant part of any species belonging to the plant kingdom, represented, sold or used to grow a plant (*Seeds Act*).

Stability: The ability of the trait to be expressed in the modified plant line and plant lines derived therefrom in a consistent, reliable, and predictable manner.

Stable population: A population is deemed stable if its relevant trait remains unchanged throughout the continuous, repeated propagation of the plant species.

Substantial equivalence: The equivalence of a novel trait within a particular plant species, in terms of its specific use and safety to the environment and human health, to those in that same

species, that are in use and generally considered as safe in Canada, based on valid scientific rationale.

Threatened and Endangered Species: Organisms listed as such by Federal authorities: in Canada the *Species At Risk Act* (SARA) is administered by Environment Canada, and endangered species are officially listed by the Committee on the Status of Endangered Wildlife in Canada (COSEWIC) (http://www.cosewic.gc.ca/index.htm); in the U.S. Departments of Interior or Commerce who jointly administer under the authority of the *Federal Endangered Species Act*.

Trait(s): The phenotypic characteristic(s) conferred to the recipient plant by specific genetic changes.

Transgenic Plant: A plant in which one or more genes, genetic constructs, or traits have been introduced using recombinant DNA techniques, including the insertion of genetic material from the same or different species.

Unconfined Release: A release into an environment of a plant with novel trait(s) that is not isolated either reproductively or physically from managed or natural environments, but may be subject to certain conditions .

Vector: An autonomously replicating DNA molecule into which foreign DNA is inserted and then propagated in a host cell.

Weed: A plant species that is a nuisance to humankind in that it occurs in "managed" ecosystems where it is unwanted. Weeds tend to spread easily in disturbed areas or among crops. Whereas it can be considered that any "plant out of place" is a weed, the emphasis of an environmental safety assessment is to determine whether a PNT could be successful in colonizing managed ecosystems at the expense of other species, in particular cultivated crop plants.

Appendix 2 Plant Biosafety Office Fee Schedule

(http://www.inspection.gc.ca/english/plaveg/bio/feepaie.shtml)

Appendix 3 Information Regarding the PNT

1. Personnel involved and status of the PNT in the application

1.1 Applicant:

1) Name
2) Address
3) Telephone Number
4) Facsimile Number

1.2 Canadian representative, if different from above:

1) Name
2) Address
3) Telephone Number
4) Facsimile Number

1.3 Is the plant material imported? If yes, was an import permit applied for under the *Plant Protection Act*? Was it granted? If yes, provide the permit number if known.

1.4 Was the plant material previously tested/grown/released in Canada? If yes, in what years?

1.5 If the PNT was derived through recombinant DNA techniques, were the gene constructs previously tested in Canada? If yes, in what plant species and in what years?

1.6 Were other government agencies, either foreign or within Canada, notified of the development of the PNT or its importation? What was the purpose of such notification?

2. Description of the PNT

2.1 Description of taxonomy

2.2 Designation given to the PNT, including all synonyms

2.3 Pedigree information of the PNT (including any relationship to a previously assessed PNT)

2.4 For transgenic PNTs, provide a unique identifier for each line designated according to the "OECD Guidance for the Designation of a Unique Identifier for Transgenic Plants" (ENV/JM/MONO(2002)7) (http://www.olis.oecd.org/olis/2002doc.nsf/LinkTo/env-jm-mono(2002)7)

2.5 Give details of the use of the PNT (e.g., to be grown as a field crop for grain production; to be grown as field crop for grain production on lands contaminated with persistent herbicide; to reclaim lands contaminated with heavy metals).

3. Description of the modification of the PNT

3.1 Novel gene products conferring the novel traits

3.2 Methods used to introduce the novel traits (briefly describe the techniques, if not through recombinant DNA)

3.3 Identify the objective of the modification, e.g., novel herbicide tolerance, male sterility/restoration, etc.

4. Description of the modification of the PNT through recombinant DNA technology

Please address the information requirements listed in this section if the PNT was derived through recombinant DNA technology.

4.1 Transformation method:

4.1.1 Describe and provide references for the transformation method, e.g. *Agrobacterium*-mediated transformation or direct transformation by methods such as particle bombardment, electroporation, polyethylene glycol transformation of protoplasts, etc.

4.1.2 For direct transformation methods, describe the nature and source of any carrier DNA used.

4.1.3 For *Agrobacterium*-mediated transformation, provide the strain designation of the *Agrobacterium* used during the transformation process, and indicate if tumor-inducing genes were present on the plasmid-based vector, and whether *Agrobacterium* was cleared from the transformed tissue. Briefly describe or provide reference(s) describing the construction of the vector.

4.1.4 For transformation systems other than *Agrobacterium*, provide the following information:

1) Does the system utilize a pathogenic organism or nucleic acid sequences from a pathogen?

2) How were any pathogenesis-related sequences removed prior to transformation?

3) Did the transformation process involve the use of helper plasmids or a mixture of plasmids? If so, describe these in detail.

4.2 Description of the genetic material potentially delivered to the recipient plant material (the modification/constructs):

4.2.1 Provide a summary of all genetic components which comprise the vector including coding regions, and non-coding sequences of known function. Example of a table

describing the DNA components of a vector (from APHIS petition #94-257-01P) is available at http://www.inspection.gc.ca/english/plaveg/bio/usda/usda03e.shtml#table1. For each genetic component provide a citation where these functional sequences were described, isolated, and characterized (publicly available database citations are acceptable) and indicate:

1) The portion and size of the sequence inserted.

2) The location, order, and orientation in the vector.

3) The function in the plant.

4) The source (scientific and common, or trade name, of the donor organism).

5) If the genetic component is responsible for disease or injury to plants or other organisms, and is a known toxicant, allergen, pathogenicity factor, or irritant.

6) If the donor organism is responsible for any disease or injury to plants or other organisms, produces toxicants, allergens or irritants or is related to organisms that do.

7) If there is a history of safe use of the source organism or components thereof.

4.2.2 If there has been a modification in the transgene relative to the native gene that affects the amino acid sequence of the protein designed to be expressed in the plant, provide the citation. If the modified amino acid sequence has not been published, provide the complete deduced sequence highlighting the modifications. Indicate whether the modifications are known or expected to result in changes in post-translational modifications or sites critical to the structure or function of the gene product. An example of such modifications might include the addition of new glycosylation sites.

4.2.3 Provide a detailed map of the vector with the location of sequences described above that is sufficient to be used in the analysis of data supporting the characterization of the DNA, including as appropriate the location of restriction sites and/or primers used for PCR and regions used as probes. Example of a detailed map of a plasmid vector (from APHIS petition #94-257-01P) is available at the following address: *http://www.inspection.gc.ca/english/plaveg/bio/usda/usda03e.shtml#figure*

4.3 Characterization of the DNA inserted in the plant:

4.3.1 For all coding regions, provide data that demonstrate if complete or partial copies are inserted into the plant's genome. Coding regions may include truncated sense constructs, sequences engineered to be nontranslatable, antisense constructs, and constructs containing ribozymes, regardless of whether or not the coding region is designed or expected to be expressed in the transgenic plant. For allopolyploid plants, information may be required indicating into which parental genome insertion has

occurred.

4.3.2 For noncoding regions associated with the expression of coding regions:

1) Data should demonstrate whether or not plant promoters are inserted intact with the coding regions whose expression they are designed to regulate. This data is relevant to consideration of points 4.4.1 and 4.4.2 below.

2) DNA analysis may be necessary for introns, leader sequences, terminators, and enhancers of plant-expressible cassettes. DNA analyses may be presented in the form of Southern analyses, DNA sequencing, PCR analyses, or other appropriate information.

3) DNA analysis may be necessary for promoters and other regulatory regions associated with bacteria-expressible cassettes.

4.3.3 For non-coding regions which have no known plant function and are not associated with expression of coding regions:

1) DNA analysis may be required for some sequences of known function (e.g., *ori V* and *ori-322*, *bom*, T-DNA borders of *Agrobacterium*, and bacterial transposable elements).

2) DNA analysis is not necessary for any remaining sequences of the plasmid backbone when the plasmid is well characterized.

4.3.4 Where appropriate, provide sequence data of the inserted material and of the surrounding regions (sequencing information may be informative in some cases, i.e., to fully characterize a partial or rearranged DNA insert).

4.4 Protein and RNA characterization and expression:

4.4.1 For all complete coding regions inserted, provide data that demonstrates whether the protein is or is not produced as expected in the appropriate tissues consistent with the associated regulatory sequences driving its expression (e.g., if the gene is inducible, determine if the gene is expressed in the appropriate tissues under induction conditions). For virus resistant plants where the transgenes are derived from a viral genome, in addition to transgene protein analysis, determine transgene RNA levels in tissues consistent with the associated regulatory regions driving expression of the transgene. The following exceptions also apply:

1) If the protein concentration is below the limits of detection, mRNA data may be substituted.

2) Protein analysis for products of genes used only as selectable markers may be waived under certain circumstances, e.g. when there is at least one complete copy

of a selectable marker gene present and the effective expression of the selectable marker gene is verified by the process used to select the transformed tissue.

3) For plants modified to express non-translatable mRNA, truncated sense constructs, antisense constructs, or constructs containing ribozymes, since the function of these genetic constructs is to specifically alter the accumulation of a specific mRNA or protein present in the transgenic plant, provide data on the level of the target protein only (e.g. native tomato fruit polygalacturonase would be the target protein of antisense polygalacturonase to achieve altered fruit ripening). If the target protein levels are below levels of detection, determine target mRNA levels.

4.4.2 When a fragment of a coding region designed to be expressed in a plant is detected, determine whether a fusion protein could be produced and in which tissues it may be located.

4.4.3 Protein or RNA characterization may not be required for fragments of genetic constructs not expected to be functional in the plant (e.g., fragments of selectable marker genes driven by bacterial promoters.)

5. Description of the inheritance and stability of introduced traits which are functional in the plant

5.1 For plants which are either male or female fertile or both, provide data that demonstrates the pattern and stability of inheritance and expression of the novel traits. If the new trait can not be directly measured by an assay, it may be necessary to examine the inheritance of the novel DNA sequences directly, and expression of the RNA.

5.2 For plants which are either infertile or for which it is difficult to produce seed (such as vegetatively propagated male-sterile potatoes), provide data to demonstrate that the novel trait is stably maintained and expressed during vegetative propagation over a number of cycles that is appropriate to the plant.

6. Description of the parental genome

In the case of an allopolyploid PNT, in which parental genome is the genetic modification?

7. Number of generations removed from the original modification

8. Description of the novel traits

8.1 Where applicable, characterize in detail the novel gene products, breakdown products, by-products and their metabolic pathways.

8.2 Is the novel trait expressed in a tissue-specific manner?

8.3 Is the novel trait expressed in a developmental stage-specific manner?

8.4 Is expression of the novel trait induced? If yes, what are the inducing agents?

8.5 Where applicable, describe the activity of the gene products, breakdown products and by-products in the host plant. Describe any changes to existing metabolic pathways (including altered accumulation and storage patterns), including those that might not be intended.

8.6 Where applicable, the toxicity of the novel gene products, breakdown products and by-products in the environment must be established. Describe:

1) potential toxigenicity to known or potential predators, grazers, parasites, pathogens, competitors and symbionts;

2) potential for adverse human health effects, e.g., exposure to toxins, irritants and antigens. Include estimated level and most likely route of human exposure to the gene products, breakdown products and by-products.

Appendix 4 Information on the Biology and Interactions of the PNT

1. Description of the biology of the plant species prior to modification

1.1 Provide common name(s) and currently accepted scientific nomenclature.

1.2 A biology document describing the biology of the plant species must be submitted with the application if it is not available in the biology document series, unless the PBO confirms that such a document has previously been submitted.

2. Selection of Counterpart

Generally the most suitable counterpart for comparative studies is the isogenic line closest to the PNT, provided that the PNT is intended to be cultivated in the same region as this line. The counterpart may be a previously authorized PNT that has been in large-scale commercial production for several years. Developers are encouraged to consult with the PBO where there are questions regarding selection of an appropriate counterpart.

3. Phenotype of the PNT

The applicant must provide information on the intended phenotype and any known unintended or unanticipated traits. The PNT should be compared to its counterpart(s) and related cultivated varieties as appropriate. If differences are detected, the applicant should address these findings in the application.

Typically, observations are made when the plants are grown in multiple sites and over more than one growing season. Confined research field trials of PNTs should take place in the intended growing region of the PNT in Canada. Data collected from field studies outside Canada can be used if the applicant demonstrates that the environment for testing the PNT is similar to the Canadian environment. In some cases, such as where there may be a potential for increased weed characteristics or if the plant is an outcrossing species, it may be appropriate to evaluate the plants outside of managed ecosystems. Depending upon the results, additional studies may be warranted to provide the required information. Applicants may provide valid scientific rationale why certain information is unnecessary or inappropriate.

3.1 Describe the breeding history of the PNT population being evaluated starting at the point of trait introduction.

3.2 Compare the PNT to its counterpart with respect to the following characteristics which influence reproductive and survival biology:

1) Habit - Note any changes in basic morphology of the plant including any abnormalities, e.g., changes in overall growth habit, pollen characteristics (such as stickiness, size), seed shattering dormancy characteristics, symbionic

associations (e.g., with vesicular-arbuscular mycorrhizal fungi, rhizobia) etc.

2) Life cycle - e.g., plants are categorized as annual, biennial, perennial. Would the presence of the introduced trait produce a change?

3) Life history characteristics such as:

i) plant height, biomass (dry/wet weight)

ii) number of flowers produced/plant

iii) number of fruits produced/plant

iv) number of pollen grains/anther

v) percentage of viable pollen

vi) time to maturity (e.g., time to flowering)

vii) number of viable seeds produced/fruit

viii) percentage of seed germination

ix) percentage of germinated seeds surviving to maturation

x) number of flowering days

4) Outcrossing frequency (within species) and/or cross fertilization frequency (between species).

5) Impact on pollinator species - this may be addressed through information on whether the same pollinator species have been seen in the field or have there been changes in the pollinators that visit the flowers (requires previous familiarity with pollinators on non PNT species).

6) Stress adaptations (specifically note which stresses were observed):

i) Biotic stress factors: Examples might include parasites or pathogens, competitors (e.g., weeds), and herbivores.

ii) Abiotic stress factors: Examples might include response to drought stress, nutrient deficiency or other stresses common to that plant.

7) Ability to overwinter (or orverseason).

3.3 Compare the compositional analysis of the PNT to its counterpart(s) including, protein,

lipids, fiber, and other parameters as appropriate. This data is used to assess secondary or pleiotropic effects and may indicate environmental impacts (e.g., changes in nutritional quality of seeds affecting birds).

3.4 Compare the PNT and its counterpart(s) with respect to levels of known naturally expressed toxicants, antinutrients and allergens known for that species.

4. Cultivation of the PNT

4.1 Description of area of cultivation

1) Describe the regions in Canada where the species is currently cultivated

2) Will the modification permit cultivation of the species in regions in Canada outside the area of current cultivation? If so, in what new regions might the PNT be cultivated? Describe the ecosystems in the new regions.

4.2 Description of cultivation practices

1) Describe the cultivation practices for the PNT, including land preparation, fertilizer usage, weed and pest control, harvest, post-harvest protocols, and other cultivation practices. Compare and contrast these practices from those traditionally used for this species. Discuss how such practices might influence agro-ecosystem sustainability, crop rotations, pesticide use, frequency of tillage, soil erosion and consequential changes in energy and soil conservation. Discuss in what ways any volunteer plants of the PNT may dictate altered management practices for succeeding crops?

2) Describe any specific deployment strategies recommended for this PNT? Deployment strategies might include geographic or temporal factors or integration with other practices.

   i) Insect Resistance Management - In the case of insect resistant PNTs, describe strategies intended to delay the development of resistance in target insect populations (see Section 7.5.1 within the Directive text for details).

   ii) Herbicide Tolerance Management - In the case of PNTs developed for tolerance to a herbicide or class of herbicides, describe appropriate strategies that are intended to delay the development of herbicide tolerance weeds and avoid significant changes in weed biotypes (see Section 7.5.2 within the Directive text for details).

5. Interactions of the PNT with sexually compatible species

Determine whether there are any sexually compatible species in areas where the

PNTs will be grown. If there are, then this section is applicable and the following questions should be considered.

5.1 Which sexually compatible species, if any, are found in areas where the plant will be cultivated, including any new areas of cultivation?

5.2 Characterize the compatible wild relative(s) with respect to weediness in managed ecosystems and/or establishment and spread into natural ecosystems

5.3 In what ways would the introduced trait itself be likely to change the ability of the PNT to interbreed with other plant species?

5.4 In cases in which there is a potential for gene flow from the PNT into sexually compatible species (e.g. same or related species as appropriate), describe the consequences for the offspring of such crosses. Characterization of the crosses between wild relatives and PNTs should be considered using the criteria described in Section 1 above for PNTs in order to address questions 5.4.1) and 5.4.2) below.

1) Is the introduced trait similar to a trait found currently in natural populations of the compatible wild relatives?

2) Does the introduced trait have the potential to increase the reproductive fitness or confer a selective advantage on the wild relative? If so would the introduced trait have a significant impact on the establishment and spread of populations of wild relatives? Consider the presence or absence of selection pressures.

i) Is the potential for the trait to increase reproductive fitness or confer a selective advantage different than the potential for this to occur from a similar trait that may already exist for the same plant?

6. Residual effects and toxicity on non-target organisms

6.1 Characterize the extent to which the gene product has been a part of the human or animal diet.

6.2 Where applicable, characterize to what extent the introduced DNA directly or indirectly leads to the expression or altered expression of a toxin or other product that is known to affect metabolism, growth, development, or reproduction of animals, plants, or microbes?

6.3 Consider potential physiological and behavioral effects to other organisms including insect, avian, aquatic, or mammalian species in the areas where the plant will be cultivated, including any new area of cultivation.

Consideration may be given to:

- threatened and endangered species in the area where the plant is to be grown.
- beneficial organisms (pollinators, predators, parasites, biological control organisms, soil microbes)
- other appropriate non-target organisms

Consider levels and routes of exposure to all plant parts that express the gene, i.e., direct feeding or other exposure to the plant or plant part, dispersed plant parts, secretion, degradation, or leaching of the novel gene product, gene introgression, or organisms that have fed on the plant.

To address the possibility of persistent toxins in the environment or persistent changes in soil ecosystem function, applicants are encouraged to undertake residual effects studies. The residual effects of the PNT in comparison to the counterpart may be assessed by crop rotation studies or other techniques. Direct measurements in soil microbial communities may be indicated if microbial toxins are expected in root exudates.

6.4 Characterize potential adverse effects on the health of humans (including workers, adults, and children) which may arise through physical contact with or use of the PNT or its parts or its raw or processed products, other than for uses for which other authorizations or reviews are required (e.g. food, feed, pharmaceuticals). The analysis might include a comparison of the transgenic and non-transgenic counterpart(s) with respect to the likely exposure to toxins, irritants, and allergens.

7. Other environmental interactions

In the case of PNTs developed using plant viral coding regions, address synergy, facilitated movement, transcapsidation, and viral recombination. For a description of these terms, see the OECD "Consensus Document on General Information concerning the Biosafety of Crop Plants Made Virus Resistant through Coat Protein Gene-Mediated Protection" No. 5, 1996, OCDE/GD(96)162 (http://www.olis.oecd.org/olis/1996doc.nsf/LinkTo/ocde-gd(96)162).

Appendix 5 Application Package Checklist

Biology Document
Have you confirmed with the PBO that a biology document has been prepared for your species? (Note that biology documents used by the PBO are posted at http://www.inspection.gc.ca/english/plaveg/bio/dir/biodoce.shtml as they are finalized).
If not, have you enclosed a draft biology document for your species, following those on the PBO web site as an example? (See Section 7.2 of the Directive).

Core Characterization
Have you considered all the questions in Appendix 3?

Environmental Characterization
Have you considered all the questions in Appendix 4? Note that data from at least two seasons of trials in multiple locations in Canada or in a similar environment are normally required to address these questions.

Detection and Identification
Have you provided a detection method capable of distinguishing your PNT from other commercial cultivars of the same species? (See Section 7.4 of the Directive).

Food and Feed Use Approvals
If your PNT is intended for food and/or feed use, have you applied to the Novel Foods Section, Health Canada and/or the Feed Section, CFIA for food and/or feed use approval as appropriate? (See Section 8.2 of the Directive).

Special Crop Management Considerations
If your PNT carries a novel insect resistance, have you provided an appropriate Insect Resistance Management (IRM) plan (Please see Section 7.5.1 of this Directive)? If your PNT carries a novel herbicide tolerance, have you provided an appropriate Herbicide Tolerance Management (HTM) plan? You are encouraged to work with seed distributors, extension personnel and growers to develop and implement an appropriate HTM plan for your PNT (Please see Section 7.5.2 of this Directive).

Please note that the PBO's decision with regards to authorizing the environmental release of a PNT expressing either a novel insect resistance or a novel herbicide tolerance, will take into consideration whether or not the applicant has provided a stewardship plan addressing the need for the responsible deployment of the novel crop in question into the environment.

Post-Release Monitoring Plan
You must provide a general plan for post-release monitoring of environmental effects of your PNT (see Section 7.6 of the Directive).

Payment
Have you enclosed the application fee, according to the guidelines provided in http://www.inspection.gc.ca/english/plaveg/bio/feepaie.shtml? Please note that review of your

application may not begin until your payment has been received.