

GUIDE FOR MAINTAINING PLANT GENETIC INTEGRITY OF CONVENTIONAL VEGETABLES

PREPARED IN NOVEMBER 2016 BY THE
International Seed Federation (ISF) Working Group AP Vegetable and Excellence Through Stewardship (ETS)



DISCLAIMER

The Guide for Maintaining Plant Genetic Integrity of Conventional Vegetables (“Guide”) provides information to assist users in developing and implementing their own organization-specific process for maintaining the integrity of their products from research and discovery through commercialization and distribution. The maintenance of plant genetic integrity (absence of GM material in conventional non-GM vegetables) is critical for achieving compliance with regulatory requirements, fulfilling customer expectations, and preventing trade disruptions. Even small amounts of material out of place can have serious consequences for a product developer and commercial trade.

The Guide is flexible and its application will differ according to the size, nature and complexity of the organization and products involved. The Guide is representative and not exhaustive. It is the user’s responsibility to consider specific circumstances (1) when developing a process specific to an organization, and (2) in meeting any applicable legal requirements.

This Guide is not, and should not be used as, a substitute for (1) the user’s individual understanding of its legal requirements, (2) consultation by the user with its legal counsel and other advisors, or (3) direct contact with appropriate regulatory agencies.

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INTRODUCTION AND PURPOSE:

Plant and seed multiplication for vegetable crops is the continuous process in which vegetables are grown according to defined standards and requirements to ensure genetic identity, maintain varietal purity, and meet certain quality standards before distribution to growers and consumers. In many countries, seed multiplication is part of a legally sanctioned system for quality control of seed production.

The entire breeding process, from new entries to a vegetable breeding program and their cross with existing material until the development of parental lines, should be managed as a controlled process. This process requires the tracking and tracing of all deliberate crosses made to maintain the integrity of the breeding process.

This guide is a collaboration between the International Seed Federation (ISF) and Excellence Through Stewardship (ETS) and is intended to provide guidance on: (1) understanding through assessment of an organization's risks of materials out of place, including the potential presence of GM material in conventional vegetable seed (known as adventitious presence or AP); (2) developing and implementing a quality management system to manage plant genetic integrity; and (3) developing an incident response plan for responding to potential incidents related to plant genetic integrity concerns. The guidance in this document is intended to be flexible and its application will differ according to the size, nature, and complexity of the organization involved, as well as the products being developed and/or commercialized. Common throughout the entire process is an emphasis on the importance of product identification and traceability, as well as on documentation and governance.

ISF represents the interests of the seed industry at a global level by engaging with public and private institutions to facilitate international seed trade. Its Working Group AP Vegetable was established in recognition of the industry needs of; identifying liability issues that could arise from the AP of GM material in conventional crops, establishing industry-wide guidelines for mitigations measures and creating communication tools.

ETS is a not-for-profit global industry-coordinated organization that promotes the universal adoption of stewardship programs and quality management systems for the full life cycle of biotechnology-derived plant products. ETS membership is global and diverse ranging from small research groups to large multinationals involved in a wide variety of seed and plant products.

ETS has developed a series of guides to cover biotechnology-derived plant products (or GM plant products) to cover maintenance of plant product integrity throughout the product life-cycle from research through commercialization, as well as Product Launch, Product Discontinuation and Incident Response, and are available on the ETS website at www.ExcellenceThroughStewardship.org.

SCOPE

This guide is primarily focused on activities associated with conventional vegetable breeding and seed production to maintain plant genetic integrity and avoid the presence of material out of place, such as adventitious presence of GM plant material.

This Guide addresses quality management systems and risk management for the full life cycle of vegetable breeding and seed production to address adventitious presence that could be present. It is applicable to all stages of the plant

product life cycle from initial research and discovery through development to commercialization and post-market activities.

SUPPORTING DOCUMENTS

[ETS Stewardship Guides](#)

- The Guide for Stewardship and Biotechnology-Derived Plant Products
- The Guide for Maintaining Plant Product Integrity of Biotechnology-Derived Plant Products
- The Guide for Incident Response Management of Biotechnology-Derived Plant Products

ACRONYMS

AP – Adventitious Presence

ETS – Excellence Through Stewardship

GM – Genetically Modified

HACCP – Hazard Analysis and Critical Control Points

ISF – International Seed Federation

LLP – Low Level Presence

OECD – Organisation for Economic Co-operation and Development

QMS – Quality Management System

SOP – Standard Operating Procedure

DEFINITIONS

[Adventitious presence](#)

Unintentional and incidental presence of trace amounts of one or more biotechnology (or GM)-derived traits in seed, grain or food product. One of the incident types this document discusses is the Adventitious Presence (AP) of GM material in conventional vegetable seed, plants or food products. There is a related concept known as Low Level Presence (LLP). For simplicity, because both AP and LLP may result in similar negative outcomes, the Guide uses the term adventitious presence (AP) to refer to both categories. The Guide uses the term “AP-related incident” for an incident of detection of unintended GM material in conventional vegetable material.

[Biotechnology](#)

As per the Convention on Biological Diversity, biotechnology is the application of a) in-vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles; or b) fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection.

[Breeder Seed](#)

Seed or vegetative propagating material, increased by the originating, sponsoring plant breeder or institution, used as the first source for further seed increase.

Construct

An engineered chimeric DNA designed to be transferred into a cell or tissue; may be synonymous with vector fragment or vector. Typically, the construct comprises the gene or genes of interest, a marker gene and appropriate control sequences as a single package.

Containment

The control of viable seed, pollen or vegetative propagating material in a manner that mitigates their release outside of their controlled development in the laboratory, greenhouse, seed conditioning or storage facilities.

Containment Facility

Any facility designed to limit access by unauthorized personnel as well as egress of controlled plant materials.

Critical Control Point

A step at which control can be applied and is essential to prevent, eliminate or reduce risks to an acceptable level from an activity that may compromise plant product integrity.

Disposition

The act or means of settlement of (i.e., what was done with) plant material (e.g., planted, devitalized, buried or stored).

Documentation

Recorded information such as specifications, quality manuals, quality plans, records and procedure documents.

Event

A genotype produced from a single transformation of a plant species using a specific genetic construct. For example, two lines of the same plant species that are transformed with the same or different constructs constitute two events.

Facility

Sites that are contiguous, under common control by a company or individual and with a grouping of equipment or individuals engaged in a common process.

Foundation Seed

Seed stocks increased from breeder seed or foundation seed, handled to maintain specific genetic identity and purity. Foundation seed is the source of certified seed, either directly or through registered seed.

Gene

The fundamental physical and functional unit of heredity. A gene is typically a sequence of DNA that encodes a specific functional product (such as a protein or RNA molecule).

Germplasm

The genetic makeup or genome of an individual, group of individuals, or a clone representing a genotype, variety, species, or culture, held in an in situ or ex situ collection.

Line

A group of individuals derived by descent from a single individual within a species.

Low level presence

Unintentional, trace amounts of biotechnology-derived trait(s) in a seed, grain or food product approved in one or more countries but not yet approved in the country of import.

Organisation for Economic Co-operation and Development (OECD)

The OECD is a voluntary association of member countries that cooperate to produce internationally agreed instruments, decisions and recommendations in areas where international cooperation is required to enable countries to profit from being integrated into global markets. One such instrument is the OECD seed schemes, through which more than 55 countries cooperate to establish international best practices and standards for the production of seed of uniform high quality. The OECD annual list of products includes about 37,000 varieties of 191 species.

Plant product integrity

Plant product integrity is the specific identity of a plant and purity of populations of the plant that are established and maintained using appropriate measures.

Protein

A molecule composed of amino acids in a specific order. Proteins are required for the structure, function, and regulation of metabolic activities in the body's cells, tissues and organs, and each protein has a unique function.

Quality Management

A component of stewardship which comprises the processes and systems to establish and maintain quality in each phase of the product life cycle.

Standard Operating Procedure (SOP)

An established, written method or set of methods that describes how to routinely perform a given task.

Standard Seed

Seed which is declared by the supplier as being true to the variety and of satisfactory varietal purity.

Stewardship

Product stewardship is the responsible management of a product from its inception through to its ultimate end and discontinuation. In agricultural biotechnology, stewardship includes careful attention to the safety of products and their market impact is essential for high value products in any industry.

Trait

A genetically determined characteristic.

Trait purity

A measure of the extent to which the intended trait(s) is present and unintended traits are absent in a population of plants.

Variety

Subdivision of a species for taxonomic classification. Used interchangeably with the term cultivar to denote a uniform, stable group of individuals that is genetically and possibly morphologically distinct from other groups of individuals in the species.

GENERAL STEWARDSHIP

Product Stewardship is the responsible management of a product throughout its life cycle. The stewardship guidelines below can assist in the identification and management of potential risks to plant genetic integrity associated with product development, commercialization, distribution and discontinuation. The concepts described in this section and in the Appendices are applicable to all stages of vegetable research, development, production, commercialization and distribution.

Quality Management Systems (QMS) and Stewardship

A properly maintained process-based and continuously improved Quality Management System (QMS) is an important component of risk assessment and mitigation. A QMS is a collection of documented procedures and work instructions reflecting the business processes of a company. These documents inform employees how certain processes and tasks should be conducted. Key elements of a QMS include processes to: (1) manage and control documentation, (2) address non-conformities; (3) trace and identify products; (4) train and measure competency of employees; (5) continuously improve systems and performance; and (6) audit and measure conformance to the system. Any mitigation measure involving changes of the set-up of processes or tasks should be included in the related documents. If measurements relating to the AP incident highlight a particular risk, they should trigger an update of the document procedures and work instructions related to the materialized risk.

The International Organization for Standardization (ISO) family of standards collectively provides a framework that an organization may use to develop, implement, and maintain a management system that incorporates a process for continual performance improvement while addressing the needs of interested parties. The ISO maintains the generally accepted standards for developing and implementing a QMS (ISO 9001:2015 and ISO 9000:2015). It requires a documentation system that contains the processes, procedures and standard operating procedures (SOPs) of the company controlled by a workflow allowing continuous improvement and accountability.

The QMS should contain a system that documents that employees are trained and are proficient to execute the task(s) and duties related to their function and that conformity to the procedures is checked regularly by an audit process. The non-conformities and corrective action that are the result of this process should lead to improved documentation and re-training of staff.

Risk Management

Risk management is an important part of sustainable business success. For the purposes of this document, proper risk management includes two major components:

1. Risk Assessment: the identification of risks related to the business through a thorough review of potential risk factors and an evaluation of their probability of occurring, and
2. Risk Mitigation: the implementation, based on the risk assessment, of appropriate stewardship measures that reduce the identified risks to an acceptable level for the company.

Each organization must conduct risk assessments and mitigation to prevent materials out of place, such as AP, or contamination due to inadvertent mixing. Failure to maintain plant genetic integrity has a potential impact on the entire vegetable industry chain, from grower to final consumer. This Guide provides guidance to identify and evaluate risks related to materials out of place, and suggests ways to help mitigate such risks. It is important to note that AP can be minimized but never completely excluded or prevented with 100% certainty.

Risk Assessment

The risk assessment includes an evaluation of potential contributing factors and their effect on the probability of an incident, such as AP. The risk assessment should include an evaluation of potential impacts, including financial, commercial trade, stakeholder reputation and/or regulatory action on registrations.

The risk assessment and risk mitigation plans developed should take into account the size, nature and complexity of the organization, its scope of activities and species handled. The ISF “toolbox” will help companies determine key activities that could contribute to an AP-related incident through the evaluation of factors and their influence on a potential incident, as well as implementation of control measure.

The following steps are designed to help an organization conduct a risk assessment.

1. Identify potential plant genetic integrity concerns, including potential sources of contamination
 - a. Understand current and historical GM presence in vegetable or sexually compatible species
 - i. Potential impact of current and historical releases of GM material into environment in field trials or commercial products in vegetables as well as in related species that are sexually compatible with these vegetables.
 - ii. Locality where these GM activities have, or are occurring, for this vegetable, or sexually compatible (cross-pollinating) species
 - iii. Information whether seed admixtures between conventional and GM vegetable material (or any material that could not be trusted) could (theoretically) happen or could have happened in the past.

ISF has launched a vegetable GM database that includes information on current and former GM vegetable field trials, vegetables GM commercialization, and GM activities of species crossable with particular vegetables species. The database strives to provide all publicly available information related to:

- pre-commercial trials of a GM event stating the known information related to the license, trait, the construct (if known); where (country and/or state) and when the trial will or has been taken place. The database will not list the known possible standard target sequences even if they are known
- commercial events stating in which countries GM vegetables are authorized for commercial sales
- discontinued events stating which GM products have been discontinued in a country.

This database is provided as is and that no responsibility and/or liability is taken by the ISF relating to the completeness and correctness of data. The database will, however, be updated and checked regularly by leading industry experts through the ISF to assess the accuracy and timeliness of the information included. Furthermore, users are requested to provide any information to further enhance the quality of the database to the ISF. The database is accessible only for ISF members upon request. isf@worldseed.org

- b. In addition to the commercial or research activities included in the database, an organization's own activities need to be taken into consideration during the risk assessment. Activities to consider include current and former:
 - i. GM containment facility activities (including laboratory, growth chamber and greenhouse activities),
 - ii. GM vegetable activities of contract partners, and
 - iii. Current and former GM commercial activities

2. Evaluate potential risks of these materials on current activities

The presence of materials identified above could be the source of AP, if risk control measure are not established. Appendix I provides examples of risk factors that may contribute to or result in an AP-related incident. Some factors have higher risk potential. The potential impact of these factors may be dependent upon the organization's scope of activities, quality management systems and stewardship practices.

ISF recommends that a company maintains a simple structure of three probability classes for the identified factors. The conditions for each factors highlighted in Appendix I. This will allow the user to focus on the critical points in developing risk mitigation measures.

The impact of an AP-related incident may lead to cost due to compensatory claims, loss of material and/or the reduced sales related to the incident and the reputational damage to the organization. While it is difficult to predict the costs associated with an AP-related incident, there could be significant negative financial consequences.

Risk potential may be lessened through implementation of appropriate avoidance measures and mitigation plans, which should be developed during the risk assessment. Appendix I includes example factors that could contribute to an AP-related incident. Each situation must be independently evaluated, because some factor(s) may not be relevant to the organization or the specific situations.

Risk Mitigation

After assessing the potential for an AP-related incident, as well as potential sources of AP, mitigation measures at critical control points should be implemented. Organizations should consider measures to reduce the risk to an acceptable level based on their business plan and model. In Appendix I, and others identified during the risk assessment process, should be addressed in the mitigation plan through the establishment of critical control points. Mitigation measures, which can significantly reduce risk, but never fully eliminate it, should be implemented to reduce the probability of an incident, as well as its potential impact.

Factors that were identified as highest in the risk assessment (see Appendix I) would be the key activities for the implementation of mitigation measures. Through these efforts the probability of an AP-related incident could be reduced and these factors could be classified lower in the future. A set of possible measures are outlined below and each company will need to determine its particular situation and which measures are worth implementing.

Note: the following suggested preventive measures are applicable only for materials that have risk of exposure to GM material.

1. Develop Mitigation Plan
Based on the potential risks identified and the probabilities,
 - a. Determine critical control points
Describe critical control points, which could include avoidance measures
 - b. Establish and Implement:
 - Preventive measures
 - Monitoring and verification procedures
 - Corrective measures
 - Incident escalation and response procedures
 - Record keeping and documentation procedures

An organization may be involved in one or more activities associated with the development and commercialization of vegetables in which there is potential for an AP-related incident. For example, an organization may only conduct research and breeding, or may only be involved in commercial seed production and sales. To accommodate these different business models, the following portion of this Guide is presented in modules. The organization can adopt the modules that are applicable to its own individual circumstance. Each module covers activities with shared operational and regulatory consideration. The Hazard Analysis and Critical Control Points (HACCP) principles have been applied to these activities, particularly to assist in the identification of critical control points where interventions are considered necessary to confirm product integrity. The critical control points outlined in each of the modules should be assessed in the development and operation of a quality management system. The selection and extent of the preventive measures for each of the identified control points should be determined by taking into account the nature of the process or product and associated aggregate controls. The extent and application of these measures should be justified.

While the preventive measures described in the following modules have been developed to mitigate potential for AP-related incidents, they should also be considered in situations where inadvertent mixing or other potential sources of contamination could occur.

MODULES

The goal of a conventional vegetable seed breeding program is to maintain plant genetic identity of the seed material, maintain varietal purity and meet quality standards before commercialization and during distribution to growers and consumers. It is important that organizations monitor activities being conducted in the vegetable crop, or sexually compatible species, that could become a potential source of adventitious presence or cross-contamination. The introduction of GM seed or plant material into a vegetable breeding program can occur through inadvertent mixing or crossing during the breeding and/or commercial seed production process. This could result in the presence of GM material in breeding and/or commercial material where such material has not been authorized by the appropriate regulatory agency(ies). This could result in substantial legal, financial, and image implications for the organization directly involved in the release as well as the owner of the introduced GM material. In addition, there could be negative implications for the global vegetable industry.

In those countries where variety registration and/or certification are required by law, there are generally four recognized stages of seed multiplication: breeder seed, foundation seed, registered seed, and certified seed¹. These are also recognized by the OECD Seed Scheme as Pre-Basic (breeder seed), Basic (Foundation/Registered seed), and Certified seed. However in the vegetable seed business the most frequently used category is standard seed that doesn't require official certification, but suppliers(seed companies) must ensure that their material meets the legal criteria.

Even in countries that do not require formal registration and certification, the following definitions are generally recognized as the different stages of seed multiplication (steps and terminology can be different in vegetable seed companies). Breeder seed (related to the process of creating new fixed lines) is directly controlled by the originating or sponsoring plant-breeding organization. The first increase of seed breeders' parental lines (fixed lines) is usually referred to as foundation seed which is handled to maintain specific genetic identity and purity. Foundation seed is used (in most organizations) to create stock seeds that are used as the basis for commercial seed, produced by the breeder originator company, or outsourced to seed production vendors.

The entire breeding process to develop parental lines should be managed as a controlled process. This process should provide traceability, including documentation of all deliberate crosses as well as any testing conducted to determine the purity and plant genetic integrity of the materials being developed or commercialized.

MODULE 1 - RESEARCH & BREEDING

This module is aimed at working with conventional vegetable seed research and breeding programs which may be at some level of risk in exposure to GM materials. The level of risk should be analyzed and a judgement made to determine which measures and procedures should be established and implemented to mitigate the identified risks. Note: not all measures and procedures will necessarily be required to maintain plant genetic integrity.

¹ http://www.aosca.org/Page/Seed_Certification.aspx?nt=96

Analyze Plant Genetic Integrity Concerns

- Exposure to GM material sources (such as through third party germplasm or internal activities).
- Misidentification.
- Mislabeling.
- Errors in tracking.
- Insufficient isolation or other control measures to prevent cross-pollination or out-crossing:
 - consideration of crop biology (e.g. strict cross-pollinator, strict self-pollinator)
 - evaluation for sexually compatible species
 - contained facilities (e.g., growth chamber, greenhouse)
 - fields.
- Inadequate facilities or controls for containment:
 - inadequate procedures or processes (e.g., pollen transfer due to clothing, equipment)
 - inadequate facility controls (e.g., air flow between growth chambers or greenhouses)
- Inadvertent physical mixing of plant material during planting, movement, processing or storage.
- Inadequate or missed testing at a hand-off, resulting in potential contamination going undetected.
- Errors in devitalization or destruction of untraceable seed, contaminated seed or materials not meeting specification.

Determine Critical Control Points

- Transfer of germplasm or plant material:
 - to, from or within the facility
 - Contained facilities (e.g., growth chambers and greenhouses)
 - Processing and packaging areas
 - to or from a third party collaborator
 - to, from or within the field.
- Labeling and tracking of GM and conventional material.
- Storage, preparation and disposition of materials.
- Segregation of GM and conventional materials throughout the processes, such as :
 - storage
 - facilities
 - fields (e.g., throughout planting, growing season and harvest).
- Isolation practices and procedures to prevent inadvertent cross-contamination during pollen flow (e.g., isolation practices, personnel movement during pollen flow).
- Destruction/devitalization of materials.
- Testing protocols and testing availability to verify genetic identity and purity of materials at key steps throughout the breeding process.

Establish and Implement

Preventive Measures

- Labeling, tracking and disposition of propagatable plant material as part of an inventory system.
- Internal work processes and SOPs for traceability.
- Procedures so that labels are recorded and information related to identity is retained.

- Verification of identity and integrity of germplasm.
- Space assignment within facility.
- Transfer protocols or processes for traceability across functions, departments, organizations or locations.
- Protocols and/or work procedures for planting (e.g. equipment used for planting is free from contaminant seed/material prior to and following use; plot design is clear and easy to follow to prevent errors).
- Protocols and/or work procedures to control reproductive isolation (e.g. isolation within the field, movement of personnel and equipment between trials during pollen flow, cleaning of equipment prior to leaving trial, disposition of plant material during season or after harvest).
- Protocols and/or work procedures for harvesting of plant materials to prevent cross contamination (e.g., ensure equipment or container (e.g. bag, envelope) used to harvest is free from contaminant seed/material before use).
- Protocols for analysis to verify genetic identity and purity of materials at key steps throughout research and breeding.

Monitoring and Verification Procedures

- Confirm plant identity prior to transfer to or from the field by documentation and/or diagnostic testing where appropriate. This applies to plant material that may be used for further multiplication or planting.
- Monitor the seed-multiplication program to confirm that management practices are in place to meet external (e.g. seed certification agencies) and internal operational requirements.
 - Confirmation of reproductive isolation and other measures required to meet the standards for breeder, foundation, registered, and certified seed.
- Confirmation of plant identity during storage.
- For materials in which there may be both GM and conventional materials developed and/or marketed, a procedure is in place to control production, shipping, and commercialization of individual lots to designated country of sales.
- If presence of GM material is detected and confirmed, a risk analysis should be conducted to identify and implement specific corrective actions.

Corrective Measures

- When plants are found to be incorrectly identified or when identity cannot be confirmed or where reproductive isolation has not been maintained, the plant material and any derivatives should be reviewed and appropriate disposition determined.
 - Correct any deficiencies identified that could affect integrity of the containment facility or practices in place.
- Correct any deficiencies identified that could affect the reproductive isolation of the field sites or practices in place.
- Incorporate corrective measures or procedural changes into SOPs as appropriate.
- If applicable, train personnel on the procedural changes incorporated.

Incident Escalation and Response Procedures

- Appropriate incident response protocols established to ensure timely and accurate reporting of corrective actions.
- Documentation to ensure that personnel are trained on the system to report and escalate any incidents where product integrity may have been lost (e.g., AP-related incident).

Record Keeping and Documentation Procedures

- Documentation of analyses, identity and traceability should be secure, accessible, and retained as appropriate.
- Methods should be established and implemented to develop and record the trial protocols that define requirements and guidance from planning through planting and in season activities to harvest and final disposition of harvested materials.
- Procedures for the retention of documentation related to non-conformities and follow up actions.

MODULE 2 - PRODUCTION, LOGISTICS AND SALES

Plant and seed multiplication is the continuous process in which plant products are grown according to defined standards and requirements to ensure genetic identity, maintain varietal purity, and meet certain quality standards before distribution to growers. In many countries, seed multiplication is part of a legally sanctioned system for quality control of seed production.

Maintaining plant genetic integrity remains important in the commercialization and distribution. The entire development, commercialization and distribution channel is often not controlled by one entity, but rather a number of entities involved with production, storage, conditioning, processing, sales and distribution to customers. It is important to ensure there is traceability and methods for ensuring genetic identity is preserved across entities. Each entity is responsible for those steps within its scope of operations.

This module provides guidance for developers, producers, and distributors. The scope of this module includes activities to produce, process, condition, treat, store, and package products. Other activities covered in this module include verifying purity of the seed lot, the movement and transport of materials, storage and control of products in various stages of processing and packaging, and transportation and distribution of products through markets to customers.

Analyze Plant Genetic Integrity Concerns

- Potential sources of contamination include :
 - exposure to genetic material from 3rd party germplasm sources
 - status of internal GM-related work
 - collaborations with third parties and understanding their exposure to GM material.
- Regulatory considerations include :
 - status of GM material in research and breeding locations
 - allowable limits of AP in country of production and market areas
 - testing requirements.

- Insufficient isolation or control measures
 - Crop biology (e.g. strict cross-pollinator, strict self-pollinator)
 - Pollen transfer (e.g. clothing, equipment)
 - Distance to GM activities internally and externally
- Seed production practices and procedures (e.g. open field, containment facility)
- Seed mixing during planting, processing and storage
- Testing and detectability of GM material
 - Testing for AP
 - Testing method meets international standard, when applicable
- Status of QMS implementation.

Determine Critical Control Points

- Isolation procedures in production fields to prevent cross-contamination during pollen flow or harvest.
- Segregation of GM and conventional materials.
- Transfer of germplasm or plant material from the facility.
- Packaging, storage and preparation of plant material for distribution and sales.
- Labeling and tracking of GM and conventional materials.
- Testing protocols and testing availability to verify genetic identity and purity of materials at key steps in the production, commercialization and distribution process.

Establish and Implement

Preventive Measures

- An appropriate quality control strategy to ascertain seed quality standards as above.
- Procedures for labeling, tracking, and disposition of plant material as part of an inventory system for activities up to and including the point of commercial distribution.
- Procedures so that information used to identify material is recorded on labels and associated with documentation pertinent to identity and production history.
- Internal work processes and standard operating procedures for trace-back.
- Transfer protocols or processes for trace-back across functions, departments, organizations and locations.
- Protocols and processes for equipment cleaning and inspection to avoid inadvertent physical mixture or cross-contamination. Dedicated equipment should be considered where appropriate.
- Seed processing, warehousing, and distribution processes to maintain plant product integrity and avoid inadvertent physical mixture.
- Protocols for analysis to verify genetic identity and purity of materials at key steps throughout production, commercialization and distribution.

Monitoring and Verification Procedures

- Confirm plant product identity prior to cleaning, packaging and transport by documentation or verify using diagnostic methods, where appropriate.
- Remedial and corrective measures.
- In the event that plant material is found to be incorrectly identified or where identity cannot be confirmed, determine appropriate disposition of the plant material and any derivatives.
- Processes for receiving, controlling and determining the disposition of returned materials.

- Incorporate procedural changes into standard operating procedures to prevent recurrence of non-conformities.
- Confirm plant product identity before and after cleaning and packaging. Verify that the plant product meets the quality standard for intended use.
- Confirm plant product identity and, as appropriate, assess trait purity prior to transport for product distribution.
- For materials in which there may be both GM and conventional materials developed and/or marketed, a procedure is in place to control production, shipping, and commercialization of individual lots to designated country of sales.

Corrective Measures

- When a plant is misidentified, a plant is correctly identified but is not the desired genotype, or when identity cannot be confirmed, the plant material and any derivatives should be reviewed and appropriate disposition determined.
- Correct any deficiencies identified that could affect the reproductive isolation of the field sites or production facilities and assess impact on plant product integrity.
- Incorporate any corrective measures or procedural changes into SOPs as appropriate.
- Establish and implement processes for product containment, withdrawal and recall.
- Establish and implement processes for receiving, controlling and determining the disposition of returned materials.
- Incorporate procedural changes into standard operating procedures to prevent recurrence of non-conformities.
- If applicable, train personnel on procedural changes incorporated.

Incident Escalation and Response Procedures

- Appropriate incident response protocol to ensure timely and accurate reporting of corrective actions
- Documentation to ensure that personnel are trained on the system to report and escalate AP-related incident

Record Keeping and Documentation Procedures

- Procedures so that documentation of identity and trace-back is secure, accessible, and retained as appropriate.
- Procedures for the retention of documentation related to non-conformities and follow up actions.

APPENDIX I – POTENTIAL FACTORS THAT MAY CONTRIBUTE TO AP-RELATED INCIDENT(S)

The following are potential factors that may contribute to or result in an AP-related incident. The potential impact of these considerations may be mitigated by the organization's scope of activities, quality management systems and stewardship practices, as well as implementation of appropriate avoidance measures and mitigation plans.

Factor			
Status of GM materials for the vegetable or in sexually compatible species	No research or commercialization is conducted with GM vegetable or sexually compatible species	Limited research (contained environment or field) with GM vegetable or sexually compatible species	Extensive field research and/or commercialization of vegetable or sexually compatible species
Scope of Testing and Commercialization of GM materials	Regulated event, only contained environment or field trials conducted; limited testing and locations (i.e. not commercialized)	Commercial GM activities in single country with early commercial withdrawal	Commercial GM activities in several countries, commercial or discontinued after long use
Understanding proximity of neighboring sexually compatible GM materials (e.g., within pollen flow distance)	No sexually-compatible GM materials in proximity	Lack of knowledge regarding what may be in the proximity, now or historically	Sexually-compatible GM materials in proximity
Source of genetic materials and/or germplasm	No use of genetic material/germplasm from external sources	Limited use of external sources of germplasm with analysis for potential AP	Regularly use external sources of genetic material/germplasm; little or no analysis for potential AP
Internal GM work	No GM work conducted in sexually-compatible materials	Contained environment work with sexually-compatible GM materials	Extensive work with sexually-compatible GM materials
Segregation of GM work internally	Strict separation between work areas for GM and conventional material	Partial separation between work areas for GM and conventional material	No separation between work areas for GM and conventional material
Movement of personnel & equipment between work areas	No movement of personnel/equipment between work areas for GM and conventional material	Limited movement of personnel and equipment between work areas for GM and conventional material; precautions taken if transfer of viable pollen is possible.	Uncontrolled movement of personnel and equipment between work areas for GM and conventional material
Pollen transfer – ie clothing, equipment, not via plant material	Pollen is extracted with great difficulty and should be used immediately for its purpose by flower to flower contact	Pollen can be extracted manually and transported and used.	Pollen viability is high and transported by air. Potential false positives may occur due to GM pollen presence on non-GMO seed

Factor			
Crop biology	Strict self-pollinator	Partly cross or self-pollinator	Strict cross pollinator
Seed production	Contained (e.g., greenhouse or cages with prevention against insect pollination or pollen flow)	Partly opened and partly contained	Open field
Inadvertent mixing of GM and conventional seed	Measures to segregate GM and conventional materials and prevent mixing in all processes	Measures to segregate GM and conventional materials implemented for some processes	No measures to prevent mixing
Distance to GM activities	Greater than isolation distance necessary to ensure no cross pollination through pollen flow or insect pollination	Within isolation distance, measures taken to prevent cross pollination	Within isolation distance, measures not taken to exclude cross pollination
Ability to detect presence of GM material	Validated test available	Test available, but not validated	No test available
Testing for AP conducted	Routinely at key steps in the breeding process	At limited steps in breeding process; may only occur if AP suspected	No testing conducted
Testing method meets international standards	Yes	Unknown	No
Low Level Presence of GM material in conventional material allowed in importing country	Yes		No
Technical definition of “zero” detection accepted	Yes	Unknown	No
Functional Quality Management System in place	Yes for all processes in the organization	Yes for some processes in the organization and/or QMS for some processes not functional	No QMS implemented

APPENDIX II: MOLECULAR TEST TO DETECT AP

Minimizing the consequences of an AP-related incident is more difficult compared to reducing the probability of an AP-related incident happening. Regular molecular testing and an incident response procedure (crisis management) are highly recommended to help to reduce the impact of an AP-related incident. With regular molecular tests the absence of specific GM targets could be confirmed. As an example of consequence estimating the detection of GM material in an early phase for the development of a new variety (e.g. first breeding cross) the consequence will probably be considerably reduced compared to the consequences of GM material detection in an already released commercial variety.

The detection of adventitious presence is difficult and requires specific molecular test(s) to be carried out by experts under well-defined laboratory conditions. The validation of such test(s) demands the involvement of defined vegetable GM material carrying the target sequences as positive references. In the absence of such positive reference material, the use of spiking non-vegetable GM with a positive reference material sample might be considered as an alternative.

Test development includes establishing the boundaries of the specific detection limit = which refers to the technical zero detection level where a single GM seed can clearly be detected in a defined number of seeds. Some parts of target sequences like promoters (e.g. 35 S promoter from Cauliflower mosaic virus) or polyadenylation signal termination sequences (e.g. nopal synthase gene (Tnos) from Agrobacterium Ti plasmid) are frequently used in molecular genetics and can be detected by molecular analysis, but caution should be taken as the detection of such a sequence could be related to GM material but might also be 'false positives' caused by natural contamination of the virus or bacteria from which these sequences have been cloned from. It is, therefore, strongly advised to only use certified laboratories for GM sequences detection to minimize the risk of generating 'false positives' results leading to confusing and invalid results

Not only the development and validation of molecular tests and the interpretation of results, but also representative sampling are of high importance. Perfectly carried out molecular analysis starting from a non-representative sample still result in non-reliable value. The 'technical zero', which is the limit by the current state of the art to detect GM material in a given pool of seeds or plant parts, needs to be known. The limits of detection should be properly understood by all involved in the risk evaluation process.

APPENDIX III: INCIDENT RESPONSE MANAGEMENT

An incident response procedure defines how to react should the company be confronted by an AP-related incident. An implemented Incident Response Management procedure will allow the affected party to act immediately and proactively and in this way to reduce adverse impacts. Without an incident response procedure in place, valuable time and energy would be spent identifying activities to be done thereby lessening the ability to reduce the potential negative impacts of an incident hence Incident Response Management is an essential part of managing AP risks. This section describes a basic response procedure and is based on the ETS Guide for Incident Response Management that can be consulted for additional detail.

The following is designed to provide guidance on the prompt management and resolution of incidents involving unwanted GM materials in vegetable products. Potentially, incidents can occur at any stage of the product life cycle, therefore, any organization should have systems, processes, procedures and resources in place to respond to potential incidents involving the presence of GM material across the life cycle of their products.

Incident-Response System

An organization should have an incident-response system in place that is tailored to its type and scope of operations and activities. This could include having:

- defined **roles and accountabilities** for incident response, including response team leadership and subject-matter experts in regulatory, legal, compliance, commercial, research, supply chain, and communications
- defined **process flow** for incident response management
- defined **escalation process** including response triggers that define appropriate reactions to specified types of incidents
- established **communication network** for dissemination of information internally and externally
- defined **stakeholder maps** to facilitate timely inclusion of key parties
- defined **documentation requirements**, as appropriate and as determined by legal counsel
- established **training program** that allows actors to respond correctly to the defined incident response system, processes and procedures of the organization.

Advance planning and preparation is important to the successful resolution of an incident. In the design, development and implementation of incident-response processes and procedures, an organization should take into account the variety of activities and types of potential incidents that may occur.

A Step-by Step Guide to Incident Response Management

The following table lists the steps of a typical incident response process. Each organization should define and implement an incident response process to meet its needs in achieving timely and effective management and solution of an incident.

Table - Response Process

Step 1	Notification of Potential Incident
Step 2	Verification of Incident
Step 3	Scope the Incident
Step 4	Convene Incident Response Team
Step 5	Develop and Implement Response Plan
Step 6	Process Improvement

Step 1: Notification of Potential Incident Internal or External

A potential incident internal is related to the detection of a biotechnology event based on the analysis of a plant product during its life cycle. Detection should lead to the following steps:

- description of incident
- time, date, and place of incident
- involved plant product
- promulgation process for information (at the local and/or global level)
- events leading up to incident
- any associated factors or circumstances
- potential indirect effects (e.g., health, safety, environment)
- proposed next steps
- name of personnel receiving report.

Potential incidents may also have been identified by external sources by testing done in the vegetable production chain by stakeholders (producers, whole sellers, supermarkets, environmental groups). As feasible, there should be response procedures established with these external sources for prompt notification of an incident to the organization. Organizations' personnel should be designated and trained to react appropriately in the process of taking information from these external sources as described above.

Step 2: Verification of Incident

Initial notification of a potential incident should be communicated to the appropriate internal contact(s) (e.g. stewardship, regulatory, quality, compliance, and/or legal), who should confirm whether there has been an incident and its nature (e.g. unauthorized release, product nonconformance). It is strongly recommended verify the test result on the same extracted DNA at another external certified lab to verify the presence of the GM material. It should be noted that testing and sampling of biotechnology events in vegetables has not been harmonized today and that, hence, when there is an incident it leaves room for data validation interpretation (see also Appendix I Risk Factors of AP-Related Incident).

Step 3: Scope the Incident

A small team of subject matter experts should rapidly scope out the potential impact and magnitude of the incident. In addition to physical consequences, and liability/litigation risks should be evaluated by reviewing the appropriate documents, such as government regulations, contracts, and legal agreements.

This initial scoping exercise should comprise the following details:

- clear definition of the incident
- initial quantification
- definition of potential impacts
- identification of potential legal requirements (e.g., reporting obligations)
- scenario analysis of actions and consequences
- identification of stakeholder (regulators, customers, grain trade, food chain, etc.)
- review of relevant agreements and potential insurance coverage under applicable policies.

Step 4: Convene Incident Response Team

The response team structure and membership will depend upon the initial assessment of the scope, the potential impact of the incident, and the expertise needed to control the situation. The response team leader should have the expertise, time and resources to manage the issue in an expedient manner. It is important to have clarity on roles and responsibilities, as well as transparency and coordination across sub-teams. Sub teams, with local or global focus, may also be needed for major incidents so that specific stakeholder needs are covered (e.g. government staff, industry trade partners, distributors, local or international media).

Step 5: Develop and Implement the Response Plan

Clear analysis with timely and effective response can lead to the successful resolution of an incident. A dedicated response team should focus on resolving the incident. Response activities should consider the framework of stakeholder commitments, regulatory requirements, contractual obligations, and other legal requirements that may include confidentiality responsibilities. Substantial efforts should be undertaken to maintain customer, trade, and public confidence. Members of the incident response team should develop a response plan and implement remedial actions. The response plan should identify the actions to be taken, the persons accountable for the actions and when the actions should be completed. Stakeholders should be identified and appropriately informed of an incident and any potential impacts on them. Communications should take place within the relevant regulatory and legal framework. Incoming questions should be adequately addressed by informed expert staff.

Step 6: Process Improvement

At an appropriate phase in managing the incident, it may be necessary to conduct an internal investigation on the root cause of an incident and to recommend process improvements that could be made to help reduce the likelihood of similar future incidents. Corrective actions should be reviewed for effectiveness after an appropriate time. A review of the organization's incident response process and procedures should also occur in a timely manner following an incident. Any necessary process improvements and training should be implemented to correct identified deficiencies.

Summary

Incidents should be dealt with quickly and effectively to minimize impact on the organization and its stakeholders. Preparation followed by directed and effective response is important to successful incident response, together with the implementation of corrective and/or preventative actions that can help reduce the likelihood of a reoccurrence. Prompt and thoughtful response actions will help to maintain strong stakeholder relations.

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