EXCELLENCE THROUGH STEWARDSHIP®

Advancing Best Practices in Agricultural Biotechnology

GUIDE FOR

Product Discontinuation

OF

Biotechnology-Derived Plant Products

DISCLAIMER

The *Guide for Product Discontinuation of Biotechnology-Derived Plant Products* ("Guide") is solely an educational tool and is guidance to assist users in developing and implementing their own organization-specific process for discontinuing plant biotechnology products.

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 responsibility of any user of this Guide to consider that user's specific circumstances (1) when developing a discontinuation process specific to its organization, and (2) in meeting any applicable legal and regulatory requirements.

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

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Introduction

For purposes of this Guide, "discontinued products" are defined as authorized commercial biotechnology-derived plant products[1] that have reached the end of their commercial life cycle and all sales of materials under the organization's control[2] have been terminated globally. This situation is separate and distinct from product recall and product withdrawal. The decision to discontinue a product is a strategic business decision that should consider many factors, including regulatory requirements, channel aspects, market dynamics and product replacement. Discontinuation is the final phase of the product life cycle. Discontinuation may be made up of a group of geography-specific discontinuations each with unique timelines that are coordinated to result in global discontinuation of a product.

The objectives of a global product discontinuation are to eliminate product inventories and prevent future market exposure to the discontinued product through the organization's research, development and/or commercial activities. Product discontinuation is a process wherein sales of the commercial product(s) are terminated and includes the following general considerations:

- Identification of product(s) to be discontinued and the geographies in which there may be development, production and/or commercialization of the product(s)
- Determination and coordination of discontinuation timelines for each respective geography
- Determination of how to handle agreements including licensing agreements (e.g., terminate, allow to run to completion)
- Compilation of type of regulatory authorizations and timing of re-authorizations including need for maintenance of authorizations beyond discontinuation, if applicable
- Country-specific tolerances for presence of the discontinued product(s) in commercial grain and processed fractions
- Varietal de-registration/de-listing, where applicable
- Cessation of research and development efforts, if applicable
- Cessation of commercial seed production, distribution and sales for the product(s)
- Utilization of commodities and their processed fractions through usual channels for end-use and consumption
- Identification and disposition of product inventories (internal and external)
- Application of appropriate quality management procedures designed to minimize the presence of the discontinued product in other products
- Communication of discontinuation to key internal and external stakeholders
- Retention of product-related documentation (e.g., molecular characterization, product information) generated throughout the product life cycle
- Documentation and verification of the discontinuation process

[1] Although this Guide refers to seed product and grain, the guidelines are applicable to other biotechnology-derived plant products. However, this Guide is not intended to address conventional varieties.

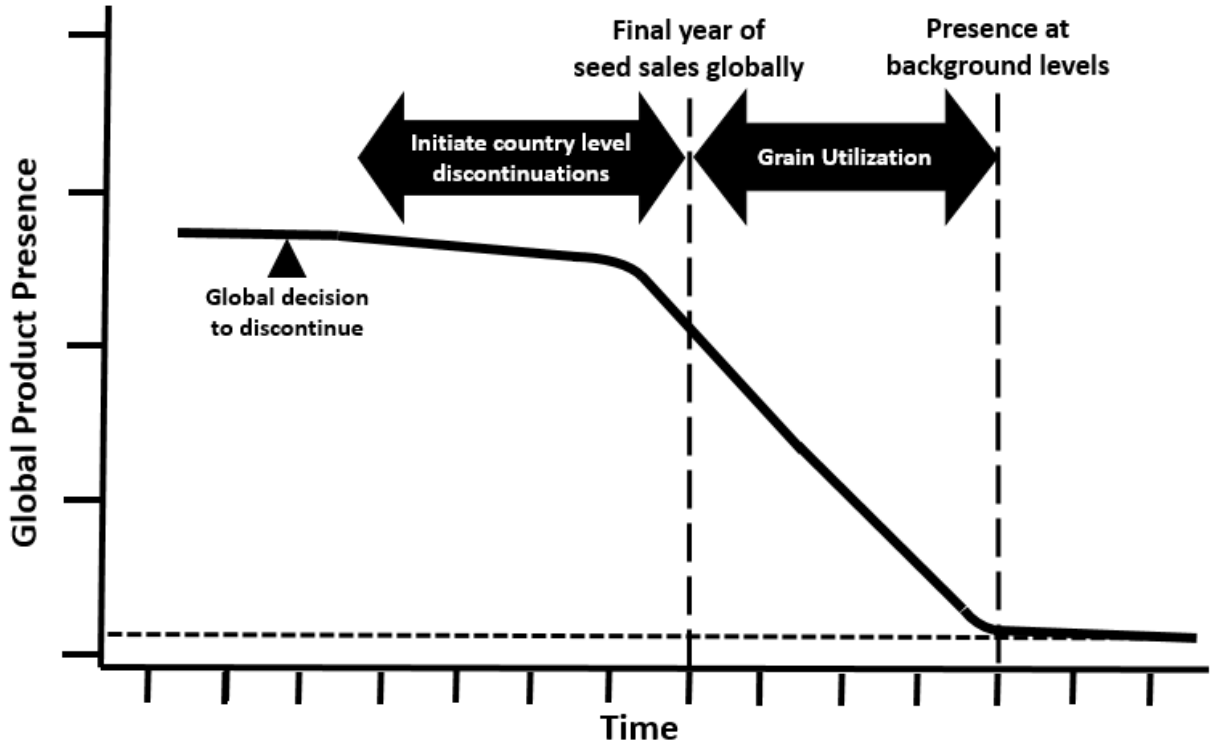
[2] Refers to materials and activities under control of the organization conducting the discontinuation and its licensees.

Discontinuation of a product may be straightforward, such as one product with limited sales in a single geography, that is not licensed to others and whose event(s) is not present in other products. Other product discontinuation scenarios may be more complex, however, and may include a combination of the scenarios below:

- One or more commercial products are being discontinued
    - A specific product that contains one or more events that:
        - Are in no other products, research or development materials
        - Are in other products, research or development materials (from the same and/or different crop) that are not being discontinued
    - All products that contain one or more events are being discontinued (i.e., the event(s) is being discontinued)
- Presence of the product (research, development, production, commercial sales, import) being discontinued in multiple geographies as well as with different levels of market penetration
- Different timing of the product discontinuation in each geography due to business needs; timing may be gradual with product being discontinued in various markets and regions over several years
- Licensing of product or event to one or more licensees
- Different regulatory requirements in different geographies
- Timing of patent expiration(s)

Generally, an organization will initiate discontinuation planning once a business decision has been made to discontinue a product. This typically occurs several years prior to the date of last sale. During this time, it is important to develop a global strategy including identifying the product(s) to be discontinued and establishing the timing of the discontinuation in each geography.

The graphic below depicts an example of the potential dynamics of a global discontinuation of a product. The level and length of time that a product may be present in the grain channel will vary depending on the type of crop and market factors. Such variables should be taken into consideration during establishment and implementation of a global discontinuation plan.



Product Discontinuation Process

An overview of the process flow for discontinuation of a biotechnology-derived plant product is in Appendix A. This process flow provides a high-level overview of key steps in the global product discontinuation process.

The product discontinuation process can be divided into four main steps:

1) Decision to Discontinue
2) Formation of Discontinuation Team
3) Development and Implementation of Global Discontinuation Plan (Note: Geography-specific plans may be included)
4) Verification and Communication of Completion of Discontinuation

Process Steps

1) Decision to Discontinue

a) Decide to discontinue product.
b) Define scope of the discontinuation and the product lines affected.
c) Identify geographies where discontinuation activities will need to occur.
d) Establish timing for completion of the global discontinuation.

2) Formation of Discontinuation Team

The Discontinuation Team is usually responsible for developing and implementing the Product Discontinuation Plan. In addition, its role typically includes monitoring and updating the Plan, and evaluating the impact of potential delays or changes to the Plan (e.g., a delay in utilization of seed stock or grain could impact decisions regarding regulatory authorizations and messaging to stakeholders). Verifications/reviews/audits should be conducted by the team or their designees so the desired endpoints are reached and the documentation is available to support the activities conducted. Once the product discontinuation is complete, the team should remain "on-call" to support any remaining discussions with stakeholders (e.g., regulators, grain trade) and to answer any inquiries or address any reports of potential remaining discontinued product.

a) Select a leader with appropriate breadth of experience.
b) Define representation on the team. This will be determined by the scope and complexity of the discontinuation. Key functional areas to be considered include, but are not limited to breeding, commercial, communications, legal, licensing, production, quality, regulatory, research, stewardship, supply chain, government affairs and public affairs.
c) Verify geographies impacted; define regional or local sub-teams, if needed.

3) Development and Implementation of Global Product Discontinuation Plan

The Global Product Discontinuation Plan is an important document for coordination of the discontinuation process and includes key actions and deliverables, timelines and responsibilities. Based on the scope of the Product Discontinuation, the Global Product Discontinuation Plan should address geography-specific and function-specific needs, enabling alignment throughout the discontinuation process. The Discontinuation Plan should be reviewed and updated as appropriate during the product discontinuation. Key components that should be included within a Global Product Discontinuation Plan are:

a) Define product(s) that is in scope.
b) Define product distribution, timelines and endpoints (e.g., final sales) by geography including allowable disposition of inventories (e.g., unsold product, breeding, development, production, third party, licensees).
    i) Third Party and Licensee considerations:
        (1) Identify all affected contracts, licenses, and sub-licenses for development and commercialization activities.
        (2) Retain records of communication wherein affected third parties and licensees were informed of the intent to discontinue the product.
        (3) Establish a discontinuation plan with third parties and licensees, appropriate to their situation, including stipulation of any actions, evidence, and documentation required to verify completion of product discontinuation.

ii) Identify seed inventory, phase-out and disposition requirements.

Identify existing internal and external seed stocks including development, breeding, and commercial seed. Inventory tracking and shipping databases are useful tools to help identify seed material and seed stocks within the organization. The Global Product Discontinuation Plan should provide guidance regarding required disposition and recordkeeping for each type of material, as well as the timeline for disposition. Each seed source should be evaluated to determine what should be retained, utilized, or destroyed. The volume of material stocks and their disposition timing should be considered in developing the proposed discontinuation plan and timeline. Following is a list of the possible areas where seed stocks may be located:

(1) Internal to the organization:
    (a) Research facilities
    (b) Greenhouse facilities
    (c) Breeding locations
    (d) Testing laboratories
    (e) Seed archives
    (f) Seed storage facilities and commercial warehouses
    (g) Regulatory laboratories/storage facilities
    (h) Contra-season nurseries
    (i) Production sites
(2) External to the organization:
    (a) Academic institutions – breeders, researchers
    (b) Cooperators
    (c) Contract Research Organizations
    (d) Third party archives/repositories for seed/trait
    (e) Licensees and licensors
    (f) Distributors and dealers
    (g) Growers
    (h) Seed tollers (i.e., 3rd party producers)
    (i) Testing facilities
    (j) Government agencies

iii) Cease Research, Development, Breeding and Production activities.

(1) Inform all research and development, breeding and supply chain functions of decision to discontinue the product and provide the timeline. Include external groups who may have materials in the appropriate communications.
(2) Establish, as appropriate, product replacements in breeding programs for all lines intended for future development.
(3) Modify and/or adapt production plans as needed.
(4) Document and implement adequate equipment cleanout for equipment used to process/handle the material being discontinued.

(5) Confirm detection method(s) are available and used in the seed quality management program to confirm, as necessary, absence of discontinued products from ongoing research, breeding, pre-commercial, and/or commercial materials.

iv) Utilize and/or dispose of excess materials and seed stock.

(1) Determine appropriate means of utilization and/or disposition[3] of excess materials and seed stock. Factors such as local regulatory requirements, commercial considerations, licensing agreements and timing may influence the methods of utilization and/or disposition. Common practice is to utilize materials via normal channels. Where this is not possible because of regulatory, customer, or stakeholder considerations, the appropriate means of destruction (e.g., autoclave, incineration, landfill) should be defined. Treated seed may require special considerations.

(2) Determine the need for and identify reference material and retained/reference samples.

(3) Once the appropriate means of utilization and/or disposition is determined, clearly communicate this information along with specific directions to the relevant personnel in a timely manner.

(4) Sell product inventories, where applicable, and track remaining inventory. Record date of last sale.

(5) Collect and dispose of remaining excess materials and seed stocks. (Note: Unsold treated seed may require special handling.)

(6) Archive examples of packaging; dispose of remainder of unused packaging and labels.

(7) Maintain documentation of disposition and/or destruction, where applicable.

c) Define regulatory needs, including re-authorizations throughout the discontinuation and beyond, as appropriate.

i) Review regulatory status of relevant products.[4]

(1) Evaluate the regulatory status of relevant countries for development, production and commercialization activities, as well as those impacted in the commodity trade channel.

(2) Evaluate each country's regulatory requirements to define the required actions pre and post discontinuation.

(a) Some countries require authorization of a stack, whereas other countries require authorization of the individual event(s).

[3] For purposes of this Guide, the term "disposition" is the act or means of settlement of plant material. For example, return to a third party, return to the inventor, or destruction of the material.

[4] Information regarding the regulatory and commercial status of agricultural biotechnology seed products is available at: *biotradestatus.com*.

(b) In some countries, authorizations do not automatically expire, so low level presence of a discontinued product may remain fully authorized.

(c) In other countries, authorizations can automatically expire, so discontinued products may be considered as a distinct case in the re-authorization process.

(d) In countries where regulations require re-authorization, exemption from new data requirements should be considered for discontinued products.

(3) Evaluate what regulatory authorizations need to be maintained post-patent due to organization's commitments (e.g., The AgAccord in the US).

ii) Develop regulatory plan regarding import, food, feed, and cultivation approvals.

(1) Give close consideration to any countries that have time-limited authorizations, and facilitate renewals of authorizations as appropriate.

(2) Consider the nature of the product authorizations and whether other organizations are selling and marketing the product without the initial registrant's approval.

(3) Consider measures to address any tolerance levels for low-level presence in seed and grain.

iii) Retain appropriate inventories of materials to serve as reference samples and make available, as appropriate, for verification purposes or stakeholder requests.

iv) Notify government regulators of the formal discontinuation decision and address regulatory requirements, as applicable.

d) Define communication strategy and develop communication plan for internal and external stakeholders.

The Global Product Discontinuation Plan should include a communication strategy that addresses communication needs for key internal and external stakeholders during the discontinuation process.

i) Identify key stakeholders, both internal and external, including groups such as direct customers, licensees, commercial partners, regulatory agencies and downstream stakeholders (including the food and feed industry) and determine levels of communication required during the discontinuation process.
ii) Provide appropriate information regarding the discontinuation plan, geographies and timelines to help achieve global discontinuation (including a reminder that discontinuation is the final phase of the product life cycle).
iii) Engage stakeholders according to their needs and concerns through dialogue and updates. Use appropriate communication tools, such as: computer databases, telephone, email, websites, trade press and media releases.
iv) Communicate the product replacement plan, if applicable.

v) Communicate deregistration of varieties and hybrids, if applicable.

e) Develop strategy to address adventitious or low-level presence, based on country-specific requirements.
   i) Understand country-specific allowances and update specifications to address presence of product/event as adventitious presence or low level presence.
   ii) Define allowances and establish quality management practices.
   iii) Determine needed changes to current quality management systems, including testing specifications and critical control points.

   Across the research, development, breeding and commercialization processes:

   i) Verify critical control points are defined and established and assign responsibilities for quality management.[5]
   ii) Establish appropriate thresholds and quality control procedures that will detect the discontinued event with appropriate specificity, sensitivity and reliability during an appropriate length of time.
      (1) Define appropriate test methods for verification purposes to be used during the discontinuation process.
      (2) Monitor output from this quality control system.
      (3) Follow up on any unexpected findings with remedial actions to:
         (a) Identify and contain materials as needed.
         (b) Appropriately dispose of materials.
         (c) Identify source(s) and implement measures to minimize reoccurrence.

f) Ensure availability of detection method(s) and reference materials (e.g., seed, protein)

g) Define documentation requirements

   Recordkeeping is an important part of a product discontinuation. It is important to identify what records (such as material disposition or testing) must be retained, along with appropriate record retention requirements.

   Examples of records that may need to be maintained include:

   i) Records related to inventory depletion, date of last sale, and disposal records[6]
   ii) Internal and external databases/website listings[7]
   iii) Third-party agreements and termination documentation
   iv) Detection methods
   v) Stewardship-relevant documents (e.g., instructions, decision records, seed quality control records)

[5] Refer to the *Guide for Maintaining Plant Product Integrity of Biotechnology-Derived Plant Products* available at www.excellencethroughstewardship.org for more information on quality management practices.

[6] The ETS website provides example forms for ETS members.

[7] External databases and websites such as *biotradestatus.com* should be updated to reflect the current regulatory and commercial status of agricultural biotechnology seed products.

vi) Regulatory documents

vii) Documents supporting internal verification process

viii) Discontinuation Team-relevant documents (e.g., membership, decision records, Discontinuation Plan, summary report)

h) Develop the strategy for verification of product discontinuation

It is important to verify that the product has been successfully discontinued and that the process has been documented. The discontinuation plan should provide details about the scope of auditing or verification, which may include management system reviews, audits of records, site inspections, or use of third party inspectors, to verify the product has been discontinued.

The verification plan should address both the organization and licensees or other partners. Product discontinuation is typically a multi-year process, and so it is important to define audit or verification processes throughout the discontinuation process.

Examples of items to verify include:

i) Documentation of utilization and/or disposition of seed stock

ii) Licensee documentation of product discontinuation

iii) Archival of quality records

iv) Archival of regulatory documents, as appropriate

v) Update of external databases/website listings

vi) Archival of stewardship-relevant records

4) Verification and Communication of Completion of Product Discontinuation

The discontinuation process is often complex, involving many materials, locations, and actions. When all materials have been appropriately disposed, the following actions will help verify and communicate completion of the product discontinuation:

a) Review product discontinuation plan and verify that important actions have been completed and documented.
b) Verify that planned audits have been completed and findings have been addressed. A final audit of facilities, records and other relevant materials may be completed.
c) Archive appropriate records.
d) Prepare summary report of product discontinuation, including date(s) of last sale and key activities completed.
e) Communicate completion of product discontinuation to both internal and external stakeholders.
f) Identify on-call team members to address subsequent questions or potential issues.

Summary

The discontinuation process outlined in this document should be adapted to the specifics of the organization and the biotechnology-derived plant product(s) involved. Completion of the discontinuation in an efficient and timely manner is achieved through establishment of a Product Discontinuation Team, who align and oversee the process. Dialogue among registrants, government regulatory authorities, relevant government trade authorities, licensees, the value chain, and other stakeholders supports successful discontinuation of a biotechnology product.

Appendix A

Process Flow for Discontinuation of a Biotechnology-Derived Plant Product