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Performance Criteria for Evaluating Regulatory Systems that Oversee Approvals of Biotechnology-Derived or Genetically Modified Crops

Summary

This document defines performance criteria that can be applied to government regulatory systems overseeing approval of biotech or genetically modified (GM) crops, focusing on the regulation of food, animal feed, and processing.

In the spirit of dialog and seeking continuous improvements for the benefit of all stakeholders, CropLife International offers these criteria to evaluate performance of regulatory systems and highlight opportunities for regulatory authorities to better meet the needs of agricultural stakeholders while ensuring comprehensive safety assessments.

Introduction

Crops developed using modern biotechnology (often called GM crops), by various public- and private-sector entities, have been commercially grown for two decades in the Americas, Asia, Africa, and Europe. GM crops have been one of the most rapidly adopted technological innovations in agricultural history; adoption rates exceed 90% in many countries. These crops have been grown and consumed without any incident impacting human or animal health, or environmental safety. Countries that have adopted wide-scale commercial use of GM crops are often able to produce more than needed to satisfy domestic demand. This allows such countries to export agricultural products to meet the demands of industries and consumers in countries that are not self-sufficient for certain commodities.

The number of GM crops at the commercial cultivation, pre-commercial or regulatory review stages more than doubled between 2008 and 2014[1]. There is an increase in development of new types of traits (e.g., quality, biofortification) and traits in new and specialty crops (e.g., rice, potatoes, sugarcane, beans). Increasingly, traits are being developed in emerging countries such as Brazil, China, India, and several African countries.

Regulatory Systems for GM Crops

Prior to regulatory approval, GM crops are subject to a comprehensive evaluation of their safety in agricultural environments and for their use as food and feed, and in processing. Countries that are major importers of agricultural products derived from GM crops, principally in Asia and Europe, have developed regulatory systems to assess the safety of these products before they can be imported and consumed. For each country, these safety assessments are generally repeated and conducted independently of related assessments by regulatory authorities in other countries, thereby missing the opportunity to leverage evaluations across countries that follow similar risk assessment approaches.

While the general risk assessment approach is similar between countries, the specific data inputs required/requested to conduct a risk assessment, and the length of time that assessment process takes, vary widely between countries. Some regulators are able to complete their assessments in timeframes measured in months, while in some countries the process can take three to five years or even longer. This

[1] Parisi, C.; Tillie, P.; Rodríguez-Cerezo, E. The global pipeline of GM crops out to 2020. *Nature Biotechnology* 34, 31–36 (2016) doi:10.1038/nbt.3449

contributes to asynchronous regulatory approvals between countries that produce and import GM crops. Regulatory asynchrony can delay access to new technologies by farmers, resulting in negative economic, environmental, and food security impacts in both producing and importing countries. Regulatory costs and delays may also discourage development of technologies that would provide benefits for specialty crops or traits that may have more limited markets, especially by public-sector scientists and for humanitarian projects.

Benefits

Quality regulatory systems for GM crops deliver significant benefits to their stakeholders, including consumers, farmers, public- and private-sector crop developers, and international traders and shippers of food and feed commodities:

1. **Safety** – Regulatory systems provide oversight of biotech products and ensure the products meet safety standards for human and animal health and the environment, as appropriate.
2. **Globally Consistent Safety Standards** – Internationally consistent safety standards facilitate shared risk assessment resources by regulatory authorities around the world.
3. **Innovation** – Improved products are made available to farmers and consumers earlier.
4. **Decreased Public Costs** – Costs to the public decrease by eliminating redundant regulatory activities, resulting in more cost-effective food production.
5. **Trade flow** – Minimizing asynchronous regulatory approvals minimizes chances for trade disruption.

Best Practices

Based on two decades of global regulatory experience, an empirical assessment of the characteristics of high-performance regulatory systems can be made. High-performance regulatory systems for GM-crop share the following attributes:

1. Risk-based data requirements
2. Science-based decisions
3. Timeliness and efficiency
4. Transparency and predictability
5. Intellectual property protection for regulatory data and materials to encourage innovation

Specific criteria to achieve each of these attributes are explored in more depth in the Appendix.

Conclusions and Recommendations

Retrospective analysis has become an important tool to improve regulatory system performance by using historical knowledge to identify areas of existing regulations that are outmoded, ineffective, insufficient, or excessively burdensome, and subsequently to propose ways to modify, streamline, expand, or repeal them in accordance with what has been learned[2]. This analysis is particularly valuable for fields where the amount of scientific and empirical information available has changed significantly. The regulatory

[2] Obama, B. Executive Order 13563 – Improving Regulation and Regulatory Review (2011), https://www.whitehouse.gov/the-press-office/2011/01/18/executive-order-13563-improving-regulation-and-regulatory-review

oversight of GM crops is one such field. Since the first large-scale introduction of GM crops in 1996, there has been a vast accumulation of experience with risk assessment and regulatory processes for GM crops. This experience can be used to identify those attributes of regulatory systems that, while ensuring human and animal health and environmental safety, enable other public policy goals, such as food security, to be met.

Due to this 20-year experience and familiarity with GM crops, CropLife International believes it is time for policy makers and regulators to assess their existing regulatory systems to ensure the framework appropriately evaluates safety while balancing the needs of agricultural stakeholders and maximizing the overall benefits to society.

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Appendix

1. Risk-based Data Requirements

CropLife International believes there are four key criteria for risk-based data requirements:

1. Data requirements for assessing food, feed, and processing (FFP) safety are distinct from data requirements for assessing cultivation safety.
2. Redundant local studies are not required for FFP safety assessment.
3. Stacked-trait products developed through conventional plant breeding do not require additional safety data without a sound scientific basis.
4. Additional data requests are based on specific and well-defined scientific hypotheses.

Distinction made between data required to support FFP and cultivation uses

The Cartagena Protocol on Biosafety[3] makes a clear distinction between products intended only for FFP and those also intended for release into the environment (e.g., as seeds). The Protocol establishes a simplified procedure for FFP uses, recognizing the limited environmental exposure. Regulatory systems, particularly environmental risk assessments, should reflect the different potential for environmental exposure between FFP and cultivation uses.

No additional local studies required for FFP applications

Local *laboratory studies* (e.g., animal feeding studies), particularly those that duplicate high-quality laboratory studies conducted in other countries, cause unjustified delays in regulatory review in importing countries. Similarly, local *field studies* are unwarranted in importing countries when products are intended only for FFP use, as these duplicate high-quality field studies conducted to support the authorization of crop cultivation in countries where the products are intended to be grown.

No additional data required for stacked-trait products developed through conventional breeding

Conventional plant breeding, which generates new combinations of genes, has a long history of safe use. There are no indications that combining genes from previously approved biotech products introduces new safety hazards. Regulation of stacked-trait products for FFP applications is scientifically unjustified without a credible hypothesis as to why specific transgenes or transgenic traits would interact to cause an adverse effect with greater risk than combinations with (and among) non-GM traits or genes.

Hypothesis-based requests for additional data

[3] The Cartagena Protocol on Biosafety [http://bch.cbd.int/protocol] is an international agreement (treaty), concluded and adopted in the framework of the Convention on Biological Diversity (CBD). The Protocol is called the Cartagena Protocol on Biosafety after the city in Colombia where it was originally scheduled to be concluded and adopted. The final text of the Protocol was agreed upon in January 2000 in Montreal and it entered into force on 11 September 2003.

Data required for risk assessment purposes must be based on clearly defined risk assessment endpoints, address scientific hypotheses, and consider both hazard and exposure. Requested information should be limited to that required to decide that there is a reasonable certainty of no harm and not for other purposes (e.g., to help defend regulatory decisions publicly or politically, or to address the scientific curiosity of regulatory experts). Conclusions of risk assessments should be based on the weight of evidence and, when that weight is sufficient, no new data should be required (e.g., to meet a local data requirement where existing data are sufficient to conclude a reasonable certainty of no harm).

2. Science-based Decisions

CropLife International believes that there are four key criteria for science-based decisions:

1. Risk assessment guidelines are established by scientific experts with risk assessment expertise.
2. There is no political intervention in the risk assessment processes.
3. The product approval process does not conclude with a political decision.
4. Mandatory post-market monitoring is not required unless clearly based on risk.

Risk assessment guidelines established by scientific experts

To ensure science-based risk assessment, data requirements should be established by scientific experts experienced in risk assessment and not by administrative authorities.

No political intervention in risk assessment processes

Risk assessment should be based exclusively on science and not subject to intervention by administrators or political influences.

Product approval process does not conclude with a political decision

Regulatory approval processes that end with a political decision have proven to be strongly influenced by shifting political biases, and have the potential to violate international obligations such as those under the World Trade Organization (WTO). Political intervention at the stage of decision making on individual products also undermines the credibility of a regulatory process, suggesting that a safety outcome is politically rather than scientifically determined.

No mandatory post-market monitoring requirements unless they are clearly risk based

Post-market monitoring requirements for products approved for FFP purposes are only appropriate when the risk assessment has identified a specific risk that justifies further monitoring (e.g., to assess whether assumptions in the risk assessment remain valid or to verify that risk management measures are being effectively implemented).

3. Timeliness and Efficiency

CropLife International believes that there are seven key criteria for timeliness and efficiency of regulatory processes:

1. There is no duplication of risk assessments.

2. Conventional breeding stacks of approved GM traits for FFP uses are not subject to further regulatory review unless there is a scientifically credible hypothesis for adverse effects.
3. Efficient review and decision-making processes are in place.
4. Defined timelines and processes are adhered to by regulators.
5. Authorizations are not time-limited.
6. Streamlined risk assessments are conducted for familiar traits and crops.
7. Public consultation is focused on scientific safety-related reviews.

No duplication of risk assessments

There is considerable commonality in the information regulatory authorities require to assess risk for FFP (import) uses (e.g., molecular characterization, protein expression, compositional equivalence). Regulatory processes that duplicate the review of this common information are inefficient and contribute to unnecessary delays in regulatory decision making.

No regulation of conventional breeding stacks of approved component GM traits

An increasing proportion of new products being commercialized contain approved stacked traits combined by conventional breeding. Not only is the regulation of most breeding stacks unjustified scientifically (see number one above), it absorbs an increasing amount of regulatory capacity and consequently causes unwarranted delays in the risk assessment of new single-trait products. Further, some regulatory systems also regulate intermediate combinations of multi-trait stacks that are not commercial products as such, and for which the safety assessment of the component single traits, combined with that of the highest-order stack, ensures the safety of such combinations. Only breeding stacks for which a scientifically credible argument can be made for possible adverse effects warrant further safety assessment.

Efficient review and decision-making processes

Regulatory systems should be designed and implemented in such a way as to avoid undue delay in risk assessment or decision making. Some examples of inefficiencies in regulatory systems include: duplication in the risk assessment; unnecessary multi-step sequential processes for risk assessment or decision making; requirements for prior country-of-origin approvals; multiple authorities accountable for decision making; and abuse of stop-clock procedures, which halt the review process while the applicant responds to requests for more information. Simplification of these processes and elimination of redundancies could significantly reduce the undue delays that result from these procedural inefficiencies without weakening the risk assessment.

Defined timelines and process adherence by regulators

Statutory timelines, established by legislative processes, should not be ignored. Regulatory systems should be resourced to ensure that statutory review timelines are complied with. For those regulatory systems that require evaluation of additional data, adequate resources should be provided by governments to avoid undue delays.

Authorizations should not be time-limited

Some countries issue time-limited authorizations, in some cases for as little as three years. Renewal of authorization generally requires a re-assessment of safety, usually according to updated guidance requirements, while ignoring the (positive) history of safe use during the period

of commercial use, and despite ongoing obligations on applicants to notify regulators of any new scientific information indicating adverse effects. The need for re-authorization contributes unnecessarily to regulatory capacity challenges. If new information regarding product safety comes to light, regulators retain the option to initiate a new risk assessment or even cancel an existing authorization.

Streamlined risk assessment for familiar traits and crops

Many new products currently subject to regulatory oversight are similar to previously approved products. For example, familiar traits/protein classes (e.g., *Bt* or herbicide tolerance proteins with well-established modes of action and safety) and crops (especially those known not to exhibit weediness characteristics) should be subject to simplified risk assessment and review processes.

Public consultation must be focused on scientific review

Some regulatory systems use a public consultation process to seek additional input on scientific risk assessments. In such cases, regulators should strictly delineate input that provides new insights on the scientific risk assessments separately from that which is a non-scientific expression of preference. Regulators should ensure that a public consultation process does not impact defined timelines for risk assessment and decision making.

4. Transparency and Predictability

CropLife International believes that there are four key criteria for transparency and predictability of regulatory processes:

1. Pre-submission consultations are permitted.
2. Post-submission dialogue between applicants and regulators is encouraged.
3. Data requirements are clearly defined and consistent over time.
4. New data requirements are not applied retroactively.

Pre-submission consultations are permitted

Pre-submission consultations between applicants and regulators provide an opportunity for applicants and regulators to align on the appropriate data to be generated to demonstrate product safety prior to regulatory submissions. This can avoid subsequent delays in risk assessment and decision making. Some regulators are averse to such pre-submission consultations to demonstrate "independence" whereas others are able to engage in dialogue while maintaining independence.

Post-submission dialogue between applicants and regulators is encouraged

Dialogue between applicants and regulators to address regulators' questions is essential for applicants to fully comprehend regulators' uncertainties and to facilitate comprehensive responses.

Data requirements are clearly defined and consistent over time

Case-by-case risk assessment is important for both applicants and regulators to adapt risk assessment to the characteristics of individual products. Notwithstanding this, predictability in basic data requirements and study protocols is essential for applicants to be compliant with regulatory requirements.

No retroactive application of new data requirements

Amendments to data requirements, particularly for long-term studies (such as field trials or animal feeding studies), and especially retroactive data requirements, lead to significant and avoidable delays in risk assessment and product approvals. Quality regulatory systems provide

consistency in data requirements and appropriate transitional arrangements in the event that data requirements are amended or changes in interpretation of existing requirements are instituted.

5. Intellectual Property Protection for Regulatory Data and Materials

CropLife International believes that there are three key criteria for protection of intellectual property:

1. Claims of confidential business information (CBI) are allowed.
2. Non-CBI regulatory data are protected from unauthorized use.
3. Biological materials are protected from unauthorized use.

Allowance of confidentiality claims

Legislation in some countries recognizes the importance of confidentiality of regulatory information to protect the intellectual property of applicants. Confidentiality of sensitive regulatory information is important to protect information subject to pending patent applications, encourage innovation, and to protect the privacy of scientists involved in risk assessment.

Regulatory authorities should clearly define what constitutes CBI, how it should be identified within applications, and how the information should be stored. They should write their evaluations in a way that does not disclose CBI.

Protection of non-CBI regulatory data from unauthorized use

Protecting the data that are used as part of the regulatory review and authorization process for plant biotechnology products is an essential part of encouraging on-going investment in plant science innovation and stimulating continued research and development. Both Article 39 of the WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)[4] and Article 21 of the Cartagena Protocol on Biosafety[5] provide protection against the disclosure and unfair commercial use of regulatory data.

Regulatory authorities should ascertain that no proprietary information is used in product applications without legitimate access or ownership.

Protection of biological materials from unauthorized use

Some regulatory systems require applicants to provide biological materials, such as seed, to regulators for the purposes of developing detection methods or for generating reference materials for detection method development. Such requirements risk abuse of the intellectual property rights of product developers and also pose liability concerns for developers in the event of improper stewardship of the materials.

[4] https://www.wto.org/English/docs_e/legal_e/27-trips_04d_e.htm
[5] http://bch.cbd.int/protocol/background/