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Review

Plants with genetically modified events combined by conventional breeding: An assessment of the need for additional regulatory data

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ABSTRACT

Crop varieties with multiple GM events combined by conventional breeding have become important in global agriculture. The regulatory requirements in different countries for such products vary considerably, placing an additional burden on regulatory agencies in countries where the submission of additional data is required and delaying the introduction of innovative products to meet agricultural needs. The process of conventional plant breeding has predictably provided safe food and feed products both historically and in the modern era of plant breeding. Thus, previously approved GM events that have been combined by conventional plant breeding and contain GM traits that are not likely to interact in a manner affecting safety should be considered to be as safe as their conventional counterparts. Such combined GM event crop varieties should require little, if any, additional regulatory data to meet regulatory requirements.

Contents

1. Introduction

Since first commercialized in 1996, genetically modified (GM) crops have established a record of food, feed and environmental safety. From a food and feed safety perspective, they have demonstrated to be at least as safe as products produced by conventional

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methods (Lemaux, 2008; Cockburn, 2002). From an environmental perspective, they can have impacts that are substantially lower than for conventionally produced products (Lemaux, 2009).

The GM crops that obtained early commercial success provided herbicide tolerance or insect protection (e.g., MON-Ø4Ø32-6 soy and SYN-BTØ11-1 maize), but generally did not combine these benefits in the same plant. The current trend, however, is to combine or 'stack' two or more single GM events to provide growers with a combination of traits that increase flexibility and improve performance. Most often, conventional plant breeding is used to combine GM events and in the past several years, multiple new combined GM event crops have been commercialized globally (James, 2007; James, 2009).

Prior to commercialization, crops containing new GM events are subject to stringent regulatory testing, and must satisfy requirements that are more demanding than those applied to crops developed through conventional breeding (Bradford et al., 2005; NRC, 2004). However, there currently is no global consensus for the regulation of crops with GM events that have been combined by conventional breeding. Consequently, individual regulatory agencies have devised their own requirements, and requested data packages may range from minimal to extensive. Additional regulatory requirements that are not based on science- and risk-based safety concerns further lengthen the review process, place an additional burden on regulatory agencies, and delay introducing innovative products to the grower.

In this paper, the current regulatory landscape for combined GM events is described. This is followed by a review of conventional plant breeding as it relates to combined GM event products, and a review of the safety assessment process applied to single GM event products. Then, the safety of combined GM events is discussed, considering the safety of the process used to create them as well as the results of additional data on combined GM events, given that these are required by some countries. Finally, based on the information described and reviewed, the scientific basis for regulatory data required for combined GM event products is evaluated and reasonable data requirements, consistent with this scientific basis, are proposed.

2. Definitions and scope

It is important to understand the difference between the terms GM trait, GM event and GM crop as they are used in this paper. A GM trait is a phenotypic characteristic expressed from DNA inserted into the plant genome during the transformation process. A GM event is defined by the insertion of DNA into the plant genome as a result of a single transformation process. Multiple DNA sequences may be inserted during a single transformation process. Thus, a single GM event may be characterized by the expression of one or more GM traits. A GM crop is one that contains one or more GM events, and phenotypically expresses one or more GM traits.

Combined GM trait products (also referred to as 'stacks' or 'pyramids' in the literature [De Schrijver et al., 2007]) may be produced using two broad approaches: (1) by conventional plant breeding, where parents with single GM events are bred to produce progeny with the combined GM events; or, (2) by molecular-based methods where two or more traits are simultaneously or sequentially transformed into a recipient crop. There are multiple ways by which the molecular-based methods can be employed to produce a crop with multiple traits (Halpin, 2005; Taverniers et al., 2008).

There are also important differences resulting from GM events combined using conventional breeding compared to molecular-based methods. Most importantly, using conventional breeding to combine GM events does not involve the transformation process; does not insert additional DNA into the genome; and does not modify the existing genomic DNA. Based on these criteria, GM events combined through conventional breeding do not constitute a new GM event. Similarly, a combined GM event product is not considered a new genetically modified organism (GMO), as defined by EU Directive 2001/18/EC (EC, 2001), nor a new living modified organism (LMO), as defined in the Cartagena Protocol on Biosafety (SCBD, 2000). Additionally, according to rules established by the Organization for Economic Cooperation and Development (OECD, 2006), each commercial transformation event is assigned a nine-digit alphanumerical unique identifier. However, a new crop variety developed from GM events combined by conventional breeding is not given a new nine-digit alphanumeric OECD unique identifier; rather, the single GM event identifiers are used together to designate the combined GM event product.

This paper focuses on combined GM event products produced through conventional plant breeding (hereafter referred to as "combined GM events"), and is limited to GM events containing genes that are not likely to interact in a manner affecting safety. The discussion of trait interaction is complex. Traits that do not interact function independently and do not exhibit synergism, potentiation or antagonism. The GM events considered in this paper are unlikely to interact in a manner that affects safety, as they either, (a) do not share the same metabolic intermediates and are not in the same metabolic pathway, or, (b) exhibit mechanisms of action that are distinct on a biochemical or cellular level. An example of combined GM events in the first category is provided by combining herbicide tolerance (e.g., from CP4 EPSPS protein expression) and insect protection (e.g., from CRY1Ab protein expression). An example of combined GM events in the second category is multiple insect protection through the expression of two different CRY proteins with specific molecular targets to protect against both coleopteran (via CRY3Bb protein expression) and lepidopteran pests (via CRY1Ab protein expression). Based

Table 1
Global data requirements for combined GM events. The information below describes the current, though fluid, status of data requirements and review complexity for combined GM events globally. All countries base their review on the approved single events. For those countries with additional data requirements (right side of table), the amount of data and the complexity of the review process varies greatly. The relative position in the table for any individual country requiring additional data (see examples, lower, right) is not meant to indicate their position in the continuum of relative data requirements. The European Union requirements for additional data requirements and review complexity are significantly higher than those in any other countries.

Data requirements:	
No additional data unless potential to interact	Continuum of additional data and complexity of review from: • Minimum data (confirm presence of traits/ lack of interaction) • Additional data if potential to interact • Minimum review complexity (short, defined review period) ⇩ (increasing data and complexity of review) to: • Comprehensive dataset regardless of interaction potential (phenotypic characterization, molecular characterization, protein levels, morphology, nutritional composition) • Additional data if potential to interact • Complex review (undefined, protracted review period)
Country or region:	
United States,Canada, Australia/NewZealand	Mexico, Colombia, Taiwan, Philippines, Japan, South Korea, South Africa, European Union

Table 2
Guidance from international groups and agencies on combined GM events and conventional breeding.

Group or Agency	Guidance
World Health Organization (WHO, 1995)	"Progeny derived from food varieties shown to be substantially equivalent would be expected themselves to be substantially equivalent. Traditional breeding practices would be expected to reject any varieties in which the inserted trait is unstable or gives rise to adverse secondary effects." "...it is likely that additional varieties will be developed by crossing varieties, each of which was obtained by genetic engineering. For example, if substantial equivalence has been demonstrated both for a tomato with a gene producing a delayed ripening phenotype and for a tomato with a gene for herbicide resistance, then crossing these two varieties would result in a new variety that would be expected to be substantially equivalent to the parents."
Food and Agriculture Organization/World Health Organization (FAO/WHO, 1996)	"Further strains/varieties may be derived from genetically modified organisms by conventional techniques, such as traditional...plant breeding. Where the genetically modified organisms have been determined to be acceptable as a result of the safety assessment, these further strains/varieties should be assessed on their own merits according to practices applied for the assessment of conventionally-derived organisms."
International Seed Federation (ISF, 2005)	"Once a new transformation event has been determined by a recognized authority to be safe for human or animal health and the environment then plants containing it should be useable in further plant breeding and any progeny containing the same transformation event should be covered by the original commercialization approval."
Crop Life International (CLI, 2005)	"Combined trait plant biotechnology products produced by conventional plant breeding practices should be subject to the same regulatory oversight that is applied to conventional crops produced using the same techniques. Additional safety assessments should be conducted only when the traits are related, or where they affect the same metabolic pathway."

on the criteria discussion here, the majority of GM events currently on the market do not interact.

3. Current regulatory situation for combined GM events

Currently, there is no global consensus for the regulation of previously approved GM events combined by conventional breeding. For example, Codex (CODEX, 2003) provides internationally recognized guidelines for conducting food safety assessments on single GM events; however, these guidelines do not explicitly address combined GM events generated through conventional breeding. Consequently, individual regulatory agencies have devised their own requirements (e.g., EFSA, 2007; CFIA, 2004; OGTR, 2007), and requested data packages may range from minimal to extensive. Table 1 identifies those countries with no additional data requirements for combined GM events that are unlikely to interact and describes the continuum of additional data requirements and complexity of review processes for other countries requiring combined GM event review.

When assessing the safety of combined GM events, it is instructive to consider international guidance regarding conventional breeding and substantial equivalence of GM events combined by conventional breeding. For example, the World Health Organization concludes that substantial equivalence should be maintained in a combined GM trait variety if substantial equivalence had been demonstrated for each of the parents. Specifically, they argue that "...if substantial equivalence has been demonstrated both for a [genetically engineered] tomato with a gene producing a delayed ripening phenotype and for a [genetically engineered] tomato with a gene for herbicide resistance, then crossing these two varieties would result in a new variety that would be expected to be substantially equivalent to the parents" (WHO, 1995). Additional international groups, including the Food and Agriculture Organization/World Health Organization (FAO/WHO, 1996), International Seed Federation (ISF, 2005), and CropLife International (CLI, 2005) similarly advocate basing the safety of combined GM events on the safety of the parental GM events (see Table 2).

Consistent with this international guidance, regulatory agencies in some countries, including the US (FDA, 2001), Canada (CFIA, 2004), and Australia (OGTR, 2007), have requested no additional regulatory data to approve combined GM events as long as the traits are not likely to interact in a manner that would affect safety and the risk assessments of the single events can reasonably be applied to the combined event product. The FDA specifically states that "narrow crosses are unlikely to result in unintended changes to foods that raise safety or other regulatory questions" – "including narrow crosses between different rDNA-modified [GM] lines" (FDA, 2001).

Contrary to this international guidance, some propose that safety testing beyond that required for the single GM events be conducted for combined GM event product approvals (De Schrijver et al., 2007). To support the regulatory approval of combined GM events, some countries (i.e., those of the EU) have conducted complex reviews of a comprehensive additional dataset as suggested by De Schrijver et al. (2007), to document that combined GM event products are no different from the parental single GM events from which they were derived or their conventional counterparts. These additional data may include phenotypic characterization, molecular characterization, protein levels, morphology, and nutritional composition.

Other countries vary in the amount of data required to confirm that the single event assessments remain applicable to the combined event (see Table 1). Many do not consider it necessary to require the development of a comprehensive dataset, or a complex data review process, in order to conclude that the safety for the combined GM event product has not changed. It is recognized that the data generated for the parental single GM events can be used to predict the safety of the combined GM event in most instances.

4. Safety considerations

4.1. Conventional plant breeding

The history of plant domestication and plant breeding dates back approximately 10,000 years (McCouch, 2004). Plant breeding has been practiced since early humans identified seeds from the most productive plants and saved them to plant in the following growing season. The modern era of plant breeding, whose beginning correlates with the rediscovery of Mendel's work in 1900 (Duvick, 1996), has led to great success in combining desirable traits in a single crop as demonstrated by improved agronomic, quality, and/or nutritional traits. These improvements have been introduced using a variety of techniques, including hybrid breeding, introgression of traits from wild relatives, mutagenesis, wide crosses, embryo and ovule rescue, double haploid technology, tissue culture and plant regeneration, and protoplast fusion, all of which are considered routine applications of traditional plant breeding. More recently, molecular marker technology has been employed to characterize progeny and streamline the breeding process.

Conventional plant breeding predictably provides safe food and feed crops which exhibit familiar phenotypic and agronomic properties in the environment. Many traits, including disease resistance, yield, stress resistance, and quality/nutrition improvements have been introgressed from wild species through conventional plant breeding (Fernie et al., 2006; Hajjar and Hodgkin, 2007). The process of identifying traits, combining them in familiar genotypes to establish a history of safe use (Constable et al., 2007) and selecting elite performing varieties is routinely employed in plant breeding. Moreover, this approach has an impressive record of food, feed, and environmental safety, and rarely gives rise to safety concerns through unintended effects (Cellini et al., 2004).

Combining multiple approved GM events using conventional breeding to produce elite performing crops is increasingly important in global agriculture (James, 2007; James, 2009). When conventional breeding is used to generate varieties with combined GM events, these varieties are screened over multiple generations and across diverse growing environments. Typically, product performance and agronomic features are evaluated and traits such as yield, field performance, and disease resistance are measured and tested to ensure that the traits are stable, heritable, and express the desired phenotype under a wide range of environmental conditions. The phenotypic characteristics evaluated during the screening step are the expressed result of the plant's genotype and are the culmination of the complex metabolic pathways that are activated in response to environmental conditions. Phenotypic characteristics allow breeders to measure the degree to which unintended effects are produced as a result of the various traits combined in the variety. Selection during the conventional breeding process is valuable in removing undesirable characteristics and thereby helps to maintain the safety and quality of the food and/or feed product (Cellini et al., 2004; NRC, 2004; WHO, 1995). Additional evaluations or analyses may be recommended for a particular crop species that may contain a novel compositional profile or have an undesirable component (e.g., allergen, toxicant, or anti-nutrient) in a final food or feed product at a level that may be of concern. These components have been identified in various publications, for example OECD Consensus Documents (OECD, 2010). The requirements for these evaluations vary by crop and country, most often based on variety registration requirements. Breeders are aware of potential changes in composition that may arise through breeding, and strict adherence to safe breeding practices and variety requirements ensure that food safety concerns are unlikely to be repeated within the current disciplined environment.

In summary, conventional breeding is widely and routinely used to combine desirable traits in new crop varieties. Careful attention to desired phenotype, progeny selection and phenotypic performance of the resulting variety affords a significant level of risk management, thereby reducing the potential for harm to humans, animals, and the environment. With few exceptions, safe food and feed products are generated from conventional plant breeding. This approach has long been employed, and is based on the underlying premise that newly generated varieties based on existing crop varieties with a history of safe use are unlikely to produce unintended effects that would be a food safety concern. More recently, the same modern plant breeding techniques used to combine conventional traits have been used to combine GM traits produced through agricultural biotechnology.

4.2. Safety of crops with single GM events

Agricultural crops improved with a single GM event are rigorously tested according to internationally recognized guidelines (CODEX, 2003; SCBD, 2000) prior to regulatory approval and commercial availability. The development and commercialization of a new GM event occurs through a lengthy and complicated process that involves the following: (1) research to identify potentially valuable genes, (2) product concept testing, (3) multiple transformations in model and target species, (4) screening to select the best transformation event with the desired trait, (5) conventional breeding into elite germplasm, followed by field efficacy testing, (6) development of a scientifically robust safety data package, (7) submission to, and evaluation and authorization by, regulatory agencies, and (8) commercialization compliant with conditions of the regulatory approval.

The regulatory review and authorization process for GM events is more rigorous and extensive than for conventionally-bred crops with similar modifications (Bradford et al., 2005; NRC, 2004). Konig et al. (2004) noted that "It can even be argued that foods from GM crops are better characterized than other non-regulated plant derived foods, due to the additional rigour in the current regulatory requirements and testing regime compared to that for conventionally-bred crops".

Before a GM event is commercialized, it must undergo a safety review and be authorized by the relevant competent agencies under all applicable regulations. The regulatory review routinely includes assessments for food, feed, and/or environmental safety using a wide range of scientific studies that can be broadly grouped into the following categories: event/molecular characterization; trait expression/characterization; substantial equivalence; food/feed safety; environmental safety; evaluations for plant incorporated protectants (PIP), if appropriate. Some specific studies for single GM events are considered in greater detail below.

The regulatory data package developed for a single GM event provides an in-depth analysis of the transformed plant, including a description of the recipient plant, and a comprehensive molecular characterization of the introduced DNA that documents stability and heritability over several generations. Multiple datasets are available that consistently demonstrate the stable inheritance of both the introduced DNA and the associated phenotype of single GM events (Heck et al., 2005; Padgette et al., 1995). An important aspect of product characterization is the stable inheritance of GM events. Stable inheritance of the individual single GM events has been recognized as sufficient to assure the stability of these events in the combined GM event product by FAO and WHO (FAO/WHO, 1991) and more recently by the UK's Advisory Committee on Releases to the Environment (ACRE, 2007). Therefore, use of the single GM event assessment is appropriate to establish stable inheritance in the combined GM event product.

Food and feed assessments are based on a full nutritional evaluation of the GM event grown in different environments that are representative of normal cultivation conditions. Although not a specific requirement under the Codex Guidelines (see paragraph 11, CODEX, 2003), an animal study is also provided. Such a study may involve oral administration of high doses of purified protein to investigate the toxicity of the protein or whole food animal feeding with test animals such as rats or chickens to establish the nutritional equivalence of the GM food compared to an equivalent conventional feed. These evaluations, coupled with field and agronomic data, establish the safety of the introduced protein. They also help to identify potential unintended effects from the genetic modification that may impact food safety, based on comparison to existing crops or foods with a history of safe use (Cellini et al., 2004; CODEX, 2003).

Single GM event crops with traits that derive from a newly introduced protein (e.g., CRY or EPSPS proteins) are examined with regard to protein structure, function, potential toxicity, and allergenicity of the introduced protein. The characteristics of the crop and the potential environmental risk of releasing the GM event are evaluated for a range of potential environmental effects. Spe-

cific assessments include the following: agronomic and phenotypic characteristics, effects on non-target organisms, gene flow, potential increase in weediness or plant pest attributes, and stability under a range of environmental conditions.

Codex Alimentarius incorporated data requirement guidelines for the evaluation of GM products for food safety in 2003 (CODEX, 2003). Most countries requiring evaluation of GM products have used these Codex guidelines as a framework to develop their own food and feed safety data requirements. With respect to evaluating environmental risk, international guideline assessments are contained within the Cartagena Protocol for Biosafety (SCBD, 2000). Even in those countries that have not ratified the Biosafety Protocol, including the US, Canada, and Australia, similar principles to evaluate environmental risk are used. The datasets described above provide information that meets the requirements of these international guidelines.

Because food and feed crops are traded internationally, the safety of a GM event available in commerce has typically been reviewed and authorized by regulatory agencies in numerous countries. Currently, some form of regulatory review is required in the fifty-seven countries that have granted regulatory approvals for GM crops (James, 2009). These include importing countries as well as countries where the crop is cultivated. These multiple independent regulatory approvals further document the safety of the GM event.

In summary, single GM events are tested according to international guidelines that are more rigorous and extensive than those required for conventionally-bred crops with similar modifications. Data submitted for regulatory review of single GM events supports assessments for food, feed and environmental safety using a wide range of scientific studies. Multiple datasets have demonstrated the genomic and phenotypic stability and reviews by regulatory agencies for fifty-seven countries globally provide multiple confirmations of the safety of the single GM event products.

4.3. Safety of GM events combined by conventional breeding

Conventional plant breeding is routinely used to improve crop performance and is specifically employed to develop plant varieties that fit particular environments and production practices (Powell et al., 2003). Section 4.1 reviewed this process and considered its safe use in the development of food and feed products, while the following Section 4.2 reviewed the rigorous safety assessment process for single GM event products. The same biological and selective principles used for conventional and single GM event crop development are used to combine previously approved GM events. Accordingly, single GM events previously assessed as safe should be safe to combine through conventional plant breeding when they are unlikely to interact in a manner affecting safety. As a result, the rigorous safety assessments conducted on single GM events, which were deemed to be as safe as their conventional counterparts, also can be used to predict the safety of the combined GM events.

There are many commercial examples of combined GM events, and an updated list can be accessed through the Biosafety Clearing-House (BCH, 2010). The safety of commercially available combined GM events has been well-demonstrated in multiple independent reports that document the continually increased acceptance and use by farmers globally (Brooks and Barfoot, 2008; James, 2009; Lemaux, 2008; Sankula, 2006). However, regulatory agencies in some countries request additional characterization of combined GM events and comparisons to single GM parental controls and conventional comparators. These additional studies may include analysis of phenotype, molecular characteristics, protein characteristics, morphology and nutritional evaluation.

It is instructive to look at the results of the additional safety studies performed on combined GM events to consider if they confirm the safety anticipated from the same studies performed on the single GM events. Analyses of combined GM events compared to parental controls have consistently revealed the following: no phenotypic differences from parental events; molecular characteristics that are the same as parental events with all events inherited stably; protein levels comparable to the single event parents; no morphological differences compared to parental events; substantial equivalence based on nutritional evaluation, with no pleiotropic or toxic effects compared to the conventional non-GM crop. These analyses are available on public websites, including those for the US EPA (EPA, 2010), Japan Biosafety Clearing-House (JBCH, 2010) and the EU (GMO Compass, 2010). In many cases, they also provide the assessment conclusions of the appropriate competent authorities providing the regulatory approval.

The results of the additional characterizations performed on the current commercial combined event products, as described above, provide scientific documentation that combining approved GM events by conventional breeding has generated no unique safety concerns. These results also demonstrate the general observation that with respect to safety, the combined GM event product is no different than either of the single GM event parents, and not substantially different from comparator conventional varieties. Specifically, no substantiated safety concerns have been identified, nor have any adverse effects been reported, for any approved commercial combined GM event product.

In summary, the safety of combined GM event products is based primarily on the use of a safe process, conventional plant breeding, to combine single GM events that had previously been determined to be safe through the regulatory review and approval process. Thus, the data packages that had been developed for the single GM events are useful in establishing the safety of the combined event product. The results from the additional data that had been submitted to countries that require them simply confirm the safety that would be expected from the use of a safe process to combine products that had been previously determined to be safe.

5. Discussion and recommendations

The use of GM crops is the most rapidly adopted crop technology in the recent history of agriculture (James, 2008). The technology has been embraced globally, and through 2009 GM maize, cotton, soy, canola, sugar beet and alfalfa have been cultivated on almost 1 billion hectares in 25 countries (James, 2009). GM crops that obtained early commercial success provided single agronomic traits (e.g., herbicide tolerance or insect protection), but generally did not combine these benefits in the same plant. The current trend, to combine or 'stack' two or more single GM events, has provided growers with increased flexibility and improved performance. Combined trait crops are clearly preferred by growers in the US, where, in 2009, more maize acres were planted with combined GM products than the sum of conventional and single GM event products (James, 2009). Not surprisingly, this trend toward planting combined GM trait crops is becoming increasingly important worldwide, where there is global pressure to increase crop productivity to remain economically competitive and minimize environmental impacts. Over a recent three year period, global planting of combined GM trait crops increased from 11.6 million hectares (11% of total) in 2006 to 28.7 million hectares (21% of total) in 2009 (James, 2007; James, 2009).

The data and information presented in previous sections describe the safety of conventional plant breeding (Section 4.1), the regulatory review process that establishes the safety of single GM events (Section 4.2), and the basis for the safety of combining

GM events by conventional plant breeding (Section 4.3). Through a review process far exceeding that employed for crops produced through conventional breeding, the single GM event products have already passed a rigorous regulatory safety review and have established stability through conventional breeding. All this supports the position that combining previously approved, single GM events by conventional plant breeding produces combined GM event food and feed products that are as safe as the parental GM single events and their conventionally-produced counterparts. Therefore, it seems reasonable to conclude that combined GM event crops generated through conventional breeding of single GM events warrant little safety concern and regulatory requirements and procedures for GM events combined through conventional breeding should reflect the predicted safety established for the single GM events. Thus, for events or traits unlikely to interact, the data on the single GM events can be effectively 'bridged' to the combined GM event product and the safety assessments performed on the single GM event parents should be sufficient to address any regulatory questions on the combined GM event product.

Given their expected safety, combined GM event crops produced through conventional breeding should be subject to little, if any, regulatory data requirements beyond the safety assessments and/or approvals of the single GM events. Thus, the regulatory approaches taken by those countries that do not require additional data for combined GM events (i.e., US, Canada, Australia/New Zealand) are scientifically justified. For regulatory agencies that desire confirmatory information, data that demonstrate the presence of the GM events and support lack of GM trait interactions affecting safety or efficacy of the product may be reasonable. These data may include greenhouse or field bioefficacy studies, gene or protein expression levels, and/or relevant composition analyses on the combined GM event product. Additional studies would be warranted if two or more of the traits present in the combined GM event product are likely to interact in a manner that would in some way change prior safety assessments. In this case, appropriate experiments should be designed to address the anticipated interaction. On the other hand, a request for extensive additional data, duplicating that developed for the single GM events, does not appear to be scientifically justified for approved GM events that are unlikely to interact as such data would be expected to generate results that are equivalent to the results obtained for the single GM event.

These recommendations assume previous or concurrent regulatory approval of single GM event products used to generate combined GM event products. In terms of efficiency and appropriate use of regulatory agency resources, the option of concurrent submission and review of data for the single GM event parents and combined GM event products should be allowed.

The recommendations made here would maintain the rigorous safety review process currently applied to GM events while allowing efficient use of limited regulatory agency resources. Careful attention to a reasonable, science-based regulatory review process will ensure the continued development and timely introduction of new GM event varieties that are needed to sustain innovative plant breeding to meet future agricultural demands.

Conflict of Interest

W. Pilacinski, A. Crawford, S. Huber, P. Hunst, L. Lahman, S. MacIntosh, M. Pohl, C. Rickard, L. Tagliani and N. Weber are employed in the agricultural biotechnology industry. R. Downey and B. Harvey declare no conflicts of interest.

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