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Stacked Trait Products Are As Safe As Non-Genetically Modified (GM) Products Developed By Conventional Breeding Practices

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Abstract

International safety assessments and independent publications conclude that stacking genetically modified (GM) traits (events) through conventional breeding poses no greater risk to food or feed safety than stacking multiple non-GM traits by conventional breeding. Stacked trait products are not substantially different from their conventional comparator or their GM parent plants. Additional safety assessment of a stacked trait product produced by conventional breeding should not be required unless there is a plausible and testable hypothesis for interaction of the traits. However, the different approaches employed for the regulation of stacked trait products between countries results in asynchronous approvals, increasing the potential for trade flow disruptions, and adds to the regulatory burden for product developers. Considering their proven safety and benefit over the past 20+ years, regulatory authorities in some countries do not regulate stacked trait products, while others have simplified the approval process based on experience and sound science, reducing or eliminating the need for additional regulatory oversight. Countries that choose to regulate stacked trait products should consider integrating the more than 20 years of safety assessment experience, history of safe use, and global regulatory experience, in their approach to reduce redundancy, simplify regulations, and minimize the likelihood for trade disruption.

Keywords: stacked trait product, breeding stack, genetically-modified plant, GM event, GM trait, single event

1. Introduction

Genetic engineering has been used for more than 25 years to incorporate novel traits into plants. This tool has provided innovative and beneficial products to farmers around the world since genetically modified (GM) plants were first commercialized in 1994. Originally, individual traits such as herbicide tolerance and insect resistance were introduced into plants. These were, and continue to be, subject to regulatory review before being authorized for commercial use [9]. Over the years, as the safety and benefits of genetically modified (GM) plants were realized, a logical progression in the evolution of product development was to introduce multiple GM traits in the same plant, resulting in a “stack” or “stacked trait product” [15] that exhibits the phenotype of each of the GM traits.

Stacking of traits is accomplished through two methods: 1) by conventional plant breeding, where parents with single GM events are crossed to produce progeny that contain two or more GM events, commonly referred to as stacked trait products (also known as “breeding stacks”), or 2) by using molecular methods, where two or more traits are simultaneously or sequentially introduced into a host plant. The difference between the two stacking methods is that stacked trait products produced via conventional breeding do not contain a new event(s) that has not been assessed and approved by regulatory authorities [11, 12]. In this rapid communication we focus on the scientific rationale that additional regulatory oversight and further safety assessment of stacked trait products produced through conventional breeding, where the individual traits have already been assessed and approved, is unnecessary.

1.1. Global importance of stacked products

Stacked trait products offer multiple solutions for the farmer in one plant, allowing for expanded and enhanced management practices to maximize productivity and realize environ-

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mental benefits through improved agronomic practices (e.g., reduced/minimum tillage). For example, stacking of insect resistant traits can result in crops that are protected from damage by multiple pests and/or provide multiple modes of action to protect against similar pests, thereby delaying the development of insecticidal resistance among the target pests. Similarly, the stacking of herbicide tolerant traits allows farmers to utilize diverse modes of action for weed management and improve product durability specific to more prevalent or problematic local environments, while providing flexibility to combat difficult-to-control and resistant weeds. In both cases, this results in options for farmers to employ best management practices to improve farming productivity and expand the use of integrated pest management systems [14]. The value of stacked trait products to agriculture is highlighted by their rapid adoption by farmers. Over 80 percent of corn acres planted in 2018 in the United States were stacked trait products, a 70 percent increase in the last 15 years [16]. This same trend has been observed globally, with a market adoption rate increase of over 115 percent in just 10 years, reflecting the rapid and widespread adoption of these products and their importance to advancing agriculture [9].

1.2. Conclusions of international regulatory bodies and independent studies

Conventional plant breeding has a long, established history of safe use (HOSU), predictably providing safe food and feed products throughout history [22]. The World Health Organization (WHO) issued food safety evaluation guidelines in 1995 recognizing that when two GM plants that are substantially equivalent to conventional varieties are crossed by conventional breeding techniques, the resulting stacked trait product is expected to be substantially equivalent to the individual events [21]. Since stacked trait products do not contain a new GM trait (event) or additional introduced DNA, they are not considered new genetically modified organisms (GMO) or new living modified organisms (LMO), as defined by the Cartagena Protocol on Biosafety [6, 12].

Today, there are significant differences in the approach to regulation of stacked trait products between countries, frequently resulting in asynchronous approvals. For example, some jurisdictions do not require pre-market authorizations or only require a notification of commercialization if stacked trait products will be introduced to the marketplace, while others require additional data to be submitted for a safety assessment. The Codex Alimentarius principles and guidelines have been broadly applied to the evaluation of the safety of single events. Once these single events have been assessed and approved for use, conventional breeding can be utilized to incorporate these events into the commercial cultivars without the need for additional safety assessment [5]. Numerous publications support the conclusion that stacking GM traits through conventional breeding poses no greater risk to food or feed safety than combining multiple non-GM traits by conventional breeding [12, 13, 20, 21], and several recent reports have demonstrated that stacked trait products are not substantially different from their conventional comparator or the GM parent plants [3, 11, 23].

Given that single GM trait products are approved after a rigorous regulatory safety review, and that this process far exceeds the review employed for non-GM crops produced through conventional breeding, it is reasonable to conclude that stacked trait products do not pose additional risk and are as safe as the parental single events, unless there is a potential for the stacked traits to interact [15].

1.3. Current trends in the regulation of stacked trait products

As stated above, international guidelines and standards state that safety assessments performed on the single GM event are sufficient to assess the safety of stacked trait products and the associated intermediate stacks (sub-stacks) when these products are developed using conventional breeding [8]. Regulatory authorities in many countries do not require additional regulatory data to approve stacked trait products, as long as the traits are not predicted to interact [4, 19, 2]. Additional studies would only be warranted if two or more of the events present in the stacked trait product can potentially interact in a manner that would in some way change the conclusions of prior safety assessments of the single events. Interactions between traits are plausible only if they are predicted based on their mechanisms of action. Usually, such an interaction can be tested directly (such as through bioassays of insect-active proteins) and, only when necessary, by studies on the safety of the stacked trait product. The potential for interaction is rare but predictable, and can typically be evaluated within the context of the single event and the mode of action of the individual traits [13, 15]. To date, there has never been a documented occurrence of trait interaction as a result of stacking that has caused a safety concern.

With experience and familiarity gained through the evaluation and adoption of stacked trait products internationally, many countries have simplified or are currently in the process of simplifying their regulations for stacked trait products, including Japan, Brazil, and Argentina. For example, based on 20+ years of experience and familiarity with stacked trait products in which no safety concerns were observed, Japan streamlined its regulations. The Ministry of Health, Labor and Welfare (MHLW) of Japan has authorized stacked trait products for food and feed import with previously approved agronomic traits that are considered category 1 traits without the need for additional data [17]. Argentina's Ministry of Production and Labor recently published a new normative regarding stacked trait products with a "low probability of synergism" (i.e., interaction) between previously assessed single events, indicating that these products will not require any further assessment before commercial release and marketing [1, 18]. Additionally, the European Food Safety Authority (EFSA) has extensively reviewed more than 30 stacked trait products without finding any safety concerns [7, 10].

2. Conclusion

Since conventional breeding and selection does not by itself introduce novel hazards, and the process of stacking GM traits has been shown to be as safe as stacking non-GM traits, the safety assessment of stacked trait products is unnecessary unless there is a plausible and testable hypothesis of trait interaction [15].

Despite a HOSU of GM plants with single traits, and extensive regulatory and commercial experience with stacked trait products, regulatory policies and data requirements for their approval differ globally. While some countries have eliminated or streamlined their stacked trait data requirements in recent years based on that experience, others continue to increase their requirements. Additional regulatory oversight and further safety assessment of stacked trait products where the individual traits are approved is unnecessary and duplicative. Simplification and streamlining of existing stacked trait product regulations would reduce regulatory burden and asynchronous approvals, while continuing to deliver innovations with a history of safe use to farmers globally.

3. Declaration of Conflicting Interest

All the authors of this paper are currently employed by, or have been employed by, the agricultural biotechnology industry.

4. Disclaimer

The findings and conclusions in this publication are those of the author(s) and should not be construed to represent any official USDA or U.S. government determination or policy.

5. Article Information

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