August 5, 2019

Dr. Alan Pearson
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APHIS
4700 River Road
Unit 98
Riverdale, MD 20737-1238

Re: APHIS-2018-0034, Movement of Certain Genetically Engineered Organisms[1]

Dear Dr. Pearson:

Thank you for the opportunity to provide comments to the United States Department of Agriculture (USDA) on its June 6, 2019, Proposed Rule regarding the movement of certain genetically engineered organisms. We commend USDA for undertaking the initiative to revise its regulatory system for genetically engineered organisms and for using its long experience in regulating these organisms as a basis for making these improvements.

Founded in 1883, the American Seed Trade Association (ASTA), located in Alexandria, Virginia, is one of the oldest trade organizations in the United States. Its membership consists of over 700 companies involved in seed production and distribution, plant breeding, and related industries in North America. ASTA members research, develop, produce and distribute all varieties of seeds – including grasses, forages, flowers, vegetables, row crops, and cereals. ASTA member seed products support agricultural producers of food products and farm commodities in the United States and around the world.

General Comments

Seed innovation is based on an increased understanding of plant genomes, refinements in breeding techniques, and identification of new traits so that farmers have a wide array of high quality, high producing seed varieties available when making their planting choices. The continuation of such innovation is crucial for both the U.S. seed industry and global food security, particularly at a time when the global population continues to grow rapidly and most nations cannot afford food shortages. Stability of food production will continue to be a global priority for all nations.

For more than three decades, numerous administrations[2] have agreed on the principles and policies that provide the foundation for effective and efficient regulatory oversight. In 2011-12, two Executive

[1] 84 Fed. Reg. 26514 (June 6, 2019)

[2] EO 12866 (Sept.30, 1993) *Regulatory Planning and Review*. http://www.archives.gov/federal-register/executive-orders/pdf/12866.pdf;OECD. 1995. Recommendation of the Council on Improving the Quality of Government Regulation.http://acts.oecd.org/

Public/Info.aspx?lang=en&infoRef=C(95)21/FINAL; OECD.1997. Report on Regulatory Reform. http://www.oecd.org/gov/regulatory-policy/2391768.pdf; APEC-OECD. 2005. Integrated Checklist on Regulatory Reform http://www.oecd.org/regreform/34989455.pdf

Orders and a memo on appropriate regulation of emerging technologies[3] reaffirmed the principles that were clearly articulated in the 1993 Executive Order on regulatory development and review:

- Regulate only when there is a significant problem that is best solved by regulation.
- If regulation is warranted, it should be designed to be cost-effective: the benefits of regulation should justify the costs, and the degree of regulation should be commensurate with the risk.
- Base regulatory decisions on the best available scientific and technical information.
- Provide sufficient flexibility to accommodate new evidence and learning, and review regulations on a regular basis to ensure they meet the regulatory objectives in the least burdensome way.
- Use clear language and provide opportunity for stakeholder and public involvement.
- If possible, regulation should promote innovation while protecting health and the environment.
- Avoid interagency duplication and inconsistency.
- Promote international coordination to minimize trade impacts.

The Coordinated Framework for the Regulation of Biotechnology (Coordinated Framework)[4], established as a formal policy by the Executive Office of the President, Office of Science and Technology Policy (OSTP) in 1986, was consistent with the principles described above. It additionally set forth a number of principles specific to Federal regulation of the products of biotechnology.

A fundamental principle articulated in the Coordinated Framework was the use of existing Federal laws to regulate biotechnology research and products. These laws provide authority to various agencies to regulate particular products and product uses. Because the uses and potential risks posed by products developed through modern biotechnology would be the same as existing products otherwise developed with similar traits, the developers of the Coordinated Framework determined that existing laws would provide adequate oversight for protecting the public and the environment. Using existing laws helped to ensure that other central regulatory principles were adhered to—that similar products be treated the same by regulatory agencies and that new products meet the same safety standards and criteria as existing products. Thus, a new food crop must be as safe to grow and as safe to eat as those food crops already on the market.

These principles were reaffirmed in a review of the Coordinated Framework in early 2017. [5]

OECD. 2005. Guiding Principles for Regulatory Quality and Performance. http://www.oecd.org/fr/reformereg/34976533.pdf;Middle East and North Africa-OECD.2009. Regional Charter for Regulatory Quality. http://www.oecd.org/mena/governance/45187832.pdf;OECD. 2012. Recommendation of the Council on Regulatory Policy and Governance http://www.oecd.org/regreform/regulatory-policy/49990817.pdf

[3] EO 13563 (January 18, 2011) *Improving Regulation and Regulatory Review* http://www.whitehouse.gov/the-press-office/2011/01/18/executive-order-13563-improving-regulation-and-regulatory-review; EO 13610 (May 10, 2012) *Identifying and Reducing Regulatory Burdens* http://www.whitehouse.gov/the-press-office/2012/05/10/executive-order-identifying-and-reducing-regulatory-burdens; Memorandum (March 11, 2011) *Principles for Regulation and Oversight of Emerging Technologies*

[4] OSTP. 1986. Coordinated Framework for Regulation of Biotechnology. 51 *Fed. Reg*. 23302, 23304

[5] https://www.aphis.usda.gov/biotechnology/downloads/2017_coordinated_framework_update.pdf

Most recently, reforms were described that will promote agricultural innovation in accordance in the report of the Interagency Task Force on Agriculture and Rural Prosperity[6] and the June 11, 2019, Executive Order on Modernizing the Regulatory Framework for Agriculture Biotechnology Products.[7] In reviewing the regulatory process under Part 340, every effort should be made to adopt the reforms in this report and the Executive Order. In particular, we note the instructions regarding regulatory streamlining and review of existing authorities, regulations and guidance with the goal of removing undue regulatory burdens for smaller developers and public researchers developing genome edited plants. The 2019 Executive Order also instructed USDA, the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) to take steps to have consistency and coordination among the three agencies. The importance of trade and international engagement was recognized as well. In March, 2018 the Secretary of Agriculture issued a statement on plant breeding innovation providing clarification on USDA's oversight of plants produced through innovative new breeding techniques.[8]

The benefits to agriculture that have resulted from, and will continue to result from, the development and commercialization of innovative plant products, including crops developed using genome editing and other precision breeding methods, should be available to all of our nation's farmers. Given USDA's experience in operating under a comprehensive and coordinated federal regulatory process for oversight of new plant products since 1986, where the science demonstrates that a product or category of products could have been produced using conventional breeding methods or in nature, such products should be excluded from premarket review.

The Plant Protection Act, in relevant part, authorizes the Secretary of Agriculture to oversee the detection, control, eradication, suppression, prevention, or retardation of the spread of plant pests. Pursuant to that broad authority, the Secretary of Agriculture may prohibit or restrict the importation, entry, exportation, or movement in interstate commerce of any plant pest, plant, plant product, or article capable of harboring a plant pest as necessary to prevent the introduction of a plant pest into the United States or the dissemination of a plant pest within the United States, and also may determine that certain articles, plants, and plant products are not plant pests and are not subject to prohibitions or restrictions on movement in interstate commerce.

ASTA commends USDA for setting a goal of improving its regulatory system for genetically engineered organisms and for using its long experience in regulating these organisms as a basis for making these improvements. ASTA is particularly pleased that USDA's proposal recognizes that some applications of gene editing result in plant varieties that are essentially equivalent to varieties developed through more traditional breeding methods and treats these varieties accordingly in the proposal. While we support excluding these categories of products from the application of Part 340, we offer some recommendations on definitions, structure and language of these exemptions. Specifically, we make recommendations with respect to definitions in §340.3, the exemptions in §340.1(b) and confirmation of the exemptions in §340.1(d). We view these recommendations as an interrelated set and request

[6] https://www.usda.gov/sites/default/files/documents/rural-prosperity-report.pdf

[7] https://www.whitehouse.gov/presidential-actions/executive-order-modernizing-regulatory-frameork-agricultural-biotechnology-products/

[8] https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation

that USDA review them as such. We also make comments on the Regulatory Status Review (RSR) process.

We begin with a discussion of the proposed sections dealing with Definitions, Applicability and Scope, which are all critical to understanding the intended coverage of the Proposed Rule.

Definitions

Genetic Engineering (GE). §340.3 of the Proposed Rule defines the term "genetic engineering" as "techniques that use recombinant or synthetic nucleic acids to modify or create a genome." As USDA points out, this would include "the use of synthetic DNA, *in vivo* DNA manipulation, and genome editing." Importantly, USDA also points out, appropriately, that the proposed definition "would not cover traditional breeding techniques, such as marker-assisted breeding, as well as tissue culture and protoplast, cell, or embryo fusion, or chemical or radiation-based mutagenesis." Finally, USDA notes that its proposed definition of "genetic engineering" is intended to clarify rather than change the coverage of its current definition.

Recommendation
ASTA recommends that USDA provide more clarity around what is meant by "synthetic nucleic acids" by stating that, for the purposes of Part 340, "synthetic nucleic acids" are those that are non-naturally occurring.

Genetically Engineered (GE) Organism. USDA uses the term "genetically engineered organism" throughout the Proposed Rule and we would recommend that this term be defined in §340.3 to provide greater clarity around which "organisms" would and would not be subject to Part 340 requirements.

Recommendation
ASTA recommends defining "genetically engineered organism" as:
"An organism developed using genetic engineering, excluding those offspring that do not retain the genetic modification of the parent. For the purposes of this part, a plant will not be considered a genetically engineered organism if it meets any of the criteria outlined in 340.1(b)(1)-(3)." Also see recommendations for §340.1(b) with respect to offspring that do not retain the genetic modification of the parent (null segregants).

We note that the term "genetic engineering" is often used synonymously with terms such as "biotechnology", "modern biotechnology", and "genetic modification". The addition of the above definition for "genetically engineered organism" would provide clarity that not all plants derived from the broad definition of "genetic engineering" in this proposal would automatically be regulated. Defining the term "genetically engineered organism" as recommended would make clear that plants derived from applications of genome editing that could be achieved through traditional breeding would not be treated as genetically engineered organisms subject to Part 340. If, contrary to the Secretary's 2018 Statement and the 2019 Executive Order, these plants were treated as genetically engineered organisms under this rule, there would be very real negative effects on the development of valuable new agricultural products and for the farmers who need those products. Imposing the Part 340 process on these products would also have serious adverse, and unnecessary, practical implications for public and private sector developers, both large and small.

We suggest that null segregants, which are offspring organisms in which the modification present in the parent organism is no longer present in the offspring organism, be excluded from the definition of a genetically engineered organism in §340.3. These organisms lack the genetic modification generated by genetic engineering. Historically APHIS has not considered organisms to be "regulated articles" under its Part 340 regulations when the plant pest genetic elements used to engineer the parent plant were removed via conventional breeding. This position has been confirmed numerous times in the "Am I Regulated" process.[9] Accordingly, these plants, by definition, are not genetically modified or engineered and should be explicitly excluded from the scope of these regulations. This approach on null segregants would also be consistent with numerous other regulations outside the U.S. that consider null segregants to be outside the scope of regulations covering genetically engineered/modified organisms.

Applicability of the Regulations

Proposed §340.1(a) specifies that the GE organisms that would be subject to Part 340 are those described in the Scope section of the rule, proposed §340.2. In proposed §340.1(b) and (c), USDA lists those categories of genetically engineered plants that would not be regulated under Part 340, including the regulatory status review provisions of proposed §340.4.[10] With certain very specific exceptions discussed below, our review of these proposed exemptions demonstrates that they are based on sound scientific principles and USDA's extensive experience in reviewing GE plants for over 30 years.

USDA states that these exemptions reflect the Secretary of Agriculture's 2018 statement that USDA does not plan to regulate plants that could otherwise have been developed through traditional breeding techniques because they would not pose any greater plant pest risk than their more traditionally bred counterparts.[11] ASTA supports the Secretary's 2018 statement; however, our review of the exemptions proposed in §340.1(b) indicates that not all of these exemptions fully reflect that statement. While we understand it is difficult to develop a generalized standard across all plant species for what could be achieved through traditional breeding, significant applications of genome editing that could be achieved in this manner would nonetheless not fall under these exemptions and would, therefore, need to go through the newly proposed Regulatory Status Review (RSR) process (see subsequent comments on the RSR process).

Plant breeders have well-established screening and quality management processes to evaluate newly developed varieties for acceptable product performance, regardless of the plant breeding method employed.[12] The U.S. seed sector has safely introduced thousands of new plant varieties into the U.S.

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[9] As an example, the 2011 reply to an "Am I Regulated? Letter: https://www.aphis.usda.gov/biotechnology/downloads/reg_loi/Dr%20Ramsey%20S%20Lewis%20NCSC%20Final.pdf]

[10] USDA requests comment on the review process to be followed for non-plant GE organisms. Any criteria or exemptions included in such a process would have to be tailored to the specific type of organism in question (e.g., criteria developed for plants would not necessarily be appropriate for microorganisms).

[11] "USDA does not regulate or have any plans to regulate plants that could otherwise have been developed through traditional breeding techniques as long as they are not plant pests or developed using plant pests." "With this approach, USDA seeks to allow innovation when there is no risk present." https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation.

[12] American Seed Trade Association (ASTA). 2016. Common Practices of Plant Breeders; ASTA. Guide to Seed Quality Management. www.betterseed.org/resources/guide-to-seed-quality-management

market for decades. A single vegetable seed company may have breeding programs in 20 different crops and can introduce hundreds of new commercial varieties every year. Field crop seed companies often work in multiple species and collectively will commercialize hundreds of hybrids and varieties in the U.S. market every year. Additionally, the production and sale of seeds are regulated activities at both the Federal and state level.

As an addendum to these comments, ASTA offers a more detailed description, with references, of common practices of plant breeders that describes the development, testing and selection involved in the development of new hybrids and varieties.

Plant genomes are not static with each individual plant having a unique genetic makeup. Plant breeders have long utilized this genetic variation to develop plant varieties with improved characteristics. Breeders have utilized various methods to utilize and introduce genetic variation into their breeding populations since the early part of the 20th century.[13] It was not until the use of molecular biology tools became commonplace that researchers began to understand and characterize the genetic variation underlying visible traits (phenotypes), and molecular markers were developed that could be used to follow segregation and inheritance of these traits. Often breeders will use many markers that span the genome and correlate with specific traits in their breeding populations. By the mid-1980s genetic maps of entire genomes could be made using observations of marker cosegregation. Markers have been used to speed up the process of elite line selection and allow the breeder to simultaneously enrich for favorable alleles while selecting away from alleles that are associated with undesired traits.

Spontaneous mutations are known to occur continuously at low frequency and these bring about genomic sequence changes that are the basis of evolution.[14] The impact of spontaneous mutations can be neutral, deleterious or beneficial for the plant, with the environment having an impact on the outcome of the mutation. Most spontaneous mutations are either neutral or have a deleterious effect. Beneficial, spontaneous mutations are relatively rare from an evolutionary perspective. However, through careful screening, plant breeders have historically taken advantage of the genetic variation created through spontaneous mutations to preserve positive characteristics.[15] Semi-dwarf cereal crops are such an example of a spontaneous mutation creating a characteristic that has helped to improve yield.

Because spontaneous mutants yield beneficial results with such a low frequency, breeders have employed methods, such as chemicals and irradiation, to increase the rate of mutations as part of their breeding programs. These induced mutations create breaks in the DNA. These “breaks” are then

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[13] S.P. Moose and R.H. Mumm (2008). Molecular Plant Breeding as the Foundation for 21st Century Crop Improvement. Plant Physiol. 147(3): 969–977.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2442525/

[14] G. S. Ladics, , et al. 2015. Transgenic Research 24(4): 587-603; J. Schnell, et al. 2015. Transgenic Research 24(1): 1-17

[15] J. Hancock. 2012. Plant evolution and the origin of crop species. CABI

"repaired" by naturally occurring DNA repair and recombination processes in the cells to result in the introduction of different types of DNA changes in the genome of an organism. At the molecular level, induced mutations are comparable to spontaneous mutations occurring due to the action of physical agents (e.g., natural radiation or UV light) or biological factors (e.g., errors of DNA replication, recombination, movement of transposons).

Plant breeders have long utilized genetic variation created through mutations to develop plant varieties with improved characteristics. In the last century thousands of plant products on the market have been developed using various selective breeding techniques.

Since the 1950s, well over 3200 crop varieties have been directly developed by selection of induced mutations alone.[16] Some examples of the successes of mutation breeding are:

- High-yielding and short barley for brewing industry
- Heat tolerance and early maturity in cotton
- Seedless watermelon
- Multiple disease resistances in tomato
- Ruby Red grapefruit
- Gold Nijisseiki disease-resistant Japanese pear
- Peanuts with tougher hulls
- Semi-dwarf rice with higher yields
- Virus-resistant cocoa
- Canola with healthy fatty acid composition
- Soybeans with improved fatty acid balance and concentrations

Thus, production and consumption of food crops derived from plant breeding programs which leverage the plasticity of plant genomes have a long history of safe use.

ASTA recommends that the scope of the exemptions in proposed §340.1(b)(1-3) should reflect the range of genetic changes that traditionally have occurred in a plant through the breeding process, including spontaneous and induced mutagenesis. The exemptions should also reflect the fact that sequence information for some crops is not robust, particularly for some specialty and newer crops.

Certain products of genome editing applications represent refinements of existing mutation breeding methods in that they allow for the targeted and precise mutations in the plant genome. In such products, a break in the DNA is induced at a targeted location in the plant genome with the subsequent utilization of the plant's natural cellular mechanism for DNA repair (so-called "double strand break repair"). Double strand break repair is also the foundation and basis for chromosomal recombination during meiosis. The deletions, insertions and rearrangements observed at the site of the DNA repair during applications of genome editing are analogous to and indistinguishable at the DNA sequence level from the deletions, insertions and rearrangements that are obtained using more traditional induced mutagenesis techniques.

The main difference between targeted gene edits through genome editing applications and induced mutations is specificity and precision. Through genome editing applications, the DNA change can be induced at a very specific site in the genome, something that is not possible through chemical- or

[16]Joint FAO/IAEA Mutant Variety Database. www.mvd.iaea.org; S. Bado, et. al., 2015. Plant Breeding Reviews. 39. doi: 10.1002/9781119107743.ch02; Y. Oladosu, et al. 2016. Biotechnology & Biotechnological Equipment 30:1, 1-16; A. Raina, et al. 2016. " Asian Res. J. Agr 2, 1-13.

irradiation-induced mutation. Prior knowledge about the functionality of the desired mutation is helpful for the successful utilization of genome editing applications in this way. Therefore, genome editing to direct a change to a trait or phenotype is guided by prior knowledge about the gene and adds a degree of precision in the ability to predict the outcome of the changed variety or hybrid.

Plant breeders also introduce genetic variation through crosses with related plants and wild relatives with valuable characteristics, such as yield, size, shape, color, taste or disease resistance. Using traditional breeding methods, it normally takes many generations of repeated cycles of selection of plants, or recurrent backcrossing to an elite parent, to generate plants with the best combination of characteristics to produce a commercial variety. Certain genome editing applications can create genetic diversity through changes in endogenous gene sequences and functions that are, in principle, possible to create using more traditional methods of breeding, such as via spontaneous/induced mutagenesis and cross-breeding.

Through the use of genome editing applications, it is possible to recreate an allele (gene variant) directly in an elite variety by using the site-directed nuclease to make a DNA break and a template to direct the repair of that break. Thus, an allele for a desirable trait (e.g., a disease-resistance gene from a wild relative) can be reproduced directly in the elite genetic material by editing an existing allele in that elite variety. This avoids the need to "breed out" the unwanted genetic material from the less agronomically desirable source of the targeted allele as the gene(s) is transferred through traditional breeding methods and maintained in subsequent selected offspring. This ability has tremendous value for those crops with long generation times, with complex or duplicated genomes, or when desired characteristics are closely genetically linked with unwanted characteristics. It also allows a breeder to make simultaneous applications, such as deletions, which is important for those crops with duplicated genomes.

Beyond the improvement of traits, genome editing is increasingly becoming a useful method for making the plant breeding process itself more efficient. An example is the use of genome editing to induce double haploids in order to more efficiently achieve homozygosity. Other methods of inducing double haploids are more laborious and less precise. Genome editing can also be used to make the recombination process in cross-breeding more efficient. In both of these examples, genome editing is not used to produce a specific characteristic or phenotype but rather to improve the breeding process.

Therefore, there is a range of applications of genome editing that produce plants that could otherwise have been obtained through more traditional breeding methods. As with other breeding methods, genome editing allows breeders to precisely and efficiently utilize existing genetic variation, induce that variation and to improve upon existing breeding methods.

Recommendation

Based upon the discussion above, ASTA thus recommends that the scope of the exemptions in proposed §340.1(b)(1-3) should reflect the range of genetic changes that occur in a plant through the breeding process, including spontaneous and induced mutagenesis. We recommend that the scope of the exemptions reflect the applications of genome editing that are no different from the applications of other breeding methods, such as producing an allele from a wild relative in an elite variety or inducing double haploids to make the breeding process more efficient.

ASTA does not recommend any revisions for §340.1(b)(1)-(2).

ASTA recommends that proposed §340.1(b)(3) be modified to accurately reflect the Secretary's March 28, 2018, statement by revising the exemption to read as follows:
(3) The genetic modification is:
(i) introducing nucleic acid sequences from within the plant's gene pool;
(ii)editing nucleic acid sequences to correspond to a sequence in that plant's gene pool; or
(iii) otherwise accessible through traditional plant breeding methods such as, but not limited to, induced or somaclonal mutagenesis, tissue culture, protoplast, cell or embryo fusion, wide and bridging crosses, haploid induction, or other methods that enable movement or rearrangement of genes within the plant's gene pool.

We further recommend that §340.1(b)(4), the exemption of "null segregants," be dropped per our recommendation to address these organisms as exclusions in the definition of "genetically engineered organism".

We believe these recommended changes to §340.1(b)(3) will also make the scope of a revised Part 340 more consistent with the direction other countries are taking. The exemptions as proposed by USDA would be more restrictive than policies in other countries such as Argentina and Chile.

Finally, USDA should not restrict the scope of these exemptions to what is technically achievable today because the improvement of technology is a continuous process. We recommend that the Agency provide a mechanism in the final rule for reviewing the existing exemptions and adding additional ones through an expedited process (e.g., via guidance) as developments occur.

Confirmation Process

Proposed §340.1(d) states that developers may request confirmation from USDA that a plant "is not within the scope" of Part 340. The preamble to the Proposed Rule indicates that this is intended to provide confirmation that the plant meets one of the exemption criteria in 340.1(b) or (c) (see 84 Fed. Reg. 26517). In essence, the proposal creates a presumption that a plant or category of plants that meets one of the criteria is exempt from regulation under Part 340. In turn, the confirmation process provides USDA with an opportunity to rebut that presumption. ASTA accepts this presumption of an exemption and USDA's rebuttal opportunity, but wants its members to have a clear regulatory pathway to request and obtain confirmation of the exemption before the exempted plant or category of plants is placed on the market.

It is likely that most developers would make use of this confirmation process because of its value in marketing their products, both domestically and in export markets, and for other commercial reasons as well. However, USDA has not laid out any specifics with respect to information needed or timelines if a developer chooses to use this option. There is a real risk that the confirmation process would become a de facto mandatory process without any assurances to the developer of how the process will, in fact, work. There is a further risk that the confirmation process will, in the end, be essentially the same as the process for the RSR, particularly with respect to the exemption criteria in 340.1(b). This uncertainty will particularly affect smaller private developers, public researchers and specialty crops because of relative lack of familiarity with the USDA Part 340 regulatory process. Additionally, if USDA does not modify the language of the proposed exemptions as discussed above, there will be categories of gene edited plants that will not fall under the scope of these exemptions and will need to go through the RSR process. The end result could be that most, if not all, gene edited plants would either go through a yet undefined confirmation process or the RSR process that is a new, untested, process. The voluntary

nature of the proposed confirmation process with regard to §340.1(c) might also limit to some extent the utility of USDA's list of plant/trait/MOA[17] combinations that had been cleared for market entry.

Recommendation

In the text of the preamble, and based on the findings of reports of the National Academies of Science, USDA states that "Thus, given the accepted safety of traditionally bred crops, and the principle that the use of recombinant DNA does not itself introduce unique risks, it is logical and appropriate to exempt from our regulation plants produced by any method if they also could have been produced by traditional breeding." (84 Fed. Reg. 26519). USDA further states: "Furthermore, plants that qualify for an exemption would not be reviewed by APHIS. For these reasons, the exemptions are based on measures that are easily recognizable and on genetic changes that could be achieved by traditional plant breeding in any system." (84 Fed. Reg. 26519-20).

ASTA recommends that USDA consider the negative impacts on innovation of having the narrower scope of exemptions, as found in proposed §340.1(b), along with the real possibility that developers, both large and small and across all crops, will either go through a confirmation process for commercial reasons or through the RSR process because a product falls outside the proposed exemptions. ASTA recommends that USDA modify the language in §340.1(b)(3) as suggested above and put in place a well-defined process for developers to use for confirmation that a product or category of products meets the exemption criteria in §340.1(b) or (c). Developers would be required to submit their confirmation requests 90 days prior to the initial placing on the market of a particular plant species/genome editing application. All other pre-commercial confirmation requests would be voluntary, as proposed by USDA. Below are recommendations on general elements that could be included in this process. We look forward to working with the Agency on guidance to provide more details to developers.

ASTA recommends that this process of confirmation should generally include the following elements:

1. The process should focus on the plant species, not the variety, as well as the purpose and type of application of genome editing, recognizing that genome editing can both be used to produce or improve on a specific characteristic or phenotype, such as silencing a disease sensitive gene, and to improve existing breeding processes themselves, such as using gene editing to more efficiently induce double haploids.
2. The type of information provided to the Agency should be a description of the crop and the justification for meeting the exclusion, similar to the "Am I Regulated Process".
3. The timeline of the review should be predictable and reasonable to help support innovation (e.g., 30-60 days).
4. The process should be efficient and not necessarily require an Agency response. A developer would notify the Agency with information to describe how a particular plant species/genome editing application meets one of the exemptions in §340.1(b). If the Agency does not respond in, for example, 30-60 days, the presumption is that one of the exemptions is met. A developer would, however, be able to specifically request a response from the Agency in its submission. There is precedent at other agencies for a notification process similar to this recommendation.
5. A developer would be free to submit a confirmation request with the Agency at any time in the pre-commercial development stage but would be required to submit 90 days prior to placing on the market of the first instance of the particular plant species/genome editing application in a product or category of products. Developers who receive confirmation of exemption in

[17] Mechanism of Action

response to a voluntary request earlier in the pre-commercial process would not have to make a second request. They would simply notify the Agency 90 days prior to placing on the market the first instance of the particular plant species/genome editing application that was included in the original confirmation.

6. Claims of Confidential Business Information (CBI) can be made in the submission and the non-CBI version of the submission would be publicly available, similar to the current "Am I Regulated" process.

We would recommend that the same elements, as described above, would apply to the § 340.1(c). Thus, where the Agency finds that a previously unlisted plant-trait-MOA combination qualifies for exemption under §340.1(c), the relevant information would be added to the publicly available list maintained by the Agency.

This approach would offer the possibility of more consistency among the U.S. regulatory agencies. If a developer has gone through the confirmation process at USDA, there should be no reason the developer would need to go through a similar process at EPA, for example. We would strongly recommend that USDA and EPA enter into a Memorandum of Understanding such that EPA would recognize the process at USDA. Similarly, such a process would provide FDA with information of what types of crops/genome editing circumstances are likely to enter the commercial food market. There will be circumstances, of course, when a developer should go to FDA for a consultation, per current FDA guidance. This coordination among USDA, FDA and EPA would be consistent with the directions given to the Agencies in the June 11, 2019 Executive Order. It would also take into account the direction that many our international partners are taking.

Regulatory Status Review

USDA proposes to use the RSR process to evaluate whether an organism would require a permit for movement based on the characteristics of the organism, including the plant, the trait and the mode of action. Developers can choose to either request an RSR or to apply for permit for movement under the regulations.

ASTA commends USDA for providing developers with regulatory options and agrees that the RSR should be predictable, timely and based on objective criteria. ASTA offers some comments on terminology used, information needed under the RSR and provisions for making claims of CBI.

We recommend that USDA use consistent language in the final rule and to incorporate terminology standard to field of risk assessments. The standard way of describing risk is in terms of both scale and likelihood of potential harm. We recommend defining Plant Pest Risk as: "*The likelihood and magnitude of direct or indirect injury, damage, or disease in any plant or plant product resulting from introducing or disseminating a plant pest or exacerbating the direct or indirect injury, damage, or disease capacity of a plant pest.*"

The phrase "unable to identify potential plant pest risks in the initial review" in §340.4(b)(2) should more rightly be phrased as "determines there is no reason to believe there is an unacceptable plant pest risk resulting from introducing or disseminating the Genetically Engineered plant" Similarly, in §340.4(b)3(iii) we recommend replacing the phrase, "found unlikely to pose a plant pest risk," with the phrase, "If the introduction of the Genetically Engineered plant is found unlikely to pose an unreasonable increase in plant pest risk and therefore, not to require regulation…"

In the proposal USDA identifies the need for information on the "genotype of the modified plant, including a detailed description of the differences in genotype between the modified and unmodified plant." Included in this information would be sequence information, including regulatory sequence information. If this information is not relevant to a plant pest review and initial assessment, it should not be required. Moreover, providing this type of information would be of concern to developers if they are not provided with an adequate opportunity to protect their CBI in accordance with Federal law. If information related to a product MOA legitimately qualifies for protection as CBI (as put forth in §340.7), it should not be excluded from being claimed as CBI. Without an option for protecting intellectual property and other proprietary information, developers are likely to be unwilling to provide this type of information which would be a discouragement to using the RSR process. If developers are not able to adequately protect their intellectual property, they will most likely not use the RSR process until a product is near to commercialization.

In conclusion, USDA should continue to play a leadership role in the development of a clear and positive US Government policy for innovation in agriculture, including the innovation in plant breeding. USDA should also work with the other US regulatory agencies to adopt consistent policies toward these products across the US Government. The US Government should continue to take a leadership position and actively engage with other governments, particularly among our trading partners, with the goal of working toward internationally consistent, science-based policies.

ASTA appreciates the opportunity to provide comments on the proposed revisions to 7 CFR Part 340. We stand ready to act as a resource throughout this process.

Sincerely,

Andrew W LaVigne
Andrew W LaVigne (Aug 5, 2019)

Andrew W. LaVigne
President/CEO

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COMMON PRACTICES OF PLANT BREEDERS

INTRODUCTION

The plant world contains hundreds of thousands of species with an amazing array of physical and chemical diversity. For over a billion years, nature has created new genes, altered existing genes, combined them in different ways, and then selected for those that survive and reproduce best. The creation and selection of certain genes and gene combinations led to plants with diverse physical structures for self-defense, support, seed dispersal and water conservation. Evolution also allowed some plant species to become 'biochemical specialists' in producing unique and characteristic phytochemicals, resulting in a broad range of compounds produced in fruits, vegetables, beans and many other plants. For example, peppers produce capsaicin, tomatoes are a good source of lycopene, and grapes produce resveratrol.

Over the last several thousand years, humans have joined Mother Nature in directing the evolution of plants by selectively saving and planting seed from wild, gathered plants with attributes humans valued: better flavors, larger fruits, fewer thorns, more nutrients and seeds that don't scatter. As soon as humans began to save some seeds for planting while discarding others, they altered the genetic makeup of the wild plants they had been gathering. The initial result of human-directed selection was the conversion of some wild plants into domesticated food crops that were easier to harvest and use and provided a reliable and convenient source of nutritious food. By 5000 BC, virtually all major food crops humans rely on today had been genetically changed from wild plants to domesticated crops. As the human population expanded into new areas, their crops moved with them to new environments, and humans continued to shape their genetic makeup so that the crops could adapt and serve human needs.

This process of constant genetic improvement continues today, though in a more formalized way, using the science and art of plant breeding. Plant breeding programs can be thought of as small-scale, human directed evolution projects that are increasingly informed by scientific understanding and facilitated by technological advances. As is true of evolution by natural selection, genetic variation is the essential resource upon which plant breeding programs are built. However, unlike biological evolution, plant breeding is goal-oriented, and the overarching goal is an array of crop varieties, with improved characteristics and traits, adapted to diverse environments. Plant breeders use cross-breeding, selection and other methods to both create new genetic variants and shape existing genetic diversity. The breeding and selection process takes multiple generations and results in plant hybrids and varieties that look, smell, taste, and yield in a more reliable and predictable way. Although each crop breeding effort may have unique practices, they all follow common selection practices with goals of improving plant productivity, quality or quantity.

During the thousands of years that humans have genetically changed plants, the value of these plants and plant products was assessed by how they looked, smelled, tasted and met human needs. From these interactions, humans learned which plant species are good sources of building materials, medicine and, most importantly, food. We learned which plants are nutritious, have useful phytochemicals, and are safe to eat, and which plants to avoid. Generally, those plants that tasted good and provided sustenance were considered safe to eat. Others were found, through trial and error, to be safe to eat only after processing or heating to inactivate factors that could negatively affect health or nutrition. Over time, as science progressed, biochemists were able to verify the chemical basis of what plant breeders had originally learned through trial and error. That same science continues to inform the ultimate evaluation of the safety and nutritional value of a given plant species as a food source.

This document provides a generalized description of the typical timelines, steps and procedures used in plant breeding programs today, focusing on hybrid breeding for both vegetables and field crops.

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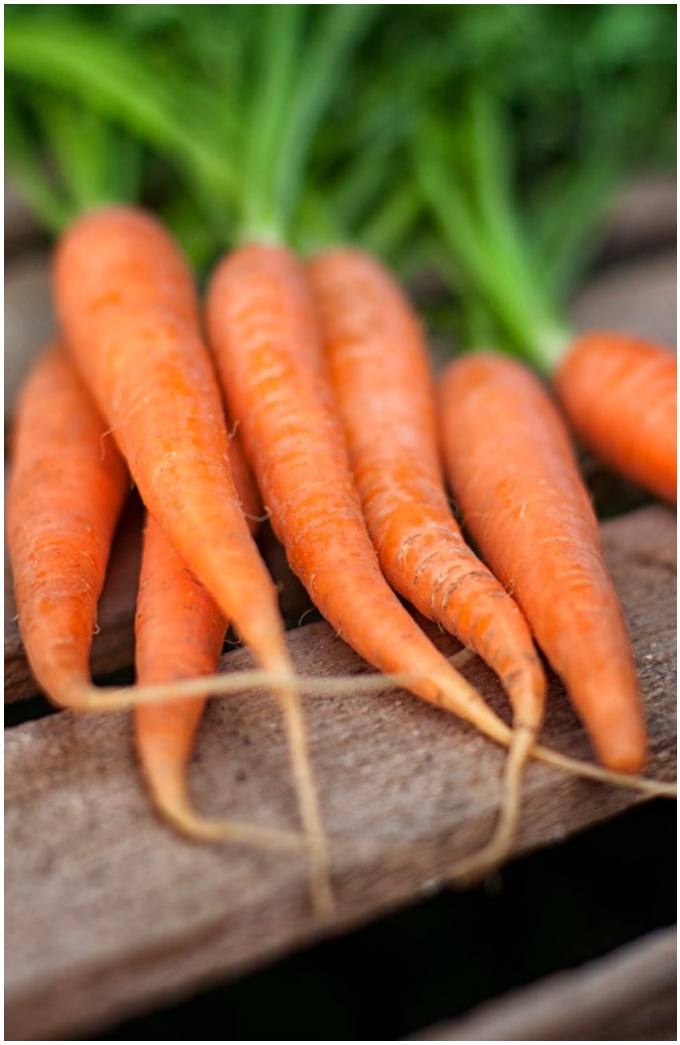
OVERVIEW OF HYBRID BREEDING

Commercial hybrids are a cross between two inbred parents, each derived from divergent genetic pools. In the hybrid breeding process, a key strategy is to identify genes in these divergent genetic pools so that the two inbreds being crossed as hybrid parents are as genetically unique as possible. Because hybrids have a full set of genes from each unique parent, they have much more genetic diversity than either inbred parent alone. Hybrids also have a combination of traits from each parent that enables the hybrids to have an overall performance that exceeds the performance of either of its inbred parents. The combination of the genetic diversity between the two inbred parents is the source of what is called "hybrid vigor" or heterosis. The value of hybrid vigor in plants can be measured in characteristics that deliver increased value to the grower, such as higher yield, larger fruit/vegetable size, better disease resistance, and broader environmental adaptability.

A hybrid breeding program normally consists of two phases: inbred development and hybrid testing. In the inbred development phase, breeders screen populations of plants that are genetically and phenotypically diverse, selecting individual plants with the desired characteristics. These individually selected plants are then self-pollinated in a repetitive fashion, called "selfing." During the selfing process, a plant acts as both mother and father to subsequent generations of seeds. The selection and selfing cycles are repeated until inbred lines that no longer show significant phenotypic variation between individuals are generated. These lines are often called "true breeding" inbred lines. Plant lines are considered inbred when the offspring (progeny) from a self-fertilized plant look identical to the parent, as well as identical to one another. In the second phase of a hybrid breeding program, the breeder crosses different inbreds to make hybrids and then conducts extensive field trials and testing of different hybrid combinations looking for the best field performance for yield, agronomic and product quality traits.

It is important to note that plant species vary in their generation time (time from seed to offspring seed). For example, some widely-grown vegetable species have a two year generation time, i.e., they are biennial. For other species it is possible to get 2 or 3 generations in a single year through special techniques such as embryo rescue. Utilization of tropical environments with year-long growing conditions can sometimes provide 5-6 generations/year for some species.



PLANT SPECIES	ONE GENERATION
Fruit Trees	5 - 6 Years
Carrot, Onion	2 Years
Tomato, Pepper	0.4 Years
Melon, Spinach	0.3 Years
Corn	0.4 - 0.2 Years
Rice	0.5 Years

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Some of the most common traits of interest in modern vegetable breeding programs include features such as reliable field performance across multiple environments, high yield, high quality, disease resistance, flavor, color, size and shape. Similarly, in field crops, the traits of interest range from disease resistance, tolerance to abiotic stress, improved processing and nutritional characteristics. Even today some of the primary tools for selecting the best plants rely upon a breeder's sense of smell and taste along with visual observations, just as has been done for thousands of years.

INBRED DEVELOPMENT

- Introduce genetic variation from (a) related plants, (b) wild relatives, or (c) random induced mutation
- Field trials, selecting and selfing
- 6-9 selfed generations to make inbred.

HYBRID TESTING

- Cross inbreds to make many experimental hybrid combinations
- Field testing at multiple locations
- Test for 3-5 growing cycles

COMMERICAL HYBRID

- Seed production of hybrids selected for commercial sale
- Commercial sale to growers

DEVELOPING INBRED LINES

In the Inbred Development Phase, the breeder begins by crossing two plants with different traits, such as yield, size, shape, color, taste, or disease resistance. The objective is to combine valuable traits from each parent to generate and select offspring containing the best characteristics of both parents. For example breeders are often trying to improve certain weaknesses that exist in one parent with complementary strengths in the other parent. The breeder's goal is to ultimately develop inbred lines with performance that results in an improvement over both of the original parents. The breeder accomplishes this thru repeated cycles of selection of plants with the best combination of characteristics and selfing.

The breeder selects the best performing inbred lines by using a breeder-directed process that includes assessing phenotypes through a field trial process. Through multiple generations (cycles) of plant selection, the breeder typically selects a few dozen elite, "true breeding," inbred plant lines from a population of thousands of individual plants. This process can last, on average, about six plant generations for typical breeding targets and through field trialing over multiple years and environments. For more complicated traits, such as multiple genes controlling a particular trait or, for example, introducing new disease resistance genes from a genetically distant wild relative, more than six plant generations may be required.

When the objective is to enhance an existing inbred line by adding a new characteristic from a donor inbred line, a technique called backcrossing is often deployed. Backcrossing minimizes changes to the inbred line, referred to as the recurrent parent. During backcrossing, the progeny of the original cross is repeatedly crossed to the recurrent parent while selecting for the target trait at each generation. When the donor of a new trait is otherwise wild or inferior to the recurrent parent, this approach enables the transfer of a trait while minimizing the dilution of other valuable traits. The contribution from the donor genome is reduced by half with each backcross. This process is illustrated below.

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50%
F1 Seed
Elite Alleles

75%
BC1 Seed
Elite Alleles

87.5%
BC2 Seed
Elite Alleles

For all selection procedures during this period, measurements undertaken by plant breeders to include or eliminate plants from subsequent generations in a breeding program depend upon the requirements of the farmer, the handler, the processor or the consumer. Such measurements may involve simple procedures such as measuring plant height or attractiveness. Others may be complex, such as measuring the response of individual plants to artificial inoculation with a plant pathogen or the chemical analysis of oil.

DEVELOPING HYBRIDS

To make hybrids, breeders cross selected members of the elite, true-breeding inbreds they have developed. The offspring seed from these crossed inbred lines are the hybrids the breeder further evaluates for field performance and quality traits to assess which hybrid combinations have the potential to be commercial hybrid variety. Each new hybrid generated goes through extensive field trialing and testing during this evaluation.

Before any new hybrid is released to the market it undergoes several years of development and testing through a stringent, multi-year process designed to identify those hybrids that have the best combination of field performance and product quality. Hybrids are grown under standard or typical production conditions side-by-side with industry leading hybrids. These leading hybrids are called "checks". Yield data is recorded from both hybrids and the checks. In addition, those hybrids with the most commercial promise are further subjected to other analytical and observational tests, as appropriate for the crop. Hundreds or even thousands of new hybrid combinations are evaluated each year. Hybrids are commercially released only if their combination of field performance and product quality will make them more competitive in some aspect compared to existing commercial hybrids. As a result, only a very small percentage--typically less than 1%-- of the hybrids originally made by the breeder are ultimately commercially released. At every point during this testing process, hybrids that are not competitive will be eliminated from the pool of candidates.

THE TESTING PROCESS

Plant breeding is often said to be a process not of selection, but of elimination. Any off-types, unstable lines, or lines showing characteristics such as significant differences in nutrient content, detrimental responses to environmental stresses, diseases, or the presence of other undesirable traits are discarded as soon as they are identified. An off-type is a seedling or plant that differs in one or more characteristic, such as flower color or height. This winnowing takes place over several years, so the remaining lines identified for prospective commercial release will perform as expected. The environment in which a crop is grown often plays a significant role in affecting plant characteristics, such as the levels of certain anti-nutrients, overall yield and flowering. The trialing process occurs over multiple geographies and multiple years in order to observe that potential variability, keeping only the varieties that will meet consumer and grower expectations.

Genetically stable, potentially commercial hybrids and varieties are normally evaluated for:

- Geographic and production system adaptation
- Performance characteristics, relative to existing commercial hybrids/varieties
- Processing characteristics appropriate for that crop, such as milling for wheat, sugar yield for sugar beets, oil quality for canola and sunflower or storage characteristics for fruits and vegetables
- End-user characteristics (as appropriate for that crop), such as protein content for soybeans, bread-making characteristics for wheat, cooking quality for rice and flavor characteristics for fruits

While this paper focuses on the process for developing new hybrid varieties, the same testing procedures occur for the development of non-hybrid varieties as well.

The majority of substances in food from plants are not toxic or harmful to humans -- less than 1/10th of one percent of all substances in all foods are toxic or otherwise harmful. Genetic changes, such as a mutation in a DNA nucleotide sequence and DNA rearrangements, were once thought to potentially produce novel, unknown toxins. In fact, however, there is not a single documented example whereby these changes have led to the production of previously unknown toxins. It is now recognized that these kinds of small genetic changes occur routinely and spontaneously in crop plants and during the breeding process. Thus, the range of natural variability that exists within a particular plant species is much broader than scientists could have previously measured and appreciated.

The advent of genomics, the ability to precisely sequence the DNA of crops, and ultimately utilize molecular knowledge about favorable traits, has led to improved efficiencies in plant breeding and plant improvement capabilities. As an example, it was discovered that corn inbred lines can vary by up to 15% in the genes that are present in specific inbred. In other words, inbred lines of corn, historic or recently developed, differ on average by 15% in the genes they contain and many genes will be absent from ones and present in others. This presence-absence variation is a natural phenomenon in corn that was only discovered by using modern genomics tools.

The discovery of this residual genomic variation may lead to new approaches to improving uniformity in products or further maximizing genetic potential. Genomics in breeding has not in any way changed the safety of the products; plants developed through breeding continue to have a record of safety while providing increased value (e.g. improved taste or disease resistance) for consumers and farmers. All reported cases of crop toxicity have been associated with the elevation of known toxins, such that testing for their presence has become a routine part of the breeding process to prevent inadvertent increases in toxin levels. This provides a very strong scientific basis to use breeding, with its genetically discernible, yet phenotypically indistinguishable variations, as a baseline for safety evaluations.

Various physical or chemical tests are used to measure product quality for new hybrids/varieties. The particular tests vary with the crop species and intended use of the final product. For example, processing tomatoes may be tested in the laboratory for fruit pH, sugar and acid levels, color, juice viscosity or even how easily they can be peeled. Fresh market tomatoes may be tested for firmness and shelf life. Hot pepper varieties may be tested for capsaicin levels, to quantitate how 'hot' they are compared to industry standards. Melons may be measured for their ability to be shipped, fruit sweetness, fruit color and for certain compounds that affect aroma and flavor. Rice is tested for stickiness or fluffiness after cooking to identify rice types for different types of dishes.

For some crops, product quality is related to the lack of certain phytochemicals. For example potatoes are selected to have very low levels of glycoalkaloids, squash is selected for low levels of cucurbitacins, soybean for low levels of trypsin inhibitors, and sweet peppers for the lack of capsaicin, canola for low glucosinolates. Some of these attributes can be measured by simple taste-testing. Detailed quantitative analysis, if appropriate, generally requires laboratory evaluations for accurate measurement. Again, these tests are performed on both candidate inbred lines and potential commercial hybrids, to be grown under a variety of environmental conditions, locations, and over multiple years to accurately measure the product quality consumers expect to see in the grocery store.

Phenotypic characteristics provide important information related to the suitability of new hybrids and varieties for commercial distribution. In the case of corn, breeders evaluate stand count and seedling vigor in the early stages of growth. As the plant matures, disease data is evaluated, such as gray leaf spot, anthracnose, fusarium and head smut infestations. As the plant continues to develop, root lodging, stalk lodging, brittle snap, time to silk, and time to shed are evaluated. The mature plant is measured for plant height, ear height, dropped ears, and husk cover. The harvested grain is measured for yield, moisture, and test weight.

CROP	TARGET MARKET	MAJOR CONSUMER QUALITY TRAITS
Sweet Corn	Fresh Market	Ear Size, Shape, Kernel Color, Flavor, Tenderness
Sweet Corn	Processing	Yield, Kernel Size, Color, Flavor, Tenderness
Vegetables	Fresh Market	Appearance, Flavor, Shelf Life
Vegetables	Processing	Yield, Appearance, 'Processibility', Flavor

Plant breeders developing new varieties of soybeans evaluate many parameters at different stages in the developmental process. In the early stages, breeders evaluate flower color, plant vigor, stand count, relative maturity, plant habit, pubescence color, hila color, pod wall color, plant morphology, days to flowering, emergence, and general disease resistance. The latter disease screening depends on the maturity and area in which the seeds are being grown. Later on, as a variety gets closer to commercialization, breeders measure yield at larger sites at increasing numbers of sites. Plants are also screened for resistance to various diseases. In some cases, breeding was directed towards specific increases in certain components, and the plant breeder would be expected to analyze for such components. For a crop, such as wheat, end-use characteristics, including milling and baking qualities, and grain quality are often identified in the initial stages of performance evaluation. Performance evaluations are carried out and include exposure to winter injury, saline soil, high soil temperatures and natural disease epidemics or insect infestations.

CONCLUSION

As our knowledge of plant genetics and biology have developed over time, new tools, technologies and strategies have been adopted by plant breeders. Thousands of years ago plant breeding was based entirely on breeders selecting plants based on their appearance, smell, taste and ease of production. As more sophisticated methods emerged to better measure plant characteristics, breeders adopted these tools. Today breeders use an array of tools such as whole genome sequencing data, computers, and digital imaging to measure plant performance and characteristics. Breeding is a living and dynamic science that is enabled by a multitude of other scientific disciplines, including but not limited to genetics, statistics, plant physiology, agronomy, entomology, plant pathology, molecular biology, computer science, soil science, ecology, and even human and animal nutrition. The effective incorporation of this vast array of scientific disciplines will continue to improve the effectiveness of plant breeding to deliver plants with even greater improvement in offering value to the global human population. Regardless of the tools used, the goal is still the same: To first create genetic diversity in a population of plants and through multiple years of field trials and testing develop new plant varieties that reliably produce safe, nutritious, good tasting food.

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