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Regulatory Analysis and Development, PPD, APHIS,
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The following are comments regarding a proposal by USDA's Animal and Plant Health Inspection Service (APHIS) to exempt plants with additional modifications that could otherwise be achieved through conventional breeding from the regulations that govern the introduction (importation, interstate movement, or release into the environment) of certain organisms modified or produced through genetic engineering. These comments are on behalf of U.S. Wheat Associates (USW) and the National Association of Wheat Growers (NAWG).

ABOUT U.S. WHEAT ASSOCIATES (USW)

USW is the export market development organization for the U.S. wheat industry. USW promotes the reliability, quality, and value of all six U.S. wheat classes to wheat buyers, millers, bakers, food processors and government officials in more than 100 countries around the world.

Its mission is to "develop, maintain, and expand international markets to enhance wheat's profitability for U.S. wheat producers and its value for their customers." Funding is made possible through checkoff dollars, goods, and services from 17 state wheat commissions and cost-share grants from the USDA's Foreign Agricultural Service (FAS).

ABOUT NATIONAL ASSOCIATION OF WHEAT GROWERS (NAWG)

NAWG is a federation of 20 state wheat grower associations that works to represent the needs and interests of wheat producers before Congress and federal agencies. Based in Washington, D.C., NAWG is grower-governed and grower-funded and works in areas as diverse as federal farm policy, environmental regulation, the future commercialization of emerging technologies in wheat, and uniting the wheat industry around common goals. Our members feel it is important to provide comments on this Docket as it impacts critical wheat research aimed at improving wheat breeding technologies.

U.S. WHEAT INDUSTRY POSITION ON BIOENGINEERING

USW and NAWG support and believe in using science-based approaches with new technologies to advance agriculture and positively impact sustainability and climate. Unfortunately, acceptance of genetically engineered crops have been limited in overseas markets coupled with a complex and costly regulatory approval process that has historically constrained wheat producers from adopting advanced breeding technologies, such as genetically modified organisms (GMOs). Recent advances in gene editing, combined with the promise of regulatory reform measures to be instituted by U.S. federal agencies, as well as other countries, provide a measure of optimism for wheat breeders to consider utilizing these technologies at some point in the future. The U.S. exports around 50% of its annual wheat production across the globe. The U.S. wheat industry would like to see these new technologies used in wheat if it does not disrupt commercial trade. U.S. farmers and the environment would benefit greatly from these new technological advancements in agriculture, while also feeding a growing population and economy.

The U.S wheat industry's position on biotechnology can be found here, principles for commercialization here, and Plant Breeding Innovation statement here.

ONGOING CONCERNS WITH THE SECURE RULE RELATED TO WHEAT BREEDING

Slightly more than one year ago, USDA's Animal and Plant Health Inspection Service (APHIS) revised regulations regarding the movement (importation, interstate movement, and environmental release) of certain genetically engineered organisms in response to advances in genetic engineering and the agency's understanding of the plant pest risk posed by genetically engineered organisms. In doing so, APHIS made steps to reduce the regulatory burden for developers of organisms developed through gene editing that are unlikely to pose plant pest risks.

The Sustainable, Ecological, Consistent, Uniform, Responsible, Efficient (SECURE) rule used science-based approaches to develop the revised rule, but the rule lacked benefits for wheat breeders, many of which are in universities and small businesses, to utilize gene editing because wheat is genetically more complex with three genomes. The wheat industry would like to see additional exemptions for applications of gene editing to plants containing additional targeted modifications to benefit wheat breeding advancements.

While the exemptions were formulated to apply to what could otherwise be achieved through conventional plant breeding techniques in any species, in reality the limited applicability of the SECURE rule exemptions to single targeted modifications was structured to favor diploid plants. As the American Seed Trade Association points out in their comments, many crops are ancient polyploids and therefore often have two copies of each gene set on different chromosomes that also need to be modified to change a phenotype. As such, extending exemptions beyond one pair of homologous chromosomes would have a tremendous positive impact on innovation in a broad range of food crops, without posing plant pest risks greater than the plant pest risks posed by plants modified by conventional breeding methods.

APHIS acknowledges that in some species, including wheat, a single targeted modification is often less than what could otherwise be developed through conventional breeding.

During development of the SECURE rule, APHIS summarized remarks of many commenters which argued that limiting the exemption in proposed § 340.1(b)(1) to a single deletion and the exemption in § 340.1(b)(2) to a single base pair substitution does not take into account that multiple base pair substitutions and/or deletions are routinely and safely introduced into plants using conventional breeding methods, including mutagenesis.

APHIS responded to these comments suggesting while multiple substitutions or deletions can occur through conventional breeding methods, including mutagenesis, that these arguments seem to be conflating the specific targeted changes that can be made via genome editing techniques with the multiple random changes that occur during conventional breeding, only one or few of which might contribute to the desired phenotype.

The U.S. wheat industry suggests that the specific, targeted changes achievable through gene editing, even when targeted on multiple chromosomes, as in polyploids, is a means by which wheat breeders can avoid untoward mutations obtained through conventional breeding techniques thereby minimizing or eliminating the need to remove these mutations by laboriously self-fertilizing or backcrossing the mutated plant for multiple generations. While APHIS acknowledges that genome editing can easily introduce multiple beneficial changes in one generation, the argument that there is a potential to observe phenotypes that have not been seen by conventional breeding does not justify maintaining a complex regulatory review process for polyploids, particularly when the end result is more likely phenotypes that have been achieved by conventional breeding, albeit at significantly greater investment in time and resources.

CURRENT PROPOSAL IS A STEP IN THE RIGHT DIRECTION

The U.S. wheat industry appreciates the effort of USDA-APHIS to expand the scope of exemptions promulgated under the SECURE rule. Among the 3 proposed exemptions, the third proposal to exempt changes resulting from cellular repair of two targeted DNA breaks on a single chromosome or at the same location on two homologous chromosomes, when the repair results in a contiguous deletion of any size in the presence or absence of a repair template, or in a contiguous deletion of any size combined with an insertion of DNA in the absence of a repair template offers limited benefits to wheat breeders.

This exemption provides an opportunity to eliminate large chromosomal segments or smaller genomic regions that are associated with negative impacts on traits. Variation in many important agronomic traits, including but not limited to heading date or grain hardiness, is associated with presence of absence of certain genes in the wheat genome. By applying gene editing technology, it would be possible to create wheat lines with deletions of genes controlling variation in these traits.

APHIS specifies that to qualify for the exemption, the plant must have mutations that are restricted to a pair of homologous chromosomes in diploids and allopolyploids or any two homologous chromosomes in autopolyploids. No specific plant pest risk is documented by

APHIS justifying continuing the complex and burdensome regulatory framework for genetic edits to two or more homeologous chromosomes.

In fact, APHIS now acknowledges and uses the hexaploid wheat mutant *ph1* as an example of a large deletion mutation obtained through conventional breeding programs.

The currently proposed regulations put polyploid wheat at a disadvantage compared to diploid crops. Genetic and genomic studies in wheat demonstrated that duplicated homoeologous genes from different wheat genomes jointly control trait variation. In wheat, because of the presence of functionally redundant copies of homoeologus genes, a mutation in only one homoeologus gene copy was shown to have small or non-detectable impact on a trait and have limited value for breeding. While a similar mutation in a diploid crop would result in easily detectable strong changes in a trait that could be used in breeding. To obtain comparable changes in agronomic traits, in polyploid wheat there is a need in editing all homoeologous copies of genes.

PROPOSAL TO EXPAND THE SCOPE OF USDA'S PROPOSED EXEMPTIONS

The U.S. wheat industry respectfully proposes that the proposed exemption criteria in the third exemption category be expanded to include "changes resulting from cellular repair of multiple DNA breaks occurring at similar locations on two or more homeologous chromosomes." Inclusion of this phrase within the third exemption category would provide expanded benefits to wheat breeders, as well as to breeders of other polyploid crops including:

The elimination of restrictions on homoeologous gene editing provides an opportunity to improve many agronomic traits in wheat. The most well-known example of homoeologous gene editing is the development of a wheat line resistant to powdery mildew created by editing all three homoeologous copies of the Mlo genes. Improvement of wheat productivity traits could be achieved by editing the homoeologous copies of recently identified genes that control grain size, grain weight, and grain number, such as TaGW2 or TaCKX2. The editing of three homoeologs of the Qsd1 gene in wheat could be used to reduce pre-harvest sprouting. Recent advances in wheat genetic and genomics accelerated identification of genes that control major agronomic traits that opens now new possibilities for improving wheat and accelerating the development of superior varieties.

U.S. Wheat Associates and the National Association of Wheat Growers appreciate the efforts of USDA to promote a transparent, science-based regulatory program based firmly on the principals of risk assessment. As there is no indication of increased plant pest risk by extending the exemptions to modifications beyond one pair of homologous chromosomes, we urge USDA to take this opportunity to remove regulatory barriers that limit or prohibit the use of advanced breeding technologies by wheat growers.

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