



United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Biotechnology
Regulatory
Services

4700 River Road
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Dr. Daria H. Schmidt
Director, Registration and Regulatory Affairs – North America
DuPont Pioneer
7100 NW 62nd Avenue
Johnston, IA 50131-1000

Re: Confirmation of Regulatory Status of CRISPR-Cas Corn with Improved Resistance to Northern Leaf Blight

Dear Dr. Schmidt:

Thank you for your letter dated March 14, 2017 inquiring whether the corn product you described in your letter is a regulated article. Thank you as well for providing clarification to our questions in your amended letter dated May 19, 2017. Your request describes a corn (*Zea mays*) product with improved resistance to Northern Leaf Blight (NLB) using only alleles from corn and generated using CRISPR-Cas9.

The Plant Protection Act (PPA) of 2000 gives USDA the authority to oversee the detection, control, eradication, suppression, prevention, or retardation of the spread of plant pests or noxious weeds to protect the agriculture, environment, and economy of the United States. The APHIS mission is to protect the health and value of American agriculture and natural resources.

APHIS regulates the importation, interstate movement and environmental release (field testing) of certain genetically engineered (GE) organisms that are, or have the potential to be, plant pests. Regulations for GE organisms that are or have the potential to be plant pests, under the PPA, are codified at 7 CFR part 340, "Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which Are Plant Pests or Which There Is Reason To Believe Are Plant Pests." Under the provisions of these regulations, a GE organism is deemed a regulated article if it has been genetically engineered using a donor organism, recipient organism, or vector or vector agent that is listed in §340.2 and meets the definition of a plant pest, or that is an unclassified organism and/or an organism whose classification is unknown, or if the Administrator determines that the GE organism is a plant pest or has reason to believe it is a plant pest.

In your amended May 19, 2017 letter, which provided additional information, you describe your corn with improved resistance to NLB as a genetic line with a targeted allele replacement. According to your letter, the corn was subjected to biolistic co-transformation with seven plasmids containing the genetic elements used to edit the NLB-sensitive allele of the corn NLB18 gene with a resistance allelic version from the same locus, resulting in the improved disease resistant phenotype. The genetic sequences that were used did not contain any plant pest sequences, nor were the sequences introduced into the parent plant with a plant pest vector. Finally, you state that any remaining extraneous plasmid DNA will be segregated out through conventional breeding, the confirmation of which will be conducted by molecular analysis.

APHIS has reviewed the information in your letter, specifically, the table which provided the source of all genetic sequences used in the genome editing, and agrees that the final CRISPR-Cas corn product with improved resistance to NLB you described was not engineered using plant pests and contains no genetic material from plant pests. APHIS has no reason to believe that the CRISPR-Cas corn product with improved resistance to NLB is a plant pest. Therefore, consistent with previous responses to similar letters of inquiry, APHIS does not consider the CRISPR-Cas corn product as described in your May 19, 2017 amended letter to be regulated pursuant to 7 CFR part 340. Additionally, corn is not listed as a Federal noxious weed pursuant to 7 CFR part 360, and APHIS has no reason to believe that the genetic alteration of your CRISPR-Cas corn would increase the weediness of corn.

Please be advised that the importation of CRISPR-Cas corn with improved resistance to NLB, like all other corn, will be subject to APHIS Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements. For further information, should you plan to import these CRISPR-Cas corn, you may contact Shailaja Rabindran at 301-851-2167 or contact PPQ general number for such inquiries at (877) 770-5990.

Please be advised that your CRISPR-Cas corn with improved resistance to NLB may still be subject to other regulatory authorities such as FDA or EPA.

Should you become aware at any time of any issues or additional information that may be inconsistent with, or affect, the Agency's conclusion regarding this inquiry, you must immediately notify the Agency in writing of the nature of the issue. We hope you appreciate our commitment to plant health and support for the responsible stewardship for the introduction of GE plants.

Sincerely,



Michael J. Firko, Ph.D.
APHIS Deputy Administrator
Biotechnology Regulatory Services
Animal and Plant Health Inspection Service
U.S. Department of Agriculture



Date