



United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Biotechnology
Regulatory
Services

4700 River Road
Riverdale, MD
20737

Dr. Glenn Bowers
Calyxt, Inc.
600 County Road D W.
Suite 8
New Brighton, MN 55112

Re: Request for regulatory status of "Nutritionally-Enhanced Wheat"

Dear Dr. Bowers:

Thank you for your letter dated February 2, 2017 inquiring whether your "Nutritionally-Enhanced Wheat" (*Triticum aestivum*) is a regulated article under 7 CFR part 340. Your letter described the wheat product as a null-segregant expressing a gene inactivated (knocked out, KO) by TALEN®Technology.

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 February 2, 2017 letter, you describe the KO wheat as a null segregant of a wheat transgenic parental line (referred to as "transgenic producer plant" in your inquiry) in which the TALEN® reagent was expressed from a stably integrated expression cassette. In the transgenic parental line, molecular analyses confirmed the

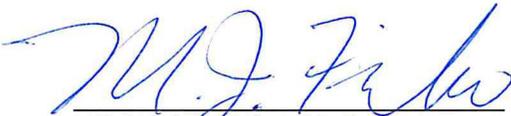
presence of the TALEN® expression cassette and the selectable marker expression cassette, as well as the targeted disruption of the gene. The letter further described that subsequent self-pollination of the transgenic parental line resulted in the wheat line that no longer contained the TALEN® expression cassette or the selectable marker expression cassette, but retained the targeted knockout (i.e., the gene product is not produced). Furthermore, your letter stated that PCR analysis confirms the absence of TALEN®-derived DNA or retention of any components of either of the expression cassettes in the genome of wheat.

APHIS has reviewed the information in your February 2, 2017 letter and based on your information, APHIS considers, consistent with previous responses to similar letters of inquiry, the KO wheat as described in your letter not regulated pursuant to 7 CFR part 340. Additionally, wheat 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 “Nutritionally-Enhanced Wheat” would increase the weediness of wheat. However, wheat is sexually compatible with a weedy relative, jointed goatgrass (*Aegilops cylindrical*). But it is APHIS’ conclusion that, if the modified trait is passed to weedy jointed goatgrass through gene flow it is unlikely to result in jointed goatgrass becoming weedier. Bread wheat and jointed goatgrass share a portion of their genome (D-genome) and they can form natural hybrids. Hybrids have low fertility, with female hybrid fertility estimated between 0.03% and 0.6% in greenhouse experiments. Backcrossing seed production rate in a field trial was 1%. Despite this low hybrid fertility, any fitness enhancing GE trait can persist and become widespread overtime in the hybrid-derived weedy populations. However, there is no evidence in the literature that trait confers a fitness advantage or enhances weediness potential. Thus it is highly unlikely that, even if gene flow occurs between GE wheat and jointed goatgrass, that it would become more weedy.

Please be advised that your KO wheat, while not regulated by APHIS under 7 CFR part 340 may still be subject to other regulatory authorities such as FDA or EPA. Please also be advised that the importation of your KO wheat, like all other wheat, will be subject to APHIS Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements. You may contact PPQ’s general number at (877) 770-5990 for such importation inquiries.

Wheat plants from this transformation that retain any inserted genetic material from plant pathogens would be considered regulated pursuant to 7 CFR part 340. Furthermore, should you become aware at any time of any issues that may 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

