



United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Biotechnology
Regulatory
Services

4700 River Road
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Dr. Karen Bohmert-Tatarev, Technology Manager
Dr. Kristi D. Snell, VP of Research & CSO
Yield10 Bioscience, Inc.
19 Presidential Way, Suite 201
Woburn, MA 01801

Re: Confirmation of Regulatory Status of a Genome-Edited Camelina Line
Developed by CRISPR/Cas Technology

Dear Dr. Bohmert-Tatarev and Dr. Snell,

Thank you for your letter dated June 12, 2017 inquiring whether the genome-edited camelina (*Camelina sativa* (L.) Crantz) line you described is a regulated article. As described in your letter, this camelina line has had a gene disrupted using CRISPR/Cas9 gene editing technology, resulting in the desired phenotype.

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 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.

As described in your June 12, 2017 letter, the parent plant of the genome-edited camelina line was genetically engineered using a plant pest vector (*Agrobacterium tumefaciens*) to deliver three expression cassettes containing DNA from plant pests, as well as other DNA elements necessary for CRISPR/Cas9 gene editing. CRISPR/Cas9 causes double-stranded breaks in the plant's DNA, which activate the plant's own



naturally-occurring repair mechanism to rejoin the DNA. You describe a genome-editing process in which no template is provided that would direct the insertion of a specific intended DNA sequence. The absence of a DNA template allows the plant's own processes to direct the DNA repair which, according to your letter, resulted in single nucleotide insertional mutations in all three copies of the target gene, inactivating its expression. Subsequently, all DNA which had been introduced for CRISPR/Cas9 gene editing was segregated from the targeted mutation through conventional breeding, thus producing progeny in which the only alterations were the single nucleotide insertions in all three copies of the gene of interest (six alleles) in the allohexaploid camelina activated by the plant's own DNA repair mechanism. In your June 12, 2017 letter you stated that the final genome-edited camelina line is devoid of plant pest sequences, T-DNA or plant vector backbone.

APHIS has reviewed the information in your June 12, 2017 letter and has concluded that the described genome-edited camelina line is not itself a plant pest. Additionally, based on the information cited in your June 12, 2017 letter, APHIS concludes that the genome-edited camelina line does not contain any of the genetic material that was inserted into the GE parent plant for CRISPR/Cas9 editing. The only genetic changes in the genome-edited camelina line are the single nucleotide insertions which resulted from the actions of the plant's own DNA repair mechanism and which were not directed by the use of a DNA template. Therefore, consistent with previous responses to similar letters of inquiry, APHIS does not consider the genome-edited camelina line described in your June 12, 2017 letter to be regulated pursuant to 7 CFR part 340. Additionally, camelina is not listed as a Federal noxious weed pursuant to 7 CFR part 360, and APHIS has no reason to believe that the intended phenotype of this genome-edited camelina line would increase the weediness of camelina.

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

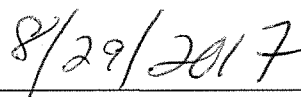
Please be advised that your genome-edited camelina line may still be subject to other regulatory authorities such as FDA or EPA.

Should you become aware at any time of any issues or additional information that may 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

