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 the Regulatory Status of Multiplex Genome-Edited Camelina Null Segregant Lines Developed using CRISPR/Cas9 Technology.

Dear Dr. Bohmert-Tatarev and Dr. Snell,

Thank you for your letter dated May 22, 2018 inquiring whether the *Camelina sativa* (L.) Crantz product described in your letter is a regulated article under 7 CFR part 340. Your letter describes null segregant *C. sativa* lines with altered product quality. The resulting desired phenotype is claimed as CBI.

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.

USDA 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.

In your May 22, 2018 letter, you stated that you used disarmed *Agrobacterium tumefaciens* to deliver a gene encoding the endonuclease Cas9, as well as three cassettes each coding for a different guide RNA to direct the Cas9 enzyme to defined targets in the *C. sativa* genome to inactivate the target site genes (target site genes are claimed as CBI). The absence of a DNA donor template during the CRISPR/Cas9-mediated genome editing process allowed the plant's own processes to direct the DNA repair which, according to your letter, resulted in mutations at the targeted loci made by the plant's own naturally-occurring DNA repair mechanism. Using DNA sequence analysis of your selected *C. sativa* lines, you were able to confirm the genetic changes and that no plant pest DNA remained in the final plant product.

Therefore, consistent with previous responses to similar letters of inquiry, USDA does not consider your null-segregant *C. sativa* lines as described in your May 22, 2018 letter to be regulated pursuant to 7 CFR part 340.

USDA is also authorized to protect American agriculture from damage caused by noxious weeds. If USDA determines that a plant poses a noxious weed risk, USDA would consider regulating the plant under the noxious weed regulation, 7 CFR part 360. USDA has the option to regulate plants under 7 CFR part 360 regardless of whether or not they meet the definition of a regulated article under 7 CFR part 340. USDA evaluated the potential for weediness of your GE *C. sativa* lines and determined that the genetic change would not increase its weediness. In addition, USDA evaluated the weediness of non-GE *C. sativa* and sexually compatible relatives should hybridization occur. Although *C. sativa* is not listed as a Federal noxious weed pursuant to 7 CFR part 360, it can be a minor weed in other crops and is sexually compatible with multiple weedy species. Based on the available information in the scientific literature, USDA has no reason to believe that the phenotypes resulting from the genetic changes described in your letter would increase the weediness of non-GE *C. sativa* or in any sexually compatible species.

USDA is committed to helping ensure that all forms of agriculture can continue to thrive and be successful. Although the genome edited *C. sativa* lines are in the early stages of development, USDA recognizes that if these plants were to be commercially released as a new variety, farmers in the vicinity may have concerns related to gene flow between GE *C. sativa* and conventional *C. sativa*, as well as the GE *C. sativa* occurring in fields of other conventional crops. Similar to the Department's experience with other crop varieties, including GE crops, USDA encourages Yield10 Biosciences to discuss these concerns with various stakeholders during the early stages of research and development of your GE *C. sativa*, and to consider developing stewardship measures to minimize gene flow and escape of your GE *C. sativa* into the environment, prior to commercialization.

Please be advised that the importation of seeds or plants of these null-segregant *C. sativa* lines, like all other *C. sativa*, will be subject to Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements. Should you plan to import these *C. sativa* seeds or plants, you may contact the PPQ Permit Services for further information at (877) 770-5990.

Please be advised that your genome-edited, null-segregant *C. sativa* lines, while not regulated by APHIS under 7 CFR part 340, may still be subject to other regulatory authorities such as the Food and Drug Administration or the Environmental Protection Agency.

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 that you appreciate our commitment to plant health and support for the responsible stewardship for the introduction of GE plants.

Sincerely,

M. J. Firko

7/07/2018

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

Date