United States Department of Agriculture

Animal and Plant Health Inspection Service

Biotechnology Regulatory Services

4700 River Road
Riverdale, MD 20737

Dr. Karen Bohmert-Tatarev, Senior Direction, Rice
Dr. Kristi D. Snell, VP of Research and CSO
Yield10 Bioscience
19 Presidential Way
Woburn, MA 01801

Re: Confirmation of the Regulatory Status of Multiplex Genome-Edited Camelina Lines Developed by CRISPR/Cas Technology

Dear Drs. Bohmert-Tatarev and Snell:

Thank you for your letter dated January 8, 2020, inquiring whether the *Camelina sativa* product described in your letter is a regulated article under 7 CFR part 340. Your letter describes genome editing of *C. sativa* using CRISPR/Cas9 technology to achieve the desired phenotype claimed as confidential business information (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 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 letter, you describe the use of disarmed *Agrobacterium tumefaciens* to deliver expression cassettes encoding the endonuclease Cas9 and guide RNAs to target endogenous Camelina genes (claimed as CBI). You describe that the inserted genetic material resulted in the inactivation of the targeted endogenous Camelina genes. The inserted transgenic cassettes were subsequently segregated out during the traditional breeding process, resulting in several Camelina lines (claimed as CBI) containing deletions of 2 to 22 nucleotides in the target genes, but not containing any of the sequences from the original transgenic construct. The absence of the transgenic insertion in the genome edited lines was confirmed by PCR analysis.

Based on the information you provided in your letter, USDA has concluded that your genome edited Camelina lines do not contain sequences inserted using a plant pest vector or sequences from a plant pest donor. Camelina is not considered a plant pest. APHIS

concludes that your genome-edited Camelina lines do 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 lines are deletions of 2 to 22 nucleotides, which resulted from the actions of the plant's own DNA repair mechanism and were not directed by the use of a DNA template. Therefore, consistent with previous responses to similar letters of inquiry, USDA does not consider your genome edited *C. sativa* lines as described in your letter to be regulated pursuant to 7 CFR part 340.

Please be advised that the importation of these genome edited *C. sativa* seeds or plants, like all other *C. sativa*, will be subject to Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements. For further information, should you plan to import these *C. sativa* seeds or plants, you may contact the PPQ general number for such inquiries at 877-770-5990. Please be advised that these genome edited lines of *C. sativa*\ may also be subject to other regulatory authorities such as the U.S. Environmental Protection Agency (EPA) or the U.S. Food and Drug Administration (FDA). To inquire about the regulatory status of your product with the EPA, please contact Alan Reynolds at 703-605-0515. To inquire about the regulatory status of your product with the FDA, please contact Robert Merker at 240-402-1226.

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,

April 23, 2020
Date

Bernadette Juarez
APHIS Deputy Administrator
Biotechnology Regulatory Services
Animal and Plant Health Inspection Service
U.S. Department of Agriculture