



United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Biotechnology
Regulatory
Services

4700 River Road
Riverdale, MD
20737

Sekhar Boddupalli, PhD
President, Ag Bio Division
Intrexon Corporation
20374 Seneca Meadows Pkwy
Germantown, MD 20876

Re: Confirmation of the regulatory status of genome edited *Lactuca sativa* (lettuce)

Dear Dr. Boddupalli,

Thank you for your letter dated September 17, 2018, inquiring whether the lettuce (*Lactuca sativa*) product described in your letter is a regulated article under 7 CFR part 340. Your letter describes genome edited lettuce lines developed with targeted deletions resulting in 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 September 17, 2018 letter, you describe the methods used to develop your genome edited lettuce lines, the intended phenotype, and supporting evidence of these claims. These genome edited lettuce lines were developed through a combination of genome editing technology (causing the mutation) and traditional breeding techniques (segregating out the introduced genetic material). The absence of a DNA donor template during the genome editing process allowed the plants 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. You stated that you used molecular screening and trait expression to identify and select progeny lacking any presence of the vector or plant pest sequences and transgenes.

Based on the information you provided in your letter, USDA has determined that your genome edited lettuce lines are not themselves plant pests. Additionally, USDA has

accepted your attestation that these genome edited lettuce lines do not to contain any introduced genetic material. Therefore, consistent with previous responses to similar letters of inquiry, USDA does not consider your genome edited lettuce lines as described in your September 17, 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 GE plant or introgression of the GE trait to a wild relative of the GE 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 has concluded that *L. sativa* is not a weed in the United States, but that two of three introduced non-native sexually compatible relatives (*L. serriola* and *L. saligna*) are common weeds of agriculture. However, based on the available information in the scientific literature, USDA has no reason to believe that the phenotypes resulting from the genome edits described in your letter would increase the weediness of *L. sativa* or its sexually compatible relatives.

Please be advised that the importation of your genome edited lettuce seeds or plants, like all other lettuce, will be subject to Plant Protection and Quarantine (PPQ), permit and/or quarantine requirements. For further information, should you plan to import these lettuce seeds or plants, you may contact PPQ Permit Services for further information at (877) 770-5990.

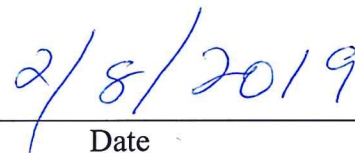
Please be advised that your genome edited lettuce lines, while not regulated by APHIS under 7 CFR part 340 may still be subject to other regulatory authorities such as FDA or EPA.

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,



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


Date