USDA
United States Department of Agriculture

Animal and Plant Health Inspection Service

Biotechnology Regulatory Services

4700 River Road
Unit 98
Riverdale, MD
20737

August 28, 2014
Dr. Luc Mathus
Cellectis Plant Sciences
600 County Road D West, Suite 8
New Brighton, MN 55112

Re: Request for Confirmation that [ ] Potato is not a regulated article

Dear Dr. Mathis:

Thank you for your letter dated July 29, 2013 inquiring whether or not the potato product described in your letter is a regulated article. This letter states that the "potato has improved consumer safety and processing attributes attributable to a single gene knock-out achieved through transient expression of a Transcription Activator-Like Effector Nuclease (TALEN)."

APHIS regulates the introduction of certain genetically engineered organisms which are, or have the potential to be plant pest. Regulations for genetically engineered organisms that have the potential to be plant pests, under the Plant Protection Act, are codified at 7 CFR part 340, "Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which Are Plant Pest or Which There Is Reason To Believe Are Plant Pests." Under the provisions of these regulations, a genetically engineered (GE) organism is deemed a regulated article if it has been genetically engineered from a donor organism, recipient organism, or vector or vector agent listed in §340.2 and the listed organism meets the definition of "plant pest" or 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 is a plant pest.

APHIS has evaluated the description of the potato product described in your July 29, 2013 letter and additional molecular analyses received on June 13, 2014. As described, the potato product was created through the transient expression of a TALEN in individual potato cells. The TALEN and the regulatory sequences used to drive the expression of the TALEN are derived from plant pest sequences (plant viral, *Agrobacterium tumefaciens*, and *Xanthomonas* spp.). The individual plant cells were genetically engineered to knock out a specific gene and used to regenerate a potato plant. The final potato plant is described as a null segregant based on molecular analyses indicating that the genetic material used to introduce the gene knock-out is no longer present in the plant.

APHIS has determined that genetic material from plant pests was used to create the potato product; however, the potato plant regenerated from genetically engineered potato cells no longer contains the introduced genetic material. Cellectis has demonstrated that the molecular analyses used to select for GE

potato plants that do not contain any inserted genetic material are adequate. Therefore, APHIS does not consider this potato product as described in your July 29, 2013 letter and confirmed through molecular analysis in your June 13, 2014 letter to be regulated under 7 CFR part 340. APHIS also considered the weediness potential of this product. Gene flow from cultivated potato to wild potato is considered a very low likelihood under natural conditions based on very limited geographic overlap and several biological barriers to hybridization and more specifically to introgression and stabilization. In addition, knockout mutations would not be expected to affect the fitness of wild potatoes.

Please be advised that the GE potato may still be subject to other APHIS regulations or other regulatory authorities such as FDA. Furthermore, GE potato plants regenerated from this transformation that retain plant pest sequences would be considered regulated under 7 CFR part 340 and would require a notification or permit for importation, interstate movement, or field release.

Sincerely,

Michael Firko
Deputy Administrator
Biotechnology Regulatory Services