United States Department of Agriculture

Animal and Plant Health Inspection Service

4700 River Road
Riverdale, MD
20737

December 16, 2011

J. Scott Thenell
1181 Keaveny Ct.
Walnut Creek, CA 94597

Re: APHIS response on the regulatory status of plants engineered using meganuclease technology

Dear Mr. Thenell:

Thank you for your letter dated September 9, 2011 regarding the regulatory status of plants that have been genetically engineered using the I-CreI meganuclease technology platform developed by Cellectis S. A. and its U.S. subsidiary Cellectis Plant Sciences (hereinafter collectively referred to as "Cellectis").

APHIS regulations for genetically engineered organisms 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 at §340.1, 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.

Your letter indicates that Cellectis has developed a genetic engineering technology that uses I-CreI meganucleases to cause plant DNA to break at a specific, targeted point in a plant genome. The I-CreI meganuclease as described in your letter is produced by the green algae Chlamydomonas reinhardtii, which is not a plant pest. Once I-CreI causes a DNA break to occur, repair of the break can create two classes of GE plants.

The first class of GE plants described in your letter contains targeted gene deletions, caused by naturally-occurring DNA repair after the break is made by the I-CreI meganucleanse. No genetic material is inserted into the plant genome.

In the second class of GE plants described in your letter, precise sequence changes are introduced into the plant genome by using specific template DNA molecules. Using a DNA template allows a range of specific changes from single nucleotide changes to the insertion of DNA sequences.

The first class of plants will not, in most cases, be regulated articles under 7 CFR part 340 because the meganuclease used is not from a plant pest and no plant pest sequences

The first class of plants will not, in most cases, be regulated articles under 7 CFR part 340 because the meganuclease used is not from a plant pest and no plant pest sequences are inserted into the plant genome using the method described in your letter. Also, there is no reason for the Agency to believe that changes to the plant genome generated by the deletion process would generate a plant pest, as long as no DNA is inserted into the plant genome during the deletion process. However, if the engineered plant is already a plant pest (i.e. a parasitic plant) or if the meganuclease is delivered into the plant using a plant pest, the engineered plant would be regulated under 7 CFR part 340. Any information that indicates that the information or data presented in your letter are not correct or are no longer correct will require the Agency revisit this evaluation.

For the second class of GE plants that use template DNA molecules, there are many potential changes to plant DNA using this type of genetic engineering. For this reason, the Agency will consider case-by-case inquiries regarding the regulatory status of these template plants. Please be aware that accidental release of a regulated article may be a violation of our regulations.

Further, please be advised that genetically engineered plants generated using Cellectis' meganuclease technology may still be subject to other applicable regulatory authorities such as EPA and FDA.

Sincerely,

Michael C. Gregoire

Michael C. Gregoire
Deputy Administrator
Biotechnology Regulatory Services