



c e r e s

January 28, 2015

Dr. Michael Firko
APHIS Deputy Administrator
Biotechnology Regulatory Services
4700 River Road, Unit 98
Riverdale, MD 20737

Re: Confirmation that TRSOG101B Transgenic Sugarcane is not a regulated article

THE FOLLOWING CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Dear Dr. Firko,

Ceres, Inc. (Ceres) is developing technology that will enable cultivated sugarcane (*Saccharum officinarum*) to have higher commercial productivity. Ceres is focused on the genetic modification of sugarcane through the use of biolistic transformation to produce sugarcane with a trait (“TRSOG101B Transgenic Sugarcane”) that will alter plant architecture, and enhance sugar yield.

Because cultivated sugarcane is not a plant pest or an invasive species, the genetic elements used to generate TRSOG101B Transgenic Sugarcane are all sourced from fully classified organisms, and the transformation process does not introduce any plant pest DNA components, there is no scientifically valid basis for concluding that our intended product, TRSOG101B Transgenic Sugarcane, is, or will become, a plant pest within the meaning of the Plant Protection Act (PPA)¹. Ceres therefore asserts that under current regulations, TRSOG101B Transgenic Sugarcane is not a regulated article within the meaning of 7 CFR §340.1 because it does not satisfy any of the regulatory criteria that would subject it to the oversight of the USDA’s Animal Plant Health and Inspection Service (APHIS).

APHIS has already determined that the genetic elements comprising the TRSOG101B recombinant DNA do not fall within the items it considers to be regulated in its responses², dated April 24, 2012 and August 6th, 2014, to the TRG101B and TRSBG101B *Am I Regulated?* letters from Ceres, respectively, for the use in *Panicum virgatum* and *Sorghum bicolor*. Before proceeding further with product development, Ceres requests that APHIS confirms that TRSOG101B Transgenic Sugarcane, modified without any plant pest elements (as described

¹ Plant Protection Act; 7 U.S.C. §7701, et seq. (2000)

² http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/biotechnology/sa_regulations/ct_am_i_reg

more fully in Table 1 below), should not be considered a regulated article within the meaning of the current regulations. If the agency does not concur with Ceres' interpretation of the current regulations, Ceres requests that the Agency provides Ceres with its scientific rationale for concluding that TRSOG101B Transgenic Sugarcane is subject to regulation.

I. Transformation Background.

To further assist APHIS in understanding the origin of our intended product, TRSOG101B Transgenic Sugarcane, a summary of information on the recipient plant, as well as the genetic and technical elements used to modify the recipient plant to make this TRSOG101B Transgenic Sugarcane product, is provided below.

A. Recipient Organism: TRSOG101B Transgenic Sugarcane (*Saccharum officinarum*)

The recipient organism targeted in our plant product, domesticated sugarcane (*Saccharum officinarum*), is not a federal noxious weed.³ In addition, cultivated sugarcane plants flower only under strict environmental conditions that are not common in the U.S., and are therefore unlikely to outcross to any wild relatives.

Historically, domesticated varieties of sugarcane were used as a feedstock for the production of sucrose, which is used as a raw material in the food industry or is fermented to produce ethanol. Sugarcane realizes maximum sugar yield in approximately 18 months. Domesticated sugarcane is adapted to warm climates and typically only grown between the 30°N and 30°S latitudes as frosts can devitalize the crop.

B. Transformation method

Transformation of sugarcane will be performed using purified DNA that is transferred by biolistic (gene gun) methods, resulting in stably integrated DNA. Such DNA transfer does not involve *Agrobacterium* transformation or any other plant pest that is currently regulated under the PPA. Table 1 below describes each genetic element and identifies its respective sources and functions. The table includes a listing of candidate genetic elements and does not imply that all elements will be used in each biolistic transformation. Some combination of promoter regulatory sequence and trait-gene will be used in each, and in some instances two or more promoter-trait combinations may be used in a single transformation.

³ <http://plants.usda.gov/java/noxious>

C. Genetic Elements

Table 1. Genetic Elements in TRSOG101B Commercial Construct for Biolistic Transformation of Sugarcane.		
GENETIC ELEMENT	SOURCE	FUNCTION
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II. APHIS' Interpretation of Its 7 CFR §340 Regulation Dictates a Finding that TRSOG101B Transgenic Sugarcane is Not a Regulated Article

A. APHIS Has Been Clear That Not All Transgenic Plants Are Subject to Regulatory Oversight

APHIS defines a “regulated article” as (Part 340.1):

Any organism which has been altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent belongs to any genera or taxa designated in §340.2 and meets the definition of plant pest, or is an unclassified organism and/or an organism whose classification is unknown, or any product which contains such an organism, or any other organism or product altered or produced through genetic engineering which the Administrator, determines is a plant pest or has reason to believe is a plant pest. Excluded are recipient microorganisms which are not plant pests and which have resulted from the addition of genetic material from a donor organism where the material is well characterized and contains only non-coding regulatory regions.⁴

Consistent with the PPA’s definition of a plant pest, APHIS further defines a “plant pest” as:

Plant pest. Any living stage (including active and dormant forms) of insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, other parasitic plants or reproductive parts thereof; viruses; or any organisms similar to or allied with any of the foregoing; or any infectious agents or substances, which can directly or indirectly injure or cause disease or damage in or to any plants or parts thereof, or any processed, manufactured, or other products of plants.⁵

⁴ *Well-characterized and contains only non-coding regulatory regions (e.g., operators, promoters, origins of replication, terminators, and ribosome binding regions).* The genetic material added to a microorganism in which the following can be documented about such genetic material: (a) The exact nucleotide base sequence of the regulatory region and any inserted flanking nucleotides; (b) The regulatory region and any inserted flanking nucleotides do not code for protein or peptide; and (c) The regulatory region solely controls the activity of other sequences that code for protein or peptide molecules or act as recognition sites for the initiation of nucleic acid or protein synthesis. (7 CFR §340.1).

⁵ 7 CFR §340.1

APHIS further claims that its regulations are consistent with the Coordinated Framework, because they apply “only [to] genetically engineered organisms or products which are plant pests or for which there is a reason to believe are plant pests, and not to...an organism or product merely because of the process by which it was produced.”⁶ APHIS has further stated that its concern arises only “when an organism or product is altered or produced by genetic engineering and one or more of its constituents (donor, vector/vector agent or recipient) comes from a family or genus of organisms known to contain plant pests.... This is because... there is a risk that certain undesirable traits may be transferred to the new organism and may survive when the organism is released into the environment.”⁷

APHIS reiterated this policy on several occasions, first when it introduced its notification and permit process for the confined release of transgenic organisms,⁸ and again during the proposed revision to its regulations.⁹ It has been clear that not all transgenic plants are to be regulated, and those that are belong to the limited group of “plant pests” as defined in the regulations.

B. TRSOG101B Transgenic Sugarcane Does Not Fall Within the Regulatory Definition of a “Regulated Article.”

Under APHIS regulations, a transgenic organism is considered a “regulated article” “if the donor organism, recipient organism, or vector agent(s) belongs to a genera or taxa designated in 7 CFR §340.2, *and* the organism meets the definition of a plant pest (emphasis added).” The language of the regulation requires that both criteria must be met to satisfy the definition of a regulated article.

For the creation of our intended product, TRSOG101B Transgenic Sugarcane, none of the donor organisms, the recipient organism, or the vectors Ceres will utilize belong to any taxa identified in §340.2. Further, none of the genetic elements described in Table 1 are sourced from any plant pest. In addition, the recipient organism, domesticated sugarcane, is not a plant pest. Therefore, our product, TRSOG101B Transgenic Sugarcane, created using the genetic elements identified in Table 1, does not satisfy either of the criteria set forth to qualify as a “regulated article”.

⁶ 51 Fed. Reg. 23352 (proposed rule); 52 Fed.Reg. 22892 (final rule where similar language is used).

⁷ Office of Science and Technology Policy’s Coordinated Framework for Regulation of Biotechnology, June 26, 1986 (51 Fed.Reg. 23302).

⁸ 57 Fed. Reg. 53036 (Feb 1991)

⁹ 73 Fed. Reg. 60008, 60010 (Oct 8, 2008)

Another definition of a “regulated article” includes transgenic organisms that are unclassified or whose classification is unknown. Other types of organisms that could raise concerns are “pathogens, predators or parasites of natural enemies of plant pests or weeds or of commercially available pollinators such as honeybees, bumble bees and alkali bees.”¹⁰ The introduced trait does not change the plants’ basic fitness characteristics and the trait’s presence does not produce a plant that would directly feed on, infect, parasitize, or contaminate plants, or adversely affect other organisms that are beneficial to plants.

III. Finding that TRSOG101B Transgenic Sugarcane is Not a Regulated Article Applies to Stacks of Other Products that are Not “Regulated Articles.”

Ceres would appreciate confirmation from APHIS that any transgene stacks, produced through molecular or breeding techniques, with other products deemed as not regulated articles, or have been granted de-regulated status, would also have the same designation, not “regulated articles” under 7 CFR §340. Such a designation of stacks such as for those under development at Ceres, all of which are combinations of what would be determined as not “regulated articles”, would allow Ceres flexibility to commercialize products with improved characteristics as feedstocks for the advanced biofuels and biopower industries.

¹⁰ 66 Fed. Reg. 51340 (Oct 9, 2001)

IV. Summary of Conclusions

In summary, the intended transformation target organism, domesticated sugarcane, is not itself a plant pest, there are no plant pest elements involved in the production of our intended product, TRSOG101B Transgenic Sugarcane, and all the native genomes that are sources for the genetic elements that will be used have been fully classified. Therefore, there is no scientifically valid basis to determine that our intended product, TRSOG101B Transgenic Sugarcane, is, or will become a plant pest within the meaning of the PPA. Likewise, a stack of any other event deemed not a “regulated article” or previously deregulated, with our product, TRSOG101B Transgenic Sugarcane, would result in a product that is not a “regulated article.”

We look forward to receiving your response, and thank you in advance for your consideration of Ceres’ position that our intended product, TRSOG101B Transgenic Sugarcane, is not a “regulated article” for the reasons described herein.

Sincerely,



Richard Hamilton
President and Chief Executive Officer
rhamilton@ceres.net

cc: Honorable Tom Vilsack, Secretary of U.S. Department of Agriculture