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October 1st, 2014

Dr. Michael J. Firko
Acting Deputy Administrator
Biotechnology Regulatory Services
4700 River Rd, Unit 98
Riverdale, MD 20737

Re: Confirmation of regulatory status of transgenic bioluminescent *Arabidopsis thaliana*

Dear Dr. Firko,

My company, Glowing Plant, Inc, is developing a range of novel ornamental plants for the consumer market. Our first product is a bioluminescent *Arabidopsis* plant, which has been genetically engineered to emit a pleasant, dim glow upon the addition of a proprietary formula. This letter does not include confidential business information.

Because *Arabidopsis* is not a plant pest or invasive species, the genetic elements introduced are all sourced from fully classified organisms, and the transformation process does not introduce any plant pest DNA components, there is no valid basis for concluding that our transgenic Arabidopsis is or will become a plant pest within the meaning of the Plant Protection Act (PPA). Therefore under current regulations, our bioluminescent *Arabidopsi*s plant is not a regulated article within the meaning of 7 C.F.R § 340.1 because there is no scientifically valid basis that it satisfies any of the regulatory criteria that would subject it to the oversight of the USDA's Animal Plant Health and Inspection Service (APHIS).

We kindly request that APHIS confirm that our bioluminescent *Arabidopsis* plant is not considered a regulated article within the meaning of the current regulations. If the agency does not concur with our interpretation of the current regulations then we ask you to provide us with the scientific rational for how our bioluminescent *Arabidopsis* is or will become a plant pest. The rest of this letter details the method for creating our plant, details of the inserted construct and our understanding of APHIS regulations which support our analysis by which bioluminescent *Arabidopsis* is not a "regulated article".

I. Description of transgenic bioluminescent *Arabidopsis* and methods used to create it

To further assist APHIS in understanding the origin of our transgenic bioluminescent *Arabidopsis*, a summary of information on the recipient plant, as well as the genetic and

technical elements used to modify the recipient plant to make it fluoresce, is provided below as per the instructions on APHIS' website.

A. Bioluminescent *Arabidopsis* Transformation

Transformation of Arabidopsis, using synthetic DNA that is transferred by biolistic (gene gun) methods, results in stably integrated DNA. Our DNA transfer does not involve *Agrobacterium* transformation nor any other plant pest that is currently regulated under the Plant Protection Act. Using the genetic elements described in Table 1 below, the genetically enhanced materials express luciferase which causes the *Arabidopsis* plant to glow with the addition of our proprietary chemical additive. Table 1 below describes each genetic element and identifies its respective sources and functions.

Table 1: Genetic Elements in Bioluminescent Luciferase Construct for Biolistic Transformation of *Arabidopsis*

Element type	Name of Element	Organism from which element is derived	Description of the elements function
Promoter	Ubq10	*Arabidopsis thaliana*	Constitutive promoter
Gene	Atffluc2	Synthetic construct modified from *Photinus pyralis* origin	Luciferase enzyme
Terminator	THsp18.2	*Arabidopsis thaliana*	Heat shock terminator
Promoter	Ubq3	*Arabidopsis thaliana*	Constitutive promoter
Gene	GFP	Synthetic construct modified from *Aequorea victoria*	Green Fluorescent Protein
Terminator	TUbq3	*Arabidopsis thaliana*	Ubiquitin 3 terminator
Gene	YFP	*Synthetic construct modified from Aequorea Victoria*	Yellow Fluorescent Protein, protein tag

B. Recipient *Arabidopsis* (*Arabidopsis thaliana*)

Arabidopsis thaliana (thale cress) is not a federal noxious weed[1]. It's a small flowering plant that was originally native to Europe, but can now be found in the United States, N. Africa and temperate Asia to Japan. A winter annual with a relatively short life cycle, the plant will grow in light (sandy), medium (loamy) and heavy (clay) soils that are acid, neutral and basic (alkaline) soils. It can grow in semi-shade (light woodland) or no shade and in dry or moist soil.

Arabidopsis is a popular model organism in plant biology and genetics. *Arabidopsis thaliana* was the first plant to have its genome sequenced, and is a popular tool for understanding the molecular biology of many plant traits, including flower development and light sensing. As a result it is the most widely studied plant today with over 11,000 researchers and 4,000 organizations around the world generating information and materials[2].

[1] http://plants.usda.gov/java/noxious
[2] http://genome.wustl.edu/genomes/detail/arabidopsis-thaliana/

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C. Intended Engineered trait/phenotype

Our transgenic *Arabidopsis* has been engineered to emit light emit a pleasant, dim glow upon the addition of a proprietary formula (which we call 'glowing plant fuel').

D. Contact information

If you have any questions or would like to discuss any of the contents of this letter, please contact us (email or phone preferred) at:

- Antony Evans
- Glowing Plant, Inc
- 665 3rd Street, Suite 250
- San Francisco, CA 94107
- Email: antony@glowingplant.com
- Tel: +1-415-779-6333

II. APHIS' Interpretation of Regulation 7 C.F.R § 340 dictates a finding that our bioluminescent transgenic *Arabidopsis* 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."

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."

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. 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."

APHIS reiterated this policy on several occasions, first when it introduced its notification and permit process for the confined release of transgenic organisms, and again during the proposed revision to it's regulations. 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. Bioluminescent transgenic *Arabidopsis* 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 C.F.R § 340.2 and the organism meets the definition of a plant pest. The language of the regulation requires that both criteria must be met to satisfy the definition of a regulated article.

For our bioluminescent transgenic *Arabidopsis thaliana* none of the donor organisms, the recipient organism nor the vectors used to transform the plant belong to any taxa identified in § 340.2. Further, none of the genetic elements identified above are sourced from any plant pest. In addition, the recipient organism, *Arabidopsis*, is not a plant pest. Therefore our bioluminescent *Arabidopsis* does not satisfy either of the criteria set forth to qualify as a "regulated article".

Another definition of a "regulated article" includes transgenic organisms that are unclassified or whose classification is unknown. The genetic donor element sources and our bioluminescent *Arabidopsis* itself are well classified and do not relate to the types of organisms that could raise concerns, such as pathogens, predators or parasites, or weeds or commercially available pollinators such as honeybees, bumble bees etc.

III. Finding that transgenic bioluminescent *Arabidopsis* is not a regulated article is consistent with previous precedents of APHIS determinations

APHIS has previously made a number of determinations that transgenic plants, analogous to our proposed bioluminescent Arabidopsis, are not "regulated articles". A number of these examples are posted and available on USDA's website.[3] A finding that bioluminescent *Arabidopsis* is not a regulated article is consistent with these other determinations.

IV. Conclusions

In summary, our bioluminescent *Arabidopsis* is not itself a plant pest and there are no plant pest elements involved in the genetic transformation, and further all sources for the genetic elements to be used have been fully classified. Therefore we respectfully ascertain that there is no basis to assume our plant is or will become a plant pest within the meaning of the Plant Protection Act.

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[3] http://www.aphis.usda.gov/wps/portal/aphis/home/?1dmy&urile=wcm%3apath%3a%2Faphis_content_library%2Fsa_our_focus%2Fsa_biotechnology%2Fsa_regulations%2Fct_reg_loi

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We thank you in advance for your consideration and prompt confirmation that our transgenic bioluminescent *Arabidopsis thaliana* plants are not a "regulated article" for the reasons described above. If you have any further questions please don't hesitate to contact us via the contact information supplied above.

Sincerely,

Glowing Plant, Inc.

By_____

Antony Evans
Chief Executive Officer

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