EPA BIOPESTICIDES AND POLLUTION PREVENTION DIVISION COMPANY NOTICE OF FILING FOR PESTICIDE PETITIONS PUBLISHED IN THE FEDERAL REGISTER (7/1/2007)

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TEMPLATE: Company submission

Circle One Global, Inc.

Pesticide Petition 7F7302

EPA has received a pesticide petition 7F7302 from Circle One Global, Inc. (Circle One), P.O. Box 28, Shellman, GA 39886-0028, proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180.1254 to establish an amendment/expansion of an existing tolerance exemption for the microbial pesticide *Aspergillus flavus* NRRL 21882 for its use on the food/feed commodity corn.

Pursuant to section 408(d)(2)(A)(i) of FFDCA, as amended, Circle One has submitted the following summary of information, data, and arguments in support of their pesticide petition. This summary was prepared by Circle One and EPA has not fully evaluated the merits of the pesticide petition. The summary may have been edited by EPA if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner.

I. Circle One Petition Summary

Pesticide Petition 7F7302

A. Product Name and Proposed Use Practices

Circle One proposes to expand the registration for afla-guard®, which is formulated with *Aspergillus flavus* NRRL 21882, to include use on corn. The product will be applied aerially at 20 pounds per acre, the rate currently approved for use on peanuts. The application to corn will be once per season at the first sign of corn tasseling.

B. Product Identity/Chemistry

1. Identity of the pesticide and corresponding residues. *Aspergillus flavus* NRRL 21882 is a naturally-occurring non-aflatoxin-producing fungal active ingredient that will be used to displace the ubiquitous *A. flavus* group of microbes, many of which can produce aflatoxins,

which are potent carcinogens. The residues resulting from treatment on corn are *Aspergillus flavus* NRRL 21882. The active ingredient is cultured from spores originally obtained from the U.S. Department of Agriculture's (USDA) Agricultural Research Service (ARS) Patent Culture Collection in Peoria, Illinois. It is cultured on a selective isolation medium and can be identified by vegetative compatibility group (VCG) assays and characterized as non-aflatoxin-producing by standard thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) procedures. Product characterization previously submitted confirmed the absence of aflatoxins (B1, B2, G1, and G2), and cyclopiazonic acid (CPA) (see *Aspergillus flavus* NRRL 21882 Biopesticides Registration Action Document (BRAD), May 24, 2004, pp. 15-16). Additionally, the manufacturer of the technical grade active ingredient routinely conducts standard microbiological assays on *Aspergillus flavus* NRRL 21882 conidia to assay for potential aflatoxins, metabolites, CPA, bacterial contaminants, and bacterial pathogens.

2. Magnitude of residues at the time of harvest and method used to determine the residue. It is expected that the percent toxic strains of total *A. flavus* found in corn grain will be reduced as a result of treatment with the registered product. A dilution plating method has been used to quantify the *A. flavus* colonization in both corn and peanuts, as well as the aflatoxin contamination (J.W. Dorner (2002) Simultaneous Quantification of *Aspergillus flavus/A. parasiticus* and Aflatoxins in Peanuts, J. of AOAC International, 85(4): 911-916).

3. A statement of why an analytical method of detecting and measuring the levels of the pesticide residue are not needed. A petition for exemption from the requirement of tolerance is being submitted with applications to add the corn use to both the manufacturing-use label for *Aspergillus flavus* NRRL 21882 and the end-use label for afla-guard®. EPA previously has determined that an exemption from tolerance is supported when the product is used on peanuts (see 69 FR 39341, June 30, 2004, codified at 40 C.F.R. § 180.1254) and temporarily when used on corn (see 72 FR 27460, May 16, 2007) in association with an Experimental Use Permit (EPA File Symbol 75624-EUP-2). In reaching these conclusions, EPA noted that *Aspergillus flavus* NRRL 21882 occurs naturally in the environment and beneficially displaces toxigenic strains of naturally-occurring *A. flavus*. EPA also noted that there is no indication of toxicity, infectivity, or pathogenicity in mammalian acute oral and pulmonary studies using *Aspergillus flavus* NRRL 21882 as the test material. Accordingly, a numerical tolerance and an analytical method to measure pesticide residues are not needed.

C. Mammalian Toxicological Profile

The toxicological profile previously has been summarized and published in the final rule to create a tolerance exemption for use on peanuts, 69 Fed. Reg. 39341 (Jun. 30, 2004) as well as in the May 24, 2004, BRAD. The pesticide is classified as Toxicity Category IV on the basis of acute oral toxicity/pathogenicity tests submitted for the exemption from tolerance for its use on peanuts. EPA also noted that there is no indication of toxicity, infectivity, or pathogenicity in mammalian acute oral, pulmonary and intravenous studies using *Aspergillus flavus* NRRL 21882 as the test material. *Aspergillus flavus* NRRL 21882 cleared all tissues examined during those tests (see 69 FR 39341, June 30, 2004). Those studies also supported the temporary exemption from tolerance for corn (see 72 FR 27460, May 16, 2007).

D. Aggregate Exposure

1. Dietary exposure. The total dietary exposure consists of the potential exposure in food and drinking water, which are discussed below. *Aspergillus flavus* NRRL 21882 is neither toxic nor infective as determined by submitted studies (see May 24, 2004, BRAD). A tolerance exemption has been granted for use on peanuts (69 Fed. Reg. 39341, Jun. 30, 2004).

i. Food. The product is proposed for use for treatment of corn at the same rate as approved for use on peanuts. Levels of *Aspergillus flavus* NRRL 21882 are not expected to exceed total levels of naturally-occurring Aspergillus fungi on corn and thus would not increase dietary exposure. *Aspergillus flavus* NRRL 21882 is a naturally-occurring strain that does not produce aflatoxins, CPA, or other known intermediates in the aflatoxin biosynthetic pathway, some of which are toxic. The use of the product reduces the aflatoxin content of treated corn when compared with untreated controls, as demonstrated by efficacy data submitted with the registration amendment application for afla-guard®. In the United States, aflatoxin levels in corn are monitored to verify they do not exceed the regulatory action levels (limits) set by the U.S. Food and Drug Administration (FDA).

ii. Drinking water. Exposure to *Aspergillus flavus* NRRL 21882 in drinking water is not expected to be greater than existing exposures to *A. flavus* strains generally. Potential risks via exposure to drinking water or runoff are mitigated adequately by, among other things, percolation through soil. The product is not applied to crops grown in water and is not likely to accumulate in drinking water if used as directed on the label. Accordingly, exposure by drinking water will not increase as a result of the proposed use on corn.

2. Non-dietary exposure. The product currently is registered for use on peanuts only. EPA has evaluated occupational, residential, ecological, and environmental exposure with the peanut use. Based on these evaluations, the only mitigation required was with respect to the exposure by pesticide handlers. To mitigate this exposure, EPA requires the use of personal protective equipment. This requirement is triggered by the properties of the *A. flavus* species, not the specific registered strain, which has had no hypersensitivity incidents reported during the 12 years handled by workers in the laboratory and in field trials. There are no residential or non-crop uses. Non-occupational exposure is not likely to be greater than that which normally exists to the naturally-occurring *A. flavus* species. This issue is discussed in further detail at 69 FR 39347 and in the May 24, 2004, BRAD.

E. Cumulative Effects

Completed toxicology studies indicate that *Aspergillus flavus* NRRL 21882 is not toxic or pathogenic to humans. It currently is registered for use on peanuts only. Another strain of *Aspergillus flavus, A. flavus* AF36, is registered under Section 3(c)(5) for use on cotton. *A. flavus* AF36 is also temporarily exempt from the requirement of a tolerance on corn in accordance with an EUP (EPA File Symbol 71693-EUP-2). Other *A. flavus* strains abound naturally in the environment. The displacement of aflatoxin-producing strains of *A. flavus* by *Aspergillus flavus* NRRL 21882 is expected to reduce aflatoxin contamination in corn, as demonstrated by the efficacy data submitted with the registration amendment for afla-guard®.

As *Aspergillus flavus* NRRL 21882 is naturally occurring, in toxicity Category IV, and atoxigenic, no cumulative incremental effect from its use on corn is expected.

F. Safety Determination

1. U.S. population. There is a reasonable certainty that no harm will result to the U.S. population from aggregate exposures to residues of *Aspergillus flavus* NRRL 21882 as a result of its use on corn. EPA has already concluded that the organism is non-toxic and non-pathogenic to animals and humans. The additional exposure to this organism from use on corn should not increase the overall exposure to *A. flavus*, and the use is expected to reduce potential exposure to potent mycotoxins. Accordingly, use of the product on corn should not change the conclusion concerning the safety of the product already reached by EPA in the context of its use on peanuts.

2. Infants and children. EPA previously has concluded that *Aspergillus flavus* NRRL 21882 is non-toxic to mammals, including human infants and children. As there are no threshold effects of concern for infants, children, and adults, no additional margin of safety was added in EPA's assessment of the product's use on peanuts. As *Aspergillus flavus* NRRL 21882 is naturally occurring, in toxicity Category IV, and atoxigenic, it can be concluded that no additional safety factor is needed.

G. Effects on the Immune and Endocrine Systems

EPA has not required submission of information on the endocrine effects of the active ingredient, *Aspergillus flavus* NRRL 21882. There is no known metabolite produced by this microorganism that acts as an endocrine disruptor. The submitted toxicity/infectivity and/or pathogenicity studies in the rodent indicate that, following oral and pulmonary routes of exposure, the immune system is intact and able to process and clear the active ingredient. Additionally, based on the low potential exposure associated with the proposed, single application per season use, no adverse effects to the endocrine or immune system are expected.

H. Existing Tolerances

An exemption from the requirement of a tolerance currently exists for residues of *Aspergillus flavus* NRRL 21882 in/on peanuts, which is published in 40 C.F.R. § 180.1254. There also is a temporary tolerance exemption for residues of *Aspergillus flavus* NRRL 21882 in/on corn when used in accordance with Experimental Use Permit 75624-EUP-2, which will expire on May 2, 2009.

I. International Tolerances

There is no Codex maximum residue level for residues of *Aspergillus flavus* NRRL 21882.