

2. *Drinking water exposure.* Exposure to AF36 via drinking water is not likely to be greater than current/existing exposures to *A. flavus* strains. Potential risks via exposure to drinking water or runoff are adequately mitigated by, among other things, percolation through soil. Thus, exposure via drinking water from the proposed use of this non-aflatoxin-producing strain of *Aspergillus flavus* is not likely to pose any incremental risk to adult humans, infants and children. In fact, displacement of the toxigenic strains of *A. flavus* by AF36 may decrease exposure and risk to the toxigenic strains of *A. flavus* in the environment.

#### B. Other Non-Occupational Exposure

1. *Dermal exposure.* The potential for non-occupational dermal exposure to AF36 is unlikely because the potential use sites, are commercial and agricultural, and because of the granular nature of the pesticide, which minimizes spray drift. As discussed earlier (see Unit III.), lack of hypersensitivity incidents, low application rates, and return of levels of *Aspergillus flavus* to background shortly after germination, poses minimal risk to populations via dermal, non-occupational exposure. Thus, dermal non-occupational exposure to the non-aflatoxin strain is not likely to be greater than the existing exposure to *A. flavus* at current levels.

2. *Inhalation exposure.* For the reasons stated immediately above, non-occupational inhalation exposure to AF36 is not expected to be greater than that which currently exists for *A. flavus* strains.

#### V. Cumulative Effects

Section 408(b)(2)(D)(v) of the FFDCA requires the Agency to consider the cumulative effect of exposure to *Aspergillus flavus* AF36 and to other substances that have a common mechanism of toxicity. These considerations include the possible cumulative effects of such residues on infants and children. *Aspergillus flavus* AF36 does not appear to be toxic or pathogenic to humans. There is no indication that the fungus *A. flavus* AF36 shares any common mechanisms of toxicity with other registered pesticides. In addition, there are no other registered pesticide products containing *Aspergillus flavus* AF36, and other *A. flavus* strains abound naturally in the environment. Moreover, the displacement of the toxigenic strain of *A. flavus* by AF36 may reduce aflatoxin contamination of cottonseed. Based on the low toxicity potential of AF36, the fact that it is non-aflatoxigenic, and the

safety net already in place to monitor for aflatoxin, no cumulative or incremental effect is expected from the use of AF36 on cotton.

#### VI. Determination of Safety for U.S. Population, Infants and Children

There is reasonable certainty that no harm will result from aggregate exposures to residues of *A. flavus* AF36, in its use as an antifungal agent, to the U. S. population, including infants and children. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. As discussed previously, there appears to be no potential for harm, from this fungus in its use as an antifungal agent via dietary exposure since the organism is non-toxic and non-pathogenic to animals and humans. The Agency has arrived at this conclusion based on the very low levels of mammalian toxicity for acute oral and pulmonary effects with no toxicity or infectivity at the doses tested (see Unit III above). Moreover, non-occupational inhalation or dermal exposure is not expected above background levels (see Unit V).

FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional ten-fold margin of exposure (safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base unless EPA determines that a different margin of exposure (safety) will be safe for infants and children. Margins of exposure (safety) are often referred to as uncertainty (safety) factors. In this instance, based on all the available information, the Agency concludes that the fungus, *A. flavus* AF36, is non-toxic to mammals, including infants and children. Because there are no threshold effects of concern to infants, children and adults when *A. flavus* AF36 is used as labeled, the provision requiring an additional margin of safety does not apply. As a result, EPA has not used a margin of exposure (safety) approach to assess the safety of *A. flavus* AF36.

#### VII. Other Considerations

##### A. Endocrine Disruptors

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its

Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific basis for including, as part of the program, the androgen-and thyroid systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority, to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

The Agency is not requiring information on the endocrine effects of this active ingredient, *Aspergillus flavus* AF36, at this time. The Agency has considered, among other relevant factors, available information concerning whether the microorganism may have an effect in humans similar to an effect produced by a naturally occurring estrogen or other endocrine effects. There is no known metabolite that acts as an "endocrine disrupter" produced by this microorganism. The submitted toxicity/infectivity or pathogenicity studies in the rodent (required for microbial pesticides) indicate that, following oral and pulmonary routes of exposure, the immune system is still intact and able to process and clear the active ingredient (see Unit III.). In addition, based on the low potential exposure level associated with the proposed single, seasonal, prebloom application of the pesticide, the Agency expects no adverse effects to the endocrine or immune systems.

##### B. Analytical Method

The Agency proposes to establish an exemption from the requirement of a tolerance without any numerical limitation. Accordingly, the Agency has concluded that for an exemption from tolerance, analytical methods are not needed for enforcement purposes for residues of *Aspergillus flavus* AF36 on treated cotton. Nonetheless, and for purposes of clarification, analytical methods are still required for product characterization, quality control, and quality assurance for manufacturing purposes [BPPD review - March 29, 1999; BPPD review - May 14, 1999]. Vegetative compatibility tests are used to screen starter cultures to identify the non-aflatoxin-producing *Aspergillus flavus* AF36 strain. Starter cultures of AF36 are also selected on the basis of