



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,  
PESTICIDES AND TOXIC  
SUBSTANCES

APR 03 1973

MEMORANDUM

**SUBJECT:** BPPD Review of Acute Pulmonary and Pathogenicity to the Rat, and Hypersensitivity Incidents - Human Data Submitted by Arizona Cotton Research and Protection Council for *Aspergillus flavus* F36 (Submission No.: S624885; DP Barcode: 286705; MRID No's.: 457981-01, 457391-01, 457982-01, and 457391-04).

**TO:** Shanaz Bacchus (PM-90), Regulatory Action Leader  
Microbial Pesticides Branch, Biopesticides and  
Pollution Prevention Division (7511C)

**FROM:** Carl Etsitty, M.S., Microbiologist  
Microbial Pesticides Branch, Biopesticides and  
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**THROUGH:** John L. Kough, PH.D., Senior Scientist  
Microbial Pesticides Branch, Biopesticides and  
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**ACTION REQUESTED:** Review the submitted data for acute pulmonary and pathogenicity to the rat, and hypersensitivity incidents - human, to determine the adequacy in support *Aspergillus flavus* atoxigenic strain AF36 for use on cotton to displace the toxigenic strain.

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**BACKGROUND:** Arizona Cotton Research and Protection Council submitted data on acute pulmonary toxicity and pathogenicity to the rat, and human hypersensitivity incidents to support their application for a registration for *Aspergillus flavus* AF36 (active ingredient), an atoxigenic fungal competitor to displace the toxigenic strain.

One of these studies is in response to the previously submitted data which indicated a number of adverse effects (deaths) in the test animals. The first data generated covered a preliminary study which were included and reported elsewhere; yet, not repeated in MRID 45739-01. Secondly, MRID 457391-01 includes "Comments on Use of Tween 80 in Protocol UAR/004" and gives an explanation of toxicity observed in UAR/004 (MRID 457981-01) attributed to use of Tween 80 in the vehicle. It also includes a number of Tween 80 literature citations confirming the attributed toxicity. Thirdly, MRID 457391-01 in the same submission includes "Comments on Use of Tween 80 in Protocol UAR/004" and gives the explanation that toxicity observed is attributable to using Tween 80 as the vehicle, and MRID 457982-01 in the same submission includes a similar study using the same test organism without using Tween 80 as the vehicle. Lastly, the registrant is reminded that it's the registrant responsibility to report any adverse reaction

*Aspergillus flavus* AF36 is labeled for outdoor use, and on cotton only to displace toxigenic *Aspergillus flavus* strains. The usage rates: 10lbs of AF36 per acre (per 13,000 linear feet based on 40 inch rows).

**CONCLUSION:** No inhalation data was provided to conclude an adequate toxicity classification; however based on MRID 457981-01, TOXICITY Category III for no foreseeable effect for inhalation data.

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## DATA REVIEW RECORD

Active Ingredient: *Aspergillus flavus* Strain AF36  
 Product Name: None given  
 Company Name: Arizona Cotton Research and Protection Council  
 ID No: 071693-R *Aspergillus flavus* AF36  
 Chemical No.: 006456 *Aspergillus flavus* 36 colonized wheat seed  
 Submission No.: S624885  
 DP Barcode: 286705  
 MRID No: 457391-01 Acute Pulmonary Toxicity/Pathogenicity - Rats  
           457391-04 Hypersensitivity Incidents  
           457981-01 Acute Pulmonary Toxicity/Pathogenicity - Rats  
           457982-01 Acute Pulmonary Toxicity/Pathogenicity - Rats

## SUMMARY OF DATA SUBMITTED:

457391-01: Acute Pulmonary Toxicity/Pathogenicity - Rats (OPPTS 885.3150)

This study was a preliminary study to investigate a suitable concentration of *Aspergillus flavus* AF36 to be used in a main study for an acute pulmonary toxicity and pathogenicity to the rat. This study concluded that  $10^8$  cfu/rat would be a suitable dose level.

CLASSIFICATION: Supplemental data to support further studies.

457391-04: Hypersensitivity Incidents (OPPTS 885.3400)

No recorded or reported adverse hypersensitivity reaction to the *Aspergillus flavus* AF36 was reported by one state council and six companies during use for 3 or 6 years.

CLASSIFICATION: ACCEPTABLE

457981-01: Acute Pulmonary Toxicity/Pathogenicity - Rats (OPPTS 885.3150)

*Aspergillus flavus* AF36 appears to have initial dosing effect resulting in 14 deaths by day 4, but was not infective or pathogenic, with clearance by day 8, when dosed with 1.2 mL/kg at  $5.30 \times 10^8$  cfu/mL (or  $1.28-1.63 \times 10^8$  cfu/animal) to the test animals.

CERTIFICATION: ACCEPTABLE

457982-01: Acute Pulmonary Toxicity/Pathogenicity - Rats (OPPTS 885.3150)

*Aspergillus flavus* AF36 appears to have initial dosing effect resulting in 1 female and 3 male rat deaths on day 2. The rest of test animals showed an initial response but rapid recovery indicating no toxicity, and that AF36 was non-infective, and/or pathogenic to rats when dosed at  $1.93-2.90 \times 10^8$  cfu/rat, with observable clearance patterns.

CERTIFICATION: ACCEPTABLE



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**Chemical:** Aspergillus flavus 36 colonized wheat seed

**PC Code:**  
006456

**HED File Code:** 41500 BPPD Tox/Chem

**Memo Date:** 4/2/2003

**File ID:** DPD286705

**Accession #:** 000-00-9002

**HED Records Reference Center**  
4/13/2007