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

DEC 12 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

Subject: Bacillus thuringiensis var. aizawai, ABG-6305 (CenTari) Technical Powder: Review of HPLC Assay For Beta-exotoxin, Status of Data Gaps, and Justification for Expanded Certified Limits.

To: Mike Mendelsohn/Phil Hutton, PM-17
Insecticide-Rodenticide Branch

From: Rita Briggs, Ph.D., Chemist ^{R.B. 12/12/91}
Science Analysis and Coordination Branch (SACB)
Health Effects Division (H7509C)

Through: Reto Engler, Ph.D., Senior Scientist
SACB/HED

DATA REVIEW RECORD

Product Name: Bacillus thuringiensis (Berliner) var. aizawai, ABG-6305
ID No: 000275-1A
Synonym: CenTari
Caswell No: 066
HED Project: 2-0714
MRID No: 420830-01 - HPLC Beta-exotoxin Validation Study; Addendum to
MRID No. 41722510.
421024-01 - HPLC Assay for Beta-exotoxin; Raw Data Addendum to
MRID No. 41722510.
11/1/91 Letter on Data Gap Status
11/12/91 Letter on Certified Limits

ACTION REQUESTED

To comment on two letters submitted by the registrant (Abbott) which (1) requests expanded certified limits for CenTari technical powder and (2) notifies the Agency of expected submission dates for several outstanding studies required to fulfill requirements for registration of CenTari. In addition, SACB is requested to review two addendums to MRID No. 4172250 (Manufacturing Process) in support of the HPLC Beta-exotoxin study.

DISCUSSION/CONCLUSION:

1. **11/1/91 Letter re: Status of CenTari Data Gaps:** Since the label has been changed from cabbage looper units to diamondback moth units, SACB concurs with the registrant that additional data using the Diamondback Moth Assay are required to evaluate biopotency (Five Lot Analysis) and storage stability for both CenTari Technical Powder and WDG, as well as physical stability data for CenTari Technical Powder.
2. **11/12/91 Letter re: Justification for Expanded Certified Limits for CenTari Technical Powder:** Based on the non-toxicity of CenTari, as demonstrated in acute toxicity studies previously submitted, SACB can support the expanded certified limits [REDACTED] provided those limits do not exceed a concentration of 10^8 CFUs of the active ingredient.
Attention: Please note that there are several points made in the discussion on the variation of active protein that, although ^{have} no bearing upon SACB's opinion on certified limits, were not clear. These points include: (1) On page 1, a range of percentages (e.g. 5-20%) were expressed as "1 std. dev.". (2) In the formula used to determine lot to lot variation (p.2), SACB believes that the z value actually is the t value.
3. **MRID #420830-01 - HPLC Beta-exotoxin Validation Study:** Based on data presented on the linearity of detector response, SACB believes that the detection limit of the method is, at least, at the lowest concentration tested (i.e. 0.81 ug/ml) and not at the 1 ug/ml level that the registrant reported it to be. It also is SACB's opinion that concentrations below 0.81 ug/ml should have been included to more fully determine the detection limit of the method. In addition, the appearance of the

QUALITY CONTROL PROCEDURE INFORMATION IS NOT INCLUDED

base lines in the chromatograms of various samples warrant, in SACB's opinion, a clarification on the sensitivity of the HPLC.

4. **MRID #421024-01 - HPLC Assay For Beta-exotoxin:** SACB has reviewed the raw data (HPLC chromatograms) submitted for evaluation of the presence of beta-exotoxin in CenTari technical powder, and has concluded the data are deficient for the following reasons:
- (1) HPLC chromatogram of beta-exotoxin standard (p.5) does not indicate how much of the standard was injected.
 - (2) Chromatograms for sample lots 41-115-BD (p.6), 44-328-BD (p.9) and 44-329-BD (p.10) show small peaks at approximately the time points for beta-exotoxin. The amounts of toxin, however, cannot be determined because the concentration of standard is unknown.
 - (3) Chromatogram for sample lot 42-221-BD (p.8) is unclear. Although a time point for beta-exotoxin is indicated, it is uncertain whether there is a peak at that point.
 - (4) With respect to chromatograms for sample Lot 44-329-BD unspiked (p.10) and spiked (p.11), the amount of beta-exotoxin added to this sample is not indicated. In addition, the chromatograms do not correspond to those shown for the same sample on page 8 of the HPLC Assay for Beta-exotoxin Validation Study, MRID No. 41722510.
 - (5) The appearance of the baselines for all the samples indicates a possible problem associated with the sensitivity of the HPLC.

OVERALL CONCLUSION: The data presented for the HPLC Beta-exotoxin study do not convince SACB that toxin is not present in the samples tested. Data on the housefly bioassay previously submitted also were inconclusive (see April 24 memo. R. Briggs to M. Mendelsohn). However, since there appears to be inherent problems in the HPLC assay itself, SACB recommends that the registrant repeat the housefly bioassay to re-evaluate the presence of toxin in CenTari, ABG-6305 Technical Powder.

20-46 ppm
 1 mths of det.
 for fly assay
 HPLC 0.4 ppm
 - 2.5