

CODING FORMS FOR SRC INDEXING

Microfiche No.	OTS0559858-1.		
New Doc ID	89020000053	Old Doc ID	8EHQ-0102-14611
Date Produced	12/20/01	Date Received	01/28/02
		TSCA Section	8E
Submitting Organization	BAYER CORP		
Contractor	BAYER TOXICOLOGY		
Document Title	SUPPORT: TSCA HLTH & SFTY STDY CVR SHEET W/FINAL RESULTS OF SUBCHRONIC TOX FEEDING STUDY OF STROBILURIN IN THE BEAGLE DOG, DATED 122001		
Chemical Category	STROBILURIN (AMS 21618)		

54653

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS: NONE

8EHQ-0102-14611

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1.0 SUBMISSION TYPE
 8(d) XX 8(e) FYI 4 OTHER: Specify _____
 - Initial Submission Follow-up Submission Final Report Submission
 Previous EPA Submission Number or Title if update or follow-up: 8EHQ-99-14611 Docket Number, if any: #
 continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e); optional for §4, 8(d) & 8(f)) X- YES <input type="checkbox"/> NO	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID 7106 4575 1292 0337 7937 01-2-36	2.3 FOR EPA USE ONLY
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3.0 CHEMICAL/TEST SUBSTANCE IDENTITY
 Reported Chemical Name (specify nomenclature if other than CAS name):
 CAS# N/A
 Purity ___%
 X- Single Ingredient
 Commercial/Tech Grade
 Mixture
 Trade Name: AMS 21618 Common Name: Scrobilurin
 CAS Number NAME % WEIGHT
 Other chemical(s) present in tested mixture
 continuation sheet attached

4.0 REPORT/STUDY TITLE
 Final Results from report "A Subchronic Toxicity Feeding Study in the Beagle Dog, Report # 109442"
 continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS [CHECK ONE]
 HEALTH EFFECTS (HE): X ENVIRONMENTAL EFFECTS (EE): ENVIRONMENTAL FATE (EF):

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)
 STUDY SUBJECT ROUTE OF EXPOSURE (HE only): VEHICLE OF EXPOSURE (HE only):
 TYPE: STOX ORGANISM (HE, EE only) DOGS EXPOSURE (HE only):
 Other: Other: Other:

6.0 REPORT/STUDY INFORMATION Study is GLP
 Laboratory Bayer Toxicology Report/Study Date 12/19/01
 Source of Data/Study Sponsor (if different than submitter) Number of pages -
 continuation sheet attached

7.0 SUBMITTER INFORMATION
 Janet M. Mostowy, Ph.D.
 VP, Product Safety & Regulatory Affairs Phone: 412-777-3490
 Bayer Corporation - 100 Bayer Road, Pittsburgh, PA. 15205
 Technical Contact: SAME AS ABOVE Phone: ()
 continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS
 This compound is a developmental pesticide.
 continuation sheet attached

Contain NO CBI



8EHQ-99-14611

Submitter Signature: [Signature] Date: 12/20/01



89020000051



9.0 CONTINUATION SHEET

Submitter: Tracking Number/Internal ID

7106 4575 1292 0337 7937
01-2-36

Continuation of 2.1

Preliminary results from this subchronic dog study were reported (8(e)HQ-93-14611) based on the damage to the kidney. The final report is now available, thus the reporting.

Summary:

Technical grade AMS 21618 was administered in the diet to Beagle dogs (4 animals per sex and treatment level) at nominal concentrations of 0, 100, 500 and 2,500 (reduced from 3,000 ppm after 8 days) of technical grade AMS 21618 mixed in the feed on the basis of the active ingredient. The purpose of this study was to characterize the general toxicity, resulting from a 90-day duration, continuous *per os* exposure of the Beagle dog to technical grade AMS 21618. In addition to the routine guideline requirements, this study investigated potential cardiac and neurologic effects. Computerized electrocardiography (ECG) and blood pressure (BP) measurements were performed. Also, neurological examinations performed that included peripheral and cranial reflex tests, task performance tests, gait and behavioral observations.

There was a compound-related decrease in food consumption and body weight (growth rate) in the mid- and high-dose females due to subchronic AMS 21618 administration. There were no clinical observations or ophthalmology findings in this study considered to be compound-related. Likewise, there were no compound-related changes found in the ECG and BP parameters measured in this study. Neurologic examination, thoracic auscultation and rectal body temperatures were all within normal limits.

The following summarizes the clinical, gross and microscopic pathology compound-related findings from this subchronic 90-day toxicology study with AMS 21618:

1. There were alterations in the following clinical pathology parameters:
 - A. Decreased T3 values at day 29 only, in the mid- and high-dose females and the high-dose males.
 - B. Decreased serum calcium levels in the mid- and high-dose females and the high-dose males.
 - C. Decreased total protein and/or serum albumin levels in the mid- and high-dose males & females.
 - D. Decreased serum cholesterol levels in the mid-dose males and high-dose males and females.
 - E. Increased alkaline phosphatase levels in the mid- and high-dose males and females.
 - F. Biologically relevant increase in liver induction enzymes included: (C demethylase and/or cytochrome P450) in the mid- and high-dose males and females. There was a slight increase in UDP-GT in the mid- and high-dose females. Increased ECOD in the mid- and high dose males and ALD and EH in the mid- and high dose males. Increased ECOD, ALD and GS-T in the mid- and high dose females, and increased EH and GLU-T in the mid- and high dose in females. Only the mid- and high-dose enzymatic changes were accompanied with adverse micropathology changes.
 - G. Decreased serum creatinine levels in the low-dose males and in the mid- and high-dose males and females were not considered biologically relevant.
 - H. A slight anemia was noted in the high-dose females at the day 29 bleeding interval, characterized by a statistical decrease in the hemoglobin and hematocrit. Subsequent bleeding intervals did not reflect persistent anemia, suggesting that an adaptive response occurred.
 - I. Decreased APTT in the high-dose males and females.
2. There were compound-related alterations in the following terminal body weight & organ weight parameters.
 - A. Decreased terminal body weights in selected mid- and high-dose females.
 - B. Non-statistical increases in the relative kidney weights of selected high-dose males, which corresponded to morphologic alterations.
 - C. Increases in the absolute and relative liver weights of the mid- and high dose males and females.
3. The following morphologic alterations were considered to be compound-related:
 - A. There was a minimal to mild hepatocytomegaly in the mid- and high-dose males and females.
 - B. There was a minimal to mild degeneration of the proximal tubules in the kidneys of the mid- and high-dose males. The female kidneys were unaffected.

This subchronic feeding study with technical grade AMS 21618 demonstrated a NOAEL (no-observed-adverse-effect level) in both sexes at 100 ppm. An intermediate level of toxicity was seen at 500 ppm based on liver and kidney findings. The MTD (maximum-tolerated-dose) was approached at 2,500 ppm, within the limits of animal welfare concerns, based on the hepatic, renal and adverse clinical pathology changes. The target organs of toxicity appeared to be the liver and kidney, with transient secondary effects on the thyroid and erythron.