

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS:

-CHECK IF THIS PAGE CONTAINS CONFIDENTIAL BUSINESS INFORMATION (CBI)

Clearly mark the confidential information with bracketing and check the box in the appropriate section (Contains CBI).
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8EHQ-0699-14479

1.0 SUBMISSION TYPE - Contains CBI <input type="checkbox"/> 8(d) <input checked="" type="checkbox"/> 8(e) <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> OTHER: Specify _____		
XX- Initial Submission -Follow-up Submission <input type="checkbox"/> Final Report Submission Previous EPA Submission Number or Title if update or follow-up: Docket Number, if any: # _____ <input type="checkbox"/> continuation sheet attached		
2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e): optional for §4, 8(d) & FYI) X - YES <input type="checkbox"/> NO	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID Cert# P 917006914 -99-2-39	2.3 FOR EPA USE ONLY
3.0 CHEMICAL/TEST SUBSTANCE IDENTITY -Contains CBI <i>Reported Chemical Name (specify nomenclature if other than CAS name):</i> CAS#: Not yet assigned Purity _____% <input type="checkbox"/> - Single Ingredient <input type="checkbox"/> Commercial/Tech Grade <input type="checkbox"/> Mixture Trade Name: ALM 1461 Common Name: Sulfonylimidazole		
4.0 REPORT/STUDY TITLE - Contains CBI Preliminary Data from a dose Range Finding Study in CD-1 Mice (Dietary Administration over 14 weeks) <input type="checkbox"/> 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 _____ VEHICLE OF EXPOSURE (HEonly) _____ TYPE: _____ ORGANISM (HE, EE only): MICE EXPOSURE (HE only): _____ Other: _____ Other: Range Finding Other: _____ Other: _____		
6.0 REPORT/STUDY INFORMATION <input type="checkbox"/> Contains CBI <input type="checkbox"/> Study is GLP Laboratory <u>Bayer Toxicology, Wuppertal</u> Report/Study Date: N/A Source of Data/Study Sponsor (if different than submitter) <u>Bayer AG</u> Number of pages _____ <input type="checkbox"/> continuation sheet attached		
7.0 SUBMITTER INFORMATION <input type="checkbox"/> Contains CBI Submitter: <u>Donald W. Lamb, Ph.D</u> Title: <u>V. P., Prod. Safety & Reg. Affrs</u> Phone: <u>412-777-7431</u> Company Name: <u>Bayer Corporation</u> Company Address: <u>100 Bayer Road</u> <u>Pittsburgh, PA 15205-9741</u> Submitter Address (if different): _____ Technical Contact: <u>Donald W. Lamb, Ph.D</u> Phone: <u>(412)777-7431</u> <input type="checkbox"/> continuation sheet attached		
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS <input type="checkbox"/> Contains CBI This compound is a developmental fungicide. The report will be submitted when available. <input type="checkbox"/> continuation sheet attached		

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59 JUN 26 PM 12:14

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99 JUN 23 AM 9:08

Submitter Signature: Donald W. Lamb Date: 6/17/99



9.0 CONTINUATION SHEET

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CONTINUED FROM COVER SHEET SECTION # 2.1

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Preliminary results from a subchronic study in CD-1 mice with ALM 1461 have revealed: 1. A significant decrease in erythrocyte count, hemoglobin concentration, and hematocrit. 2. Hepatocellular necrosis and pericholagniolar monuclear infiltrates. 3. Bronchio-alveolar adenoma (one male). 4. Focal bronchio-alveolar hyperplasia in one male (different male from the one with the adenoma) and one female. As these findings are considered to be of serious toxicological concern, the preliminary findings are being reported.

Abstract

ALM 1461 was administered via the diet to CD-1 mice (10 males and 10 females per dose), at doses of 0, 280, 1400, and 7000 ppm over a period of 14 weeks. This resulted in a test compound intake of 57.4, 292.2, and 1403.6 mg/kg body weight/day for males and 114.1, 482.6, and 2497.2 mg/kg body weight/day for females.

Treatment with ALM 1461 did not induce any effects on general condition, behavior, mortality, body weight development, and food consumption. Water intake was slightly increased in females at 7000 ppm.

Erythrocyte count, hemoglobin concentration, and hematocrit were significantly decreased in both sexes at 7000 ppm. Leukocyte count and differential blood count were unaffected.

Effects on liver function at 280 ppm (females) and morphology at 1400 ppm and above (both sexes) are derived from an increased incidence of centrilobular hepatocellular hypertrophy (both sexes 1400 and 7000 ppm), cytoplasmic change (males 1400 ppm, both sexes 7000 ppm), GSTP-positive centrilobular hepatocytes (females 280 ppm, both sexes 1400 ppm and above), hepatocellular necroses (males 7000 ppm), and pericholangiolar mononuclear infiltrates (females 1400 ppm, both sexes 7000 ppm). Livers were enlarged (both sexes 7000 ppm) and mean activities of ALAT and ASAT (1400 ppm males, 7000 ppm both sexes), APh (7000 ppm both sexes), and plasma cholesterol concentrations (1400 and 7000 ppm both sexes) were increased. In liver tissue, activities of ECOD (1400 ppm males, 7000 both sexes), EROD (7000 ppm both sexes), GS-T (280 ppm females, 1400 and 7000 ppm both sexes), EH (1400 and 7000 ppm, females), and GLU-T (7000 ppm females) were increased, while ALD was marginally but significantly reduced (1400 and 7000 ppm males). In the lungs, a bronchio-alveolar adenoma (one male) and focal brochio-alveolar hyperplasia (another male, one female) were seen at 7000 ppm. Gross and histopathological investigations into other organs and tissues gave no indication of test-compound-related functional or morphological changes in either sex.

Under the conditions described, the administration of ALM 1461 to mice was tolerated without adverse effects at 280 ppm by male and female CD-1 mice.