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CODING FORMS FOR SRC INDEXING

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Date Produced	10/05/99	Date Received	10/12/99	TSCA Section	8E
Submitting Organization		BAYER CORP			
Contractor		BAYER TOXICOLOGY			
Document Title				INITIAL SUBMISSION: TSCA HLTH & SFTY STUDY CVR SHT W/CONTINUATION SHT SUMMARIZING PILOT STUDY ON DEVELOPMENTAL TOXICITY IN RATS AFTER ORAL ADMINISTRATION OF ALM 2647, DATED 100599	
Chemical Category		EXPERIMENTAL FUNGICIDE, ALT 2647			

A 03

TSCA HEALTH & SAFETY STUDY COVER SHEET

8EHQ-1099-14565

TSCA CBI STATUS:

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

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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 8(d), 8(d) & FYI) X - YES <input type="checkbox"/> NO	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID Cert# P 917006933 99-2-70	2.3 FOR EPA USE ONLY
3.0 CHEMICAL/TEST SUBSTANCE IDENTIFY - 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 checked="" type="checkbox"/> Mixture Trade Name: ALM 2647 Common Name: _____		
4.0 REPORT/STUDY TITLE - Contains CBI Pilot Study on Developmental Toxicity in Rats after Oral Administration (Study T7067897) <input type="checkbox"/> Continuation sheet attached		
5.1 STUDY/TSCATS INDEXING TERMS [CHECK ONE] HEALTH EFFECTS (HE): <input checked="" type="checkbox"/> ENVIRONMENTAL EFFECTS (EE): _____ ENVIRONMENTAL FATE (EF): _____		
5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes) STUDY _____ SUBJECT _____ ROUTE OF _____ VEHICLE OF _____ TYPE: <u>TOX</u> ORGANISM (HE, EE only): <u>RATT</u> EXPOSURE (HE only): _____ EXPOSURE (HE only): _____ Other: <u>DEVELOPMENTAL</u> Other: _____ Other: _____		
6.0 REPORT/STUDY INFORMATION <input checked="" type="checkbox"/> Contains CBI <input type="checkbox"/> Study is GLP Laboratory: <u>Bayer Toxicology, Wuppertal</u> Report/Study Date: 9/13/99		
Source of Data/Study Sponsor (if different than submitter): <u>Bayer AG</u> Number of pages: 2 <input type="checkbox"/> continuation sheet attached		
7.0 SUBMITTER INFORMATION <input checked="" 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 checked="" type="checkbox"/> Contains CBI This compound is an experimental fungicide (Pilot Study - No report to be issued) <input type="checkbox"/> continuation sheet attached		

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8EHQ-99-14565

Submitter Signature: Donald W. Lamb

Date: 10/5/99

Page 1 of 2



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9.0 CONTINUATION SHEET

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Submitter Tracking Number/Internal ID

P917006933 99-2-70

CONTINUED FROM COVER SHEET SECTION # 2.1

Reporting is based on the decrease in fetal weight in the 100 mg/kg/day dose group.

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ALM 2647

Pilot study on developmental toxicity in rats after oral administration

(T7067897)

8 mated female Wistar rats each were daily treated orally by gavage with ALM 2647 in 0.5% aqueous carboxymethylcellulose from day 6 to day 19 p.c. with doses of 0, 10, 30 and 100 mg/kg body weight (bw)/day (dose-volume 10 ml/kg bw). The fetuses were delivered by cesarean section on day 20 p.c. Investigations were performed on general tolerance of the test compound by the females as well as on its effect on intrauterine development. 2/3 of fetuses underwent skeletal evaluation while 1/3 of fetuses were evaluated viscerally.

Mortality and appearance of the dams were not affected by treatment, while feed spillage occurred mainly at the end of treatment in the 100 mg/kg dose group. Distinctly reduced feed intake was seen during the whole treatment period up to the end of gestation (with increasing severity) at the 100 mg/kg dose level as well. Reduced amount of feces was observed at a dose level of 30 mg/kg and above together with light colored feces in the 100 mg/kg group. Water intake and urination were increased at the 30 mg/kg dose level and above. Body weight loss occurred after the start of treatment (day 6-8 p.c.) and intermittently thereafter (days 11-12 p.c.; 13-14 p.c.; 19-20 p.c.) at the 100 mg/kg dose level resulting in distinctly reduced mean body weight, body weight gain, carcass weight and corrected body weight gain. Necropsy revealed no toxicologically relevant gross pathological alterations at a dose level up to and including 100 mg/kg bw/day.

Reproductive parameters i.e. gestation rate, postimplantation loss, number of live fetuses per litter, fetal sex distribution and placental appearance were not affected to a toxicological significant degree by treatment at a dose level up to and including 100 mg/kg. Placental and fetal weights were either slightly (within the range of historical controls) or distinctly (below the range of historical controls) reduced in the 100 mg/kg dose group.

External, visceral and skeletal evaluation of fetuses showed no clearly treatment-related alterations up to and including a dose level of 100 mg/kg. Visceral evaluation revealed one case each of liver hemorrhage in the 30 and 100 mg/kg group but due

T7067897

ALM 2647

to lack of clear dose-relationship and comparable findings in historical controls toxicological relevance is not assumed. Skeletal evaluation showed a marginally increased incidence of 14th rib (variation) at a dose level of 30 mg/kg and above. Since dose relationship was not clearly evident on a fetal and litter basis, treatment relationship is not assumed, however final evaluation is not possible due to the low number of females in a pilot study. No treatment-related fetal malformations were observed at a dose level up to and including 100 mg/kg.

Summarizing all findings test compound related effects on the maternal organism were evident at the 30 mg/kg (reduced amount of feces, increased water intake and urination) and 100 mg/kg dose level (same findings as in the 30 mg/kg group together with feed spillage, decreased feed intake, body weight loss, reduced body weight gain) while an effect on intrauterine development (decreased placental and fetal weight) was observed at a dose of 100 mg/kg bw/day.

September 13, 1999

Dr. A.-M. Klaus