

A 01

CODING FORMS FOR SRC INDEXING

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New Doc ID		88000000010		Old Doc ID		8EHQ-1099-14570					
Date Produced		10/14/99		Date Received		10/18/99		TSCA Section		8E	
Submitting Organization				BAYER CORP							
Contractor				BAYER TOXICOLOGY							
Document Title				INITIAL SUBMISSION: TSCA HLTH & SFTY STUDY CVR SHT W/CONTINUATION SHT SUMMARIZING DEVELOPMENTAL TOXICITY STUDY IN RATS WITH EXPERIMENTAL FUNGICIDE, ALM 2552, DATED 101499							
Chemical Category				EXPERIMENTAL FUNGICIDE, ALM 2552							

A 03

TSCA HEALTH & SAFETY STUDY COVER SHEET

MA 27633

TSCA CBI STATUS:

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

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**1.0 SUBMISSION TYPE** - Contains CBI  
 8(d)  8(e)  FYI  4  OTHER: Specify 8EHQ-1009-14570  
 Initial Submission  Follow-up Submission  Final Report Submission  
 Previous EPA Submission Number or Title if update or follow-up:  
 Docket Number, if any: #  
 continuation sheet attached

1999 OCT 18 11:10:58

**2.1 SUMMARY/ABSTRACT ATTACHED** (may be required for 8(e): optional for §4, 8(d) & FYI)  
 YES  NO

**2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID**  
 Cert# P 917006939  
 99-2-73

**2.3 FOR EPA USE ONLY**

**3.0 CHEMICAL/TEST SUBSTANCE IDENTITY** - Contains CBI  
 Reported Chemical Name (specify nomenclature if other than CAS name):  
 CAS#: Not yet assigned  
 Purity \_\_\_\_\_ %  
 Single Ingredient  
 Commercial/Tech Grade  
 Mixture  
 Trade Name: ALM 2552 Common Name: \_\_\_\_\_

Contains No CBI

**4.0 REPORT/STUDY TITLE** - Contains CBI  
 Developmental Toxicity Study in Rats (Study T8067898)  
 Continuation sheet attached

**5.1 STUDY/TSCATS INDEXING TERMS**  
 [CHECK ONE]  
 HEALTH EFFECTS (HE):  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: TOX ORGANISM (HE, EE only): RATS Other: DEVELOPMENTAL Other: \_\_\_\_\_

**6.0 REPORT/STUDY INFORMATION**  Contains CBI  Study is GLP  
 Laboratory: Bayer Toxicology Report/Study Date: 10/12/99  
 Source of Data/Study Sponsor (if different than submitter): Bayer AG  
 continuation sheet attached Number of pages - \_\_\_\_\_

**7.0 SUBMITTER INFORMATION**  Contains CBI  
 Submitter: Donald W. Lamb, Ph.D. Title: V. P. Prod Safety & Reg. Affrs. Phone: 412-777-7431  
 Company Name: Bayer Corporation Company Address: 100 Bayer Road  
Pittsburgh, PA 15205-9741  
 Technical Contact: Donald W. Lamb, Ph.D. Submitter Address (if different): \_\_\_\_\_  
 continuation sheet attached Phone: (412)777-7431

**8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS**  Contains CBI  
 This compound is an experimental fungicide.  
 (Pilot Study - No report to be issued)  
 continuation sheet attached



BEHQ-99-14570

Submitter Signature: Donald W. Lamb

Date: 10/14/99

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## 9.0 CONTINUATION SHEET

## TSCA CBI STATUS:

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CONTINUED FROM COVER SHEET SECTION # 2.1

In this study, a compound-related effect on fetal development (reduced fetal weights) was evident in the 160 mg/kg bw/day dose group and cannot be completely excluded for the 100 mg/kg bw/day dose group. Furthermore, compound-related ovarian cysts were evident for dams in the 100 and 160 mg/kg bw/day dose groups. Ovarian cysts were also observed in the 30 mg/kg bw/day dose group, and this finding cannot be completely excluded from being compound-related. Therefore information is being submitted.

**Abstract**

Eight inseminated Wistar rats per dose group were treated daily by gavage with ALM 2552 in 0.5% aqueous carboxymethylcellulose from day 6 to day 19 p.c. with doses of 0, 30, 100, and 160 mg/kg bw/day 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 the general toxicity of ALM 2552 to the dams, as well as the effect of ALM 2552 on intrauterine development. Two thirds of the fetuses underwent a skeletal evaluation and 1/3 of the fetuses underwent a visceral evaluation.

None of the treated females died during the study, but compound-related findings were clearly evident in the 100 mg/kg bw/day dose group and were severe in the 160 mg/kg bw/day dose group. All females in these dose groups had transient swelling in the area of the thyroid (individually differently between days 7-15 p.c.). Further findings consisted of feed spillage and transiently reduced feed intake (days 6-9 p.c.), increased water intake and urination, and body weight loss (days 6-9 p.c.) with a subsequent reduction in body weight gain, resulting in decreased final body weight, corrected body weight change, and carcass weight. Additionally, decreased feed intake together with body weight loss was observed at the end of gestation (days 18-20 p.c.) in the 160 mg/kg bw/day dose group, and light colored feces was observed in this dose group.

No toxicological relevance is assumed for the marginal body weight loss which occurred on day 6-7 p.c. in the 30 mg/kg bw/day dose group, since this finding was based on 2 females only. However, final evaluation is not possible due to the low number of females used in a pilot study.

Necropsy revealed a single case of renal pelvis dilatation in the 160 mg/kg bw/day dose group as well as ovarian cysts in all pregnant females in the 100 and 160 mg/kg bw/day dose groups. One case of ovarian cysts was seen in the 30 mg/kg bw/day group. While the kidney finding is assumed to be incidental, at the higher dose levels a compound-related effect has to be assumed for the finding of ovarian cysts. Toxicological relevance remains questionable for the single case of ovarian cysts in the 30 mg/kg bw/day dose level, since ovarian cysts do occur in historical control groups. However, final evaluation is not possible due to the low number of females used in a pilot study.

Reproductive parameters (i.e., gestation rate, postimplantation loss, number of live fetuses per litter, fetal sex distribution, and placental appearance) were not affected by ALM 2552. A marginal reduction of fetal weight for the 100 mg/kg bw/day dose group cannot be completely excluded as being compound-related, since values were at the lower range of the historical control data. In the 160 mg/kg bw/day dose group, placental weights were slightly reduced (at the lower range of historical controls) and fetal weights were distinctly reduced (below the range of historical controls).

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One case each of fetal microphthalmia (30 and 100 mg/kg bw/day dose-groups) or anophthalmia (160 mg/kg bw/day dose group) was observed, but due to comparable findings in the historical controls treatment relationship is not assumed. External and visceral evaluation of fetuses showed no compound-related effects. At all dose levels tested, skeletal investigations revealed retarded ossification of skull bones with an incidence approximately twice as high as the control group. However, dose relationship was not evident and the incidence of these findings were in the range of the historical control data. Therefore, a compound-related effect is not assumed.

Summarizing all findings, compound-related effects on the maternal organism were equivocal in the 30 mg/kg bw/day dose group (transiently marginal body weight loss and ovarian cysts), were clearly evident in the 100 mg/kg bw/day dose group (swelling in the area of the thyroids, reduced feed intake and feed spillage, increased water intake and urination, body weight loss, reduced body weight gain, and ovarian cysts), and were severe in the 160 mg/kg bw/day dose group (swelling in the area of the thyroids, reduced feed intake and feed spillage, increased water intake and urination, body weight loss, reduced body weight gain, ovarian cysts, and light colored feces). A compound-related effect on intrauterine development cannot be completely excluded for the 100 mg/kg bw/day dose group (marginally reduced fetal weights). However, there was definitely a compound-related effect in the 160 mg/kg bw/day dose group (slightly reduced placental weight and distinctly reduced fetal weight).