

8EHQ-0699-14478

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).  
Submit a sanitized cover sheet with CBI deleted. Mark the sanitized copy, "Public Display Copy" in the heading.

<b>1.0 SUBMISSION TYPE</b> <input type="checkbox"/> Contains CBI <input type="checkbox"/> 8(d) <b>XX 8(e)</b> <input type="checkbox"/> FYI <input type="checkbox"/> 4 <input type="checkbox"/> OTHER: Specify _____ <input checked="" type="checkbox"/> Initial Submission <input type="checkbox"/> 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		
<b>2.1 SUMMARY/ABSTRACT ATTACHED</b> (may be required for 8(e): optional for §4, 8(d) & FYI) X- YES <input type="checkbox"/> NO	<b>2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID</b> P917-006-903 99-2-37	<b>2.3 FOR EPA USE ONLY</b>
<b>3.0 CHEMICAL/TEST SUBSTANCE IDENTITY</b> <input type="checkbox"/> Contains CBI Reported Chemical Name (specify no CAS#) _____ CAS# <u>N/A</u> Purity _____ % X- Single Ingredient <input type="checkbox"/> Commercial/Tech Grade <input type="checkbox"/> Mixture Trade Name: <u>DRS 4917</u> Common Name: _____ CAS Number _____ NAME _____ % WEIGHT _____ Other chemical(s) present in tested mixture: _____ <input type="checkbox"/> continuation sheet attached		
<b>4.0 REPORT/STUDY TITLE</b> <input type="checkbox"/> Contains CBI Preliminary Data from DRS 4917 Developmental Toxicity Screening in Rats After Oral Administration continuation sheet attached		
<b>5.1 STUDY/TSCATS INDEXING TERMS</b> [CHECK ONE] HEALTH EFFECTS (HE): <u>X</u> ENVIRONMENTAL EFFECTS (EE): _____ ENVIRONMENTAL FATE (EF): _____		
<b>5.2 STUDY/TSCATS INDEXING TERMS</b> (see instructions for 4 digit codes) STUDY SUBJECT ROUTE OF VEHICLE OF TYPE: _____ ORGANISM (HE, EE only): <u>RATS</u> EXPOSURE (HE only): <u>GAV</u> EXPOSURE (HE only) _____ Other: Developmental Tox Other: _____ Other: _____		
<b>6.0 REPORT/STUDY INFORMATION</b> <input type="checkbox"/> Contains CBI <input type="checkbox"/> Study is GLP Laboratory <u>Bayer AG Toxicology Lab, Wuppertal, Germany</u> Report/Study Date <u>N/A</u> Source of Data/Study Sponsor (if different than submitter) _____ Number of pages _____ <input type="checkbox"/> continuation sheet attached		
<b>7.0 SUBMITTER INFORMATION</b> <input type="checkbox"/> Contains CBI Submitter: <u>Donald W. Lamb</u> Title: <u>VP, Product Safety &amp; Regulatory Affairs</u> Phone: <u>412-777-7431</u> Company Name: <u>Bayer Corporation</u> Company Address: <u>100 Bayer Road, Pittsburgh, PA. 15205</u> Submitter Address (if different): _____ Technical Contact: <u>Same as above</u> Phone: ( ) _____ <input type="checkbox"/> continuation sheet attached		
<b>8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS</b> <input type="checkbox"/> Contains CBI This compound is an experimental herbicide Note: This is all the information we have at this time. The completed report will be submitted when we receive. <input type="checkbox"/> continuation sheet attached		

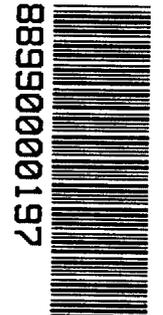


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Submitter Signature: Donald W. Lamb Date: 6/16/99

## 9.0 CONTINUATION SHEET

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**Submitter Tracking Number/Internal ID**

P917 006 903  
99-2-37

### Continuation of 2.1

The TSCA 8(e) Reporting Guidance states that "serious adverse developmental effects (e.g., significant embryo or fetal lethality, significantly reduced fetal/birth weights, significantly retarded/incomplete skeletal ossification) should be reported." The TSCA 8(e) Reporting Guidance further states that "Statistically or biologically significant increases in teratogenic effects or other serious embryotoxic or fetotoxic effects (e.g., significant embryo or fetal lethality, spontaneous abortion) should be reported regardless of the level of maternal toxicity observed in the study". In this study, all females revealed total resorption at the 10 mg/kg level. The dose of 1 mg/kg revealed decreased fetal weights and an increased incidence of common skeletal malformations and variations. Final evaluation of these findings, however, should be based on a succeeding guideline study and not on the limited data available from this screening study.

#### Abstract

4 (10 and 100 mg/kg) or 3 (1000 mg/kg) inseminated Wistar rats each were treated daily by gavage with 10, 100, or 1000 mg of DRS 4917/kg body weight/day in 0.5 % carboxymethylcellulose in demineralized water from day 6 to day 19 p.c. Cesarean sections were performed on day 20 p.c. (Study No. T1067143). All females in the 100 and 1000 mg/kg dose groups were found dead or were killed for humane reasons between days 8 and 12 p.c. Sunken flunks, high stepping gait, piloerection, nearly no feed intakes, reduced feces, decreased water consumption, and severe body weight loss occurred in these dose groups.

Gross necropsy showed tightly filled stomachs (all females) or reddish discolored small intestines (females found dead) in the females in the 1000 mg/kg dose group. The females in the 100 mg/kg group had enlarged liver and kidneys.

All females in the 10 mg/kg group had total (late) resorptions of all implants, without systemic maternal toxicity.

Based on these results an additional study was performed, in which 7 females were treated with 0 (Study No. T5061314) or 1 mg of DRS 4917/kg body weight/day in 0.5 % carboxymethylcellulose in demineralized water from day 6 to day 19 p.c. The fetuses were delivered by cesarean section on day 20 p.c. Investigations were performed to evaluate the general toxicity of the test compound to the females, which included hematology and clinical chemistry, as well evaluation of effects on intrauterine development (pregnancy rate, number of fetuses and resorptions, external findings in the fetuses, fetal weight and fetal skeletal malformations and variations (wavy ribs only) ( Study No. T1068034).

There was no indication of a treatment related effect on feed intake and excretory products as well as on body weight gain at the 1 mg/kg level. Furthermore, hematology parameters (i.e., LEU, ERY, HB, HCT, MCV, MCH, MCHC, RETI, erythrocyte morphology, THRO) and clinical chemistry (i.e., ASAT, ALAT, APH in the plasma, Cyt P-450 in the liver) did not reveal treatment related effects at the 1 mg/kg dose level. Total bilirubin in the plasma was slightly, however, statistically significantly increased at the 1 mg/kg level. Gross necropsy did not reveal any treatment-related effects at the 1 mg/kg dose level.

The pregnancy rate, the resorption rate and correspondingly the number of fetuses were unaffected at the 1 mg/kg level. The fetal weight was distinctly decreased in three litters and was unaffected in the remaining three litters, resulting in a marginally decreased overall mean fetal weight for the 1 mg/kg dose level. External evaluation of the fetuses did not reveal treatment related effects. Skeletal evaluation showed findings in the three litters with distinctly decreased fetal weights. Dysplasia of the long bones of forelimbs and of the scapula occurred in 8 fetuses from two litters and wavy ribs occurred in 19 fetuses from three litters. A treatment related effect is assumed for these findings, as the incidence of fetuses with dysplasia of forelimb bones (11.8 %) and of wavy ribs (27.9 %) exceeded the current and historical control range.