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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 ADMIN OF PLT 2930, DATED 100599		
Chemical Category	EXPERIMENTAL INSECTICIDE, PLT 2930		

A 03

8EHQ-1099-14564

TSCA HEALTH & SAFETY STUDY COVER SHEET

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 §4, 8(d) & FYI) X - YES <input type="checkbox"/> NO	2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID Cert# P 917006933 -99:2-69.	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: PLT 2930 Common Name: BEHQ-99-14564		
4.0 REPORT/STUDY TITLE - Contains CBI Pilot Study on Developmental Toxicity in Rats after Oral Administration (Study T7067888) <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 EXPOSURE (HE only): _____ VEHICLE OF EXPOSURE (HE only): _____ TYPE: <u>TOX</u> ORGANISM (HE, EE only): <u>RAT</u> Other: <u>DEVELOPMENTAL</u> 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: <u>9/13/99</u> Source of Data/Study Sponsor (if different than submitter): <u>Bayer AG</u> Number of pages: <u>2</u> <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 an experimental insecticide (Pilot Study - No report to be issued) <input type="checkbox"/> continuation sheet attached		



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Submitter Signature: Donald W. Lamb Date: 10/5/99

PR 27407

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9.0 CONTINUATION SHEET

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Submitter Tracking Number/Internal ID

P917006933
99-2-69

CONTINUED FROM COVER SHEET SECTION # 2.1

Reporting is based on:

1. the decrease in fetal weight in the 1000 mg/kg/day dose group,
2. compound effects on skeletal development in the 1000 mg/kg/day dose group and a possible effect in the 10 mg/kg/day dose group and,
3. abnormal findings in the adrenal gland of fetuses in the 1000 mg/kg/day dose group.

Contain NO

PLT 2930

Pilot study on developmental toxicity in rats after oral administration

(T7067888)

10 mated female Wistar rats each were daily treated orally by gavage with PLT 2930 in 0.5 % carboxymethylcellulose in demineralized water from day 6 to day 19 p.c. in doses of 0, 10 and 1000 mg/kg body weight (b.w.)/day. Due to an incidentally low fertility rate 6 further mated females were added to the 10 mg/kg group. The fetuses were delivered by cesarean section on day 20 p.c. and blood was taken of the females by cardiac puncture together with maternal fatty tissue (renal fat) as well as one fetus each of the first 5 litters per group for toxicokinetic investigations (will be reported separately). Investigations were performed on general tolerance of the test compound by the females as well as on its effect on intrauterine development with external and skeletal evaluation of fetuses. Additionally macroscopically altered fetal adrenal glands were evaluated histopathologically.

Mortality, appearance and behavior of the females were not affected by treatment. Marginally reduced feed intake and reduced amount of feces were observed in the 1000 mg/kg group while light colored feces were seen in both dose groups, however the latter finding was restricted at the 10 mg/kg dose level to a single female for 2 days and may be based on the high amount of white colored test substance given in the 1000 mg/kg group. Further on water intake and urination were increased in females of the 1000 mg/kg dose group. Increased urination for a single day was observed in one female of the 10 mg/kg group as well. Since findings regarding excretion at the 10 mg/kg dose level were restricted to single transient cases toxicological relevance is not assumed for these findings. Maternal body weight development was not affected by treatment at a dose level up to and including 1000 mg/kg and gross necropsy of the animals did not reveal treatment related effects. 8, 12 and 7 females of the 0, 10 and 1000 mg/kg dose group respectively, had viable fetuses. One female of the 1000 mg/kg dose group started delivery just prior to cesarean section and its data were excluded from evaluation while fetuses/pups were included for external, skeletal and histological evaluation.

T7067888

PLT 2930

The reproductive parameters, namely gestation rate, mean number of implantation sites, postimplantation loss, mean number of viable fetuses and fetal sex ratio were not affected by treatment at a dose level up to and including 1000 mg/kg.

While placental weight was not affected, increased incidence of necrotic placental borders as well as one case each of engorged placenta were observed in both dosed groups. Since dose relationship was not seen on a litter basis and incidence lay in the range of historical control data, toxicological relevance of these findings remains questionable.

Fetal weight was decreased below the range of historical control values in the 1000 mg/kg dose group and in 8 fetuses (out of 4 litters) the adrenal gland(s) were dark red discolored. Histopathological evaluation of these organs revealed increased blood content and dilated blood vessels, in one case together with minimal amount of single cell necroses.

One case of microphthalmia was observed in the 1000 mg/kg group for which due to single appearance and comparability to historical controls toxicological relevance is not assumed.

Skeletal evaluation of fetuses revealed a variation i.e. the 7th cervical vertebral arch (uni- and/or bilateral) had the shape of a 6th cervical vertebral arch in all groups tested resulting in a fetal incidence of 1.12%, 5.18% and 63.35% (together with an as well altered shape of the atlas at the 1000 mg/kg dose level) for the control, 10 mg/kg and 1000 mg/kg group, respectively. At the 1000 mg/kg dose level the exoccipital bone was thinner as well and incidence of 14th ribs (variation) was increased. Due to these findings, a treatment related effect on fetal skeletal development is evident at the 1000 mg/kg dose level and may not be excluded at the 10 mg/kg dose level.

2 cases of dysplastic scapulae (in 2 litters) were seen at the 10 mg/kg dose level and one case in the 1000 mg/kg dose group. Due to lack of dose relationship and comparable findings in historical controls, treatment relationship is not assumed for dysplastic scapulae.

Summarizing these findings an effect on fetal development may not be excluded at the 10 mg/kg dose level and was evident at the 1000 mg/kg dose level (10 mg/kg: altered shape of 7th cervical vertebral arch; 1000 mg/kg: together with effects on atlas, exoccipital bone and 14th rib, findings on adrenal glands and reduced fetal weights) while maternal toxicity was slightly evident at the 1000 mg/kg dose level (reduced feed intake and increased water intake and urination).

September 13, 1999

Dr. A.-M. Klaus