

CODING FORMS FOR SRC INDEXING

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		TSCA Section	8E
Submitting Organization	BAYER CORP		
Contractor	BAYER TOX LAB		
Document Title	INITIAL SUBMISSION: TSCA HLTH & SFTY STUDY CVR SHT REPORTING PRELIM DATA IN A REPRODUCTIVE TOXICITY STUDY OF BYF 6476 WITH THE WISTAR RAT, W/ATTCHMTS & DATED 122299 (SANITIZED)		
Chemical Category	BYF 6476 (CONFIDENTIAL)		

**INITIAL
SUB-
MISSION**

03

TSCA HEALTH & SAFETY STUDY COVER SHEET

8EHP-1299-146245

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: _____ <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 917006946 99-2-80	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 _____ % <input type="checkbox"/> - Single Ingredient <input type="checkbox"/> Commercial/Tech Grade <input type="checkbox"/> Mixture Trade Name: _____ Common Name: BYF 6476 <p style="text-align: center; font-size: 1.2em;">Confidential Information Has Been Sanitized</p>		
4.0 REPORT/STUDY TITLE Contains CBI Preliminary data from "A Reproductive Toxicity Study in the Wistar Rat" <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 (HE only): _____ VEHICLE OF EXPOSURE (HE only): _____ TYPE: TOX ORGANISM (HE, EE only): RATS Other: _____ Other: _____		
6.0 REPORT/STUDY INFORMATION Contains CBI - Study is GLP Laboratory : Bayer Tox Lab, Stilwell, KS Report/Study Date: N/A Source of Data/Study Sponsor (if different than submitter) _____ Number of pages 17 <input type="checkbox"/> continuation sheet attached		
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 Submitter Address (if different): _____ Technical Contact: Donald W. Lamb, Ph.D Phone: (412)777-7431 <input type="checkbox"/> continuation sheet attached		
8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS - Contains CBI Preliminary data only, no study available. <input type="checkbox"/> continuation sheet attached		

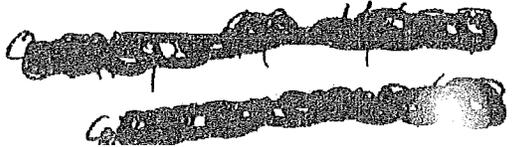
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Submitter Signature: Donald W Lamb Date: 12/22/99

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9.0 CONTINUATION SHEET

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CONTINUED FROM COVER SHEET SECTION # 2.1

ABSTRACT:

There were findings in the high-dose group of a decrease in the number of estrous cycles during a three week period and an increase in estrous cycle length.

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**A Reproductive Toxicity Study
with [REDACTED] in the Wistar Rat
(Preliminary Results Summary)**

<u>FIRST GENERATION</u>	<u>DOSE (mg/kg)</u>			
	0	10	100	750
<u>P Males</u>				
Premating/Mating				
Clinical Signs	-	-	-	Urine Stain
Body Weight Gain (decreased day65-104) -	-	-	7%	
Food Consumption (increased week 2,4-9) -	-	-	10%	
<u>P Females</u>				
Premating/Mating				
Clinical Signs	-	-	-	Urine Stain
Body Weight Gain	Confidential Information Has Been Sanitized			-
Food Consumption	-	-	-	-
Estrous Cycle -number(decreased)	3.4	3.2	3.2	2.7*
Estrous Cycle-length(increase)	4.3	4.2	4.4	5.1*
Mating Index	90	100	100	100
Fertility Index	89	100	97	97
Gestation Index	100	100	100	97
Gestation Length	-	-	-	-
Total Number Implantations	-	-	-	-

* = significantly different from control ($p \leq 0.05$).

A Reproductive Toxicity Study

with [REDACTED] in the Wistar Rat
(Results Summary, Continued)

<u>FIRST GENERATION</u>	<u>DOSE (mg/kg)</u>			
	0	10	100	750
<u>P Females</u>				
Gestation				
Clinical Signs	-	-	-	Urine Stain
Body Weight Gain (decrease days 0-20)	-	-	-	9%
Food Consumption	-	-	-	-
Lactation				
Clinical Signs	-	-	-	-
Body Weight Gain	-	-	-	-
Food Consumption	-	-	-	-
<u>F1 Pups</u>				
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Clinical Signs	-	-	-	-
Pup Body Weight(decrease)				
Birth	-	-	-	-
Day 4	-	-	-	9%*
Day 7	-	-	-	14%*
Day 14	-	-	-	17%*
Day 21	-	-	-	14%*
Gain	-	-	-	17%*
Birth Index	-	-	-	-
Live Birth Index	-	-	-	-
Viability Index	-	-	-	-
Lactation Index	-	-	-	-

* = significantly different from control ($p \leq 0.05$).

A Reproductive Toxicity Study

with [REDACTED] in the Wistar Rat
(Preliminary Results Summary)

FIRST GENERATION

	<u>DOSE (mg/kg)</u>			
	0	10	100	750
Litter Size	-	-	-	-
Pups Missing	-	-	-	-
Pups Found Dead	-	-	-	-
Vaginal Opening	-	-	-	-
Preputial Separation(delayed)	-	-	-	6%*
Sperm Analysis (not yet analyzed)				

Absolute Organ Weights

Males

Terminal Body Weight(decrease)	-	-	-	9%*
Adrenals	-	-	-	-
Brain	-	-	-	-
Kidney	-	-	-	-
Liver(increase)	-	-	9%*	12%*
Spleen	-	-	-	-
Testes	-	-	-	-
Epididymis	-	-	-	-
Prostate	-	-	-	-
EpiCauda	-	-	-	-
Seminal Vesicles(increase)	-	-	14%*	-

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* = significantly different from control (p ≤ 0.05).

A Reproductive Toxicity Study

with [redacted] in the Wistar Rat
(Preliminary Results Summary)

	0	10	100	750	
<u>Absolute Organ Weights - Males (cont.)</u>					
Pituitary	-	-	-	-	-
Thymus(decrease)	-	-	-	-	22%*
<u>Relative Organ Weight/Body Weight - Males</u>					
Adrenals	-	-	-	-	-
Brain(increase)	-	-	-	-	7%*
Kidneys(increase)	-	-	-	-	15%*
Liver(increase)	-	-	7%*	22%*	
Spleen	-	-	-	-	-
Testes	-	-	-	-	-
Epididymis(increase)	-	-	-	-	9%*
Prostate	Confidential Information Has Been Sanitized				-
EpiCauda	-	-	-	-	-
Seminal Vesicles(increase)	-	-	13%*	16%*	
Pituitary	-	-	-	-	-
Thymus(decrease)	-	-	-	-	15%*

* = significantly different from control ($p \leq 0.05$).

A Reproductive Toxicity Study

with [REDACTED] in the Wistar Rat
(Preliminary Results Summary)

FIRST GENERATION

DOSE (mg/kg)

0 10 100 750

Absolute Organ Weights

Females

Term Body Weight(increase)	-	5%*	-	-
Adrenals	-	-	-	-
Brain	-	-	-	-
Kidneys	-	-	-	-
Liver(increase)	-	11%*	-	19%*
Ovaries	-	-	-	-
Spleen	-	-	-	-
Uterus(decrease)	-	-	-	26%*
Pituitary	-	-	-	-
Thymus(decrease)	-	-	19%*	28%*

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Relative Organ Weight/Body Weight

Females

Adrenals	-	-	-	-
Brain	-	-	-	-
Kidneys	-	-	-	-
Liver(increase)	-	-	-	18%*

* = significantly different from control (p ≤ 0.05).

A Reproductive Toxicity Study

with [REDACTED] in the Wistar Rat

(Preliminary Results Summary)

FIRST GENERATION

	<u>DOSE (mg/kg)</u>			
	0	10	100	750

Relative Organ Weight/Body Weight (cont.)Females

Ovaries	-	-	-	-
Spleen	-	-	-	-
Uterus(decrease)	-	19%* ¹	(+3%)	27%*
Pituitary(decrease)	-	14%*	(+8%)	10%*
Thymus	-	-	20%*	29%*

Absolute Organ Weights - Pups (M + F)

Day 21 Body Weight(decrease)	-	-	-	14%*
Brain	-	-	-	-
Thymus	Confidential Information Has Been Sanitized			
Spleen(decrease)	-	-	-	22%*

Relative Organ/Body Weight - Pups (M + F)

Brain(Increase)	-	-	-	15%
Thymus	-	-	-	-
Spleen	-	-	-	9%*

* = significantly different from control ($p \leq 0.05$).**A Reproductive Toxicity Study**

with [REDACTED] in the Wistar Rat

¹Effect noted for uterus and pituitary thought to be related to the increased terminal body weight. Thus decreasing the organ/body weight ratio effect. The lack of a dose response, as noted by the 100 mg/kg group, also point to the potentiality of these findings as being incidental to treatment.

(Preliminary Results Summary)

SECOND GENERATION

DOSE (mg/kg)

0 10 100 750

F1 Males

Premating/Mating

Clinical Signs	-	-	-	-
Body Weight(mean decrease 0-70)	-	-	7%*	16%*
Food Consumption(mean increase 0-70)	-	-	-	11%*

F1 Females

Premating/Mating

Clinical Signs	-	-	-	-
Body Weight(decrease)	-	-	-	6%*
Food Consumption(mean increase)	-	-	-	12%*
Estrous Cycle (number)	3.6	3.4	3.5	3.1
Estrous Cycle (length)	4.4	4.5	4.4	4.8
Mating Index	100	100	100	97
Fertility Index	90	87	97	93
Gestation Index	100	100	97	93
Gestation Length	-	-	-	-
Total Number Implantations(decrease-median)	-	-	-	18%*

* = significantly different from control (p ≤ 0.05)

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A Reproductive Toxicity Study

with [REDACTED] in the Wistar Rat
(Preliminary Results Summary)

<u>Second Generation</u>	<u>DOSE (mg/kg)</u>			
<u>F1 females</u>	0	10	100	750
Gestation				
Clinical Signs	-	-	-	Urine Stain
Body Weight Gain(decrease)	-	-	-	-
Food Consumption	-	-	-	-
lactation				
Clinical Signs	-	-	-	-
Body Weight Gain	-	-	-	-
Food Consumption	-	-	-	-
<u>F2 Pups</u>				
Clinical Signs	-	-	-	-
Pup Body Weight(decrease)				
Birth	-	-	-	-
Day 4	-	-	-	-
Day 7	-	-	-	-
Day 14	-	-	-	12%*
Day 21	-	-	-	8%*
Gain	-	-	-	10%*
Birth Index	-	-	-	-
Live Birth Index	-	-	-	-
Viability Index	-	-	-	-
Lactation Index	-	-	-	-

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* = significantly different from control ($p \leq 0.05$).

A Reproductive Toxicity Study

with [REDACTED] in the Wistar Rat
(Preliminary Results Summary)

SECOND GENERATION

	<u>DOSE (mg/kg)</u>			
	0	10	100	750
<u>F2 Pups, cont.</u>				
Litter Size(decrease)	-	-	-	23%*
Pups Missing	-	-	-	-
Pups Found Dead	-	-	-	-
Anogenital Distance (not yet analyzed)				
Sperm Analysis (not yet analyzed)				

pathology data not yet analyzed
IN-LIFE COMPLETE

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