TSCA HEALTH & SAFETY STUDY COVER SHEET

8EHQ-0198-14014

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.

1.0 SUBMISSION TYPE - *Contains CBI*

☐ 8(d) X 8(e) ☐ FYI ☐ 4 ☐ OTHER: Specify_____

- Intial Submission **X** - Follow-up Submission ☐ Final Report Submission

Previous EPA Submission Number or Title if update or follow-up: Docket Number, if any: #

Follow-up to our 8/25/97 submission " Dose range-finding Developmental Tox Study with Propylene Thiourea in the Sprague-Dawley Rat, Report # 107648.

☐ continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e): optional for §4, 8(d) & FYI)	**2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID**	**2.3 FOR EPA USE ONLY**
X - YES ☐ NO	Cert# P917 006 727 98-2-1	

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY -*Contains CBI*

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS#: 2122-19-2 4-Methyl-2-imidazolidinethione

Purity __99 +____%

PDCN: 88970000264

X - Single Ingredient

☐ Commerical/Tech Grade

☐-Mixture *Trade Name:* _____ *Common Name:* Propylene Thiourea

4.0 REPORT/STUDY TITLE - *Contains CBI*

Contains No CBI

A Developmental Toxicity Study with Propylene Thiourea in the Sprague-Dawley Rat
Report # 108018

☐ 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 TYPE: CTOX	SUBJECT ORGANISM (HE, EE only): RATS	ROUTE OF EXPOSURE (HE only): ORAL	VEHICLE OF EXPOSURE (HEonly)_____
Other:	*Other:*	*Other:*	*other:*

6.0 REPORT/STUDY INFORMATION ☐ *Contains CBI* X- Study is GLP

Laboratory Bayer Agricultural Toxicology Lab Report/Study Date 12/8/97

Source of Data/Study Sponsor (if different than submitter) _____ Number of pages 604

☐ 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

☐ continuation sheet attached

8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS ☐ *Contains CBI*

8EHQ-97-14014

☐ continuation sheet attached

Submitter Signature: Donald W Lamb **Date:** 1/8/98

89980000095

9.0 CONTINUATION SHEET

TSCA CBI STATUS:

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Submitter Tracking Number/Internal ID

P917 006 727
98-2-1

CONTINUED FROM COVER SHEET SECTION # 2.1

This study assessed the potential for propylene thiourea (PTU) to promote gestational effects and/or alter the growth and development of the conceptus. Inseminated dams were administered nominal doses of 0, 1, 7, or 50 mg PTU/kg body weight (analytically confirmed doses of 0, 1.0, 7.0, and 51.4 mg PTU/kg, respectively) by oral gavage on days 6 through 19 of gestation. Maternal toxicity, as demonstrated by clinical signs and changes in body weight gain and food consumption during gestation, was characterized. All dams were sacrificed on gestation day 20, at which time gross external and internal necropsies were performed, the uterus was examined, and the fetuses were removed by cesarean section. All fetuses were evaluated for external anomalies. Approximately half of each litter was examined for visceral effects, and the other half underwent a skeletal examination.

Test compound-related maternal effects were observed in the 7 and 50 mg/kg dose groups. Gravid dams in the 50 mg/kg dose group demonstrated decreased body weight gain and food consumption, and decreased net body weight and net body weight change (subtraction of gravid uterus). Additionally observed at the high-dose were an increase in thyroid weight and a decrease in liver and kidney weight. Related to the affect on thyroid weight was an increase in TSH (thyroid stimulating hormone) and decreases in circulating T3 and T4 levels. Evidence of maternal toxicity in the 7 mg/kg dose group was limited to affected thyroid hormone levels: increased TSH levels and decreased T4 levels.

No maternal effects were observed in the 1 mg/kg dose group. There were no test-compound related effects on the gestation index, or any embryologic endpoints: pre/post-implantation loss and resorptions observed in any dose group. There were no statistically significant effects on litter size or the number of fetuses per implantation site. A test compound-related litter finding was observed in the 50 mg/kg dose group: statistically significantly decreased fetal weight (male, female, and combined). Fetal findings noted in the high-dose group included test compound-related fetal malformations and variations, observed during both the external and visceral examinations. External anomalies were observed in all body regions. In contrast, visceral findings were limited to enlarged thyroids and cranial malformations. No effects on fetal external or visceral malformations or variations were observed in the 1 or 7 mg/kg dose groups. A statistically significant increase in fetal skeletal malformations was observed in the 50 mg/kg dose group. Malformations included abnormal radius, lordosis, and fetuses exhibiting multiple skeletal anomalies. The majority of the skeletal variations were statistically significantly increased at the highest dose level, however several findings were also significantly increased in the 1 and 7 mg/kg dose groups. The fetal skeletal variations observed in the 1 mg/kg dose group were not considered test compound-related as they were all within the range of historical controls for the individual findings. In contrast the incidence of many of the skeletal variations observed in the 7 mg/kg dose group fell outside the range of historical controls. As would be expected given the fetal observations, there was a significant increase in both the fetal and litter incidence of total malformations and variations observed at the highest dose level. Also observed at this dose level was a significant difference in the incidence of malformations between males and females. No effects on the incidence of total malformations or variations, or any gender-related differences in fetal effects were observed in the 1 or 7 mg/kg dose groups.

Propylene thiourea, administered as described in this study, produced maternal toxicity at doses of 7 and 50 mg/kg body weight. The 1 mg/kg dose was free of test compound-related maternal effects. Developmental effects were observed in the 7 and 50 mg/kg dose groups. In the 50 mg/kg dose group, developmental effects included reduced fetal weight and increased external, visceral, and skeletal anomalies. In the 7 mg/kg dose group developmental effects were limited to skeletal variations. No test compound-related developmental effects were observed in the 1 mg/kg dose group and no embryotoxicity was observed at any dose level. Both the maternal and developmental no-observed-effect-levels (NOEL) were 1 mg/kg.

Agriculture Division
Report Number
108018

A Developmental Toxicity Study with Propylene Thiourea in the Sprague-Dawley Rat

Data Requirement

40 CFR Part 158
US-EPA-FIFRA, Section 158.135, Guideline 83-3

Author

A. Barry Astroff

Study Completion Date

December 8, 1997

Test Facility

Bayer Corporation
Agriculture Division
Toxicology
17745 South Metcalf
Stilwell, Kansas 66085-9104

RECEIVED
OPPT NCIC
98 JAN 20 AM 9: 18

Study Number

97-612-KR

STATEMENT OF DATA CONFIDENTIALITY

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA Section 10(d)(1)(A), (B), or (C).

Company: Bayer Corporation, Agriculture Division

Company Agent: J. H. Thyssen, Vice-President, Toxicology

Signature

Dec. 8, 97
Date

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with the FIFRA Good Laboratory Practice Standards of 40 CFR Part 160, the OECD Principles of Good Laboratory Practice, GD(92)32 (Paris, 1992), and the Japanese Ministry of Agriculture, Forestry, and Fisheries (MAFF) "Good Laboratory Practice Standards" (59 NohSan No. 3850).

SUBMITTER

BAYER CORPORATION

J. H. Thyssen: _____ Date: Dec. 8-97
Vice President, Toxicology
Agriculture Division

SPONSOR

AGRICULTURE DIVISION

J. H. Thyssen: _____ Date: Dec. 8, 97
Vice President, Toxicology

STUDY DIRECTOR

A. B. Astroff: _____ Date: 12.8.97

FLAGGING STATEMENT

I have applied the criteria of 40 CFR 158.34 for flagging studies for potential adverse effects to the results of the attached study. This study neither meets nor exceeds any of the applicable criteria.

SUBMITTER

BAYER CORPORATION

J. H. Thyssen: Date: Dec. 8-97
Vice President, Toxicology
Agriculture Division

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SPONSOR

Bayer Corporation
Agriculture Division
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Kansas City, Missouri 64120-0013

TEST FACILITY

Bayer Corporation
Agriculture Division
Toxicology
17745 South Metcalf
Stilwell, Kansas 66085-9104

DATES

Study Initiation (protocol signed by study director): February 4, 1997
Initiation of mating (first day of co-housing): February 24, 1997
Experimental initiation (first day of dosing): March 3, 1997
Termination (last day of necropsy): March 31, 1997

PERSONNEL AND RESPONSIBILITIES

Toxicology and Sponsor Representative:	J. H. Thyssen	
Toxicology Laboratory:	G. K. Sangha	
Study Direction:	A. B. Astroff	
Study Conduct:	A. D. Young	
	M. J. Brown	
Pathology Services:	B. P. Stuart	
Animal Care:	R. E. Mueller	
Analytical Chemistry:	K. D. Moore	
Quality Assurance:	D. M. Wallace	

QUALITY ASSURANCE STATEMENT

Audit reports have been submitted to the study director and laboratory management documenting the status of compliance with applicable departmental standard operating procedures, the study protocol, and Good Laboratory Practice regulations.

The Quality Assurance Unit monitored selected phases of this study, and at least annually functions of all support areas for this study type. The following are the audit dates, phases inspected, auditors, and report dates of quality assurance inspections of this study and, if applicable, of this study type as well as relevant support areas:

AUDITS			REPORT TO STUDY DIRECTOR AND MANAGEMENT
Date	Phase of Study	Auditor	
01/17/97	Active Ingredient Check & Material Accountability	C.A. Cox	01/17/97
02/04/97	Protocol Checklist	C.A. Cox	02/04/97
02/17/97	Animal Receipt, Shipment Examination, Quarantine, Feeding, Animal Inventory, Cage Identification (Cage Cards), AM Observations	C.A. Cox	02/18/97
02/24/97	Animal Release for Study Use	C.A. Cox	02/24/97
02/24/97	Identification of Males (Tailmarking), Identification of Females (Tattooing), Co-Housing, Feeding, Initial Body Weight Collection for Determination of ±20% of the Mean	C.A. Cox	02/25/97
02/26/97	Dose Preparation, Sample Submission	C.A. Cox	02/27/97
03/02/97	Gestational Body Weights, Food Consumption, Oral Dosing, Clinical Observations, Dose Storage	C.A. Cox	03/04/97
03/04/97	AM Vaginal Smears, Randomization & Transfer of Sperm Positive Females to Nesting Cages, Cage Identification (Cage Cards), Tailmarking of Females	C.A. Cox	03/04/97
03/19/97	Blood Collection	C.A. Cox	03/19/97

QUALITY ASSURANCE STATEMENT (Continued)

AUDITS			REPORT TO STUDY DIRECTOR AND MANAGEMENT
Date	Phase of Study	Auditor	
03/20/97	Gestation Day-20 Dams: Euthanasia, External Examinations, Necropsy, Determination of Pregnancy, Organ Weight Collection, Counting of Corpora Lutea, Noting & Characterization of Implantation Sites, Placental Weights Fetuses: Fetal Weights, External Examinations, Status, Sexing, Identification (Tagging), Euthanasia, Visceral Examinations, Storage	C.A. Cox	03/21/97
05/03/97	Wilson's Technique	C.A. Yount	06/04/97
06/02/97	Fetal Processing: Dehydration	C.A. Yount	06/04/97
06/03/97	Fetal Eviscerations	C.A. Yount	06/04/97
06/03/97	Fetal Processing: Staining/Macerating	C.A. Yount	06/04/97
06/05/97	Fetal Processing: Clearing	C.A. Yount	06/05/97
06/06/97	Fetal Processing: Holding, Fetal Storage	C.A. Yount	06/06/97
07/23/97	Skeletal Examinations	C.A. Yount	07/24/97
11/17-18, 20-21/97	Final Report Review	K.F. Yount	11/21/97
	Analytical Chemistry Support Functions		
1/10/97	Sample Preparation & Analysis	S. Bailey	01/22/97
	Animal Care Support Functions		
01/08/97	Filter Check/Change	C.A. Cox	01/09/97
01/08/97	Rat Polycarbonate Rack Preparation	C.A. Cox	01/09/97

QUALITY ASSURANCE STATEMENT (Continued)

Date	AUDITS Animal Care Support Functions	Auditor	REPORT TO STUDY DIRECTOR AND MANAGEMENT
01/08/97	Rat Wire Mesh Cage/Rack Preparation	C.A. Cox	01/09/97
01/27/97	Rat DACB Bedding Change	C.A. Cox	01/27/97
01/28/97	Rat Polycarbonate Rack/Bedding Change	C.A. Cox	01/30/97
01/28/97	Room Disinfection	C.A. Cox	01/28/97
02/19/97-02/20/97	Cleaning of Rat Wire Mesh Racks, Cages, Trays, and Feeders	C.A. Cox	02/20/97
02/19/97-02/20/97	Cleaning of Rat Polycarbonate Racks & Cages	C.A. Cox	02/20/97
03/19/97	Rat Rack Change (Wire Mesh)	C.A. Cox	03/19/97
	Clinical Chemistry Support Functions		
09/08/97-09/09/97	T3, T4, & Thyroid Stimulating Hormone Determinations	T. Bormann	09/25/97
	Developmental Tox Support Functions		
06/03/97	Staining/Macerating Solution Preparation & Storage	C.A. Yount	06/04/97
06/05/97	Clearing and Holding Solution Preparation & Storage	C.A. Yount	06/05/97
07/15/97	Preparation of Alizarin Red Stain	C.A. Yount	07/16/97

In compliance with the Good Laboratory Practice regulations, this final report for study number 97-612-KR has been reviewed by the Quality Assurance Unit. The results presented in this report accurately describe the methods and standard operating procedures and reflect the raw data collected during the conduct of the study.

K. F. Yount, Quality Assurance Auditor

12/5/97
Date

ABSTRACT

This study assessed the potential for propylene thiourea (PTU) to promote gestational effects and/or alter the growth and development of the conceptus. Inseminated dams were administered nominal doses of 0, 1, 7, or 50 mg PTU/kg body weight (analytically confirmed doses of 0, 1.0, 7.0, and 51.4 mg PTU/kg, respectively) by oral gavage on days 6 through 19 of gestation. Maternal toxicity, as demonstrated by clinical signs and changes in body weight gain and food consumption during gestation, was characterized. All dams were sacrificed on gestation day 20, at which time gross external and internal necropsies were performed, the uterus was examined, and the fetuses were removed by cesarean section. All fetuses were evaluated for external anomalies. Approximately half of each litter was examined for visceral effects, and the other half underwent a skeletal examination.

Test compound-related maternal effects were observed in the 7 and 50 mg/kg dose groups. Gravid dams in the 50 mg/kg dose group demonstrated decreased body weight gain and food consumption, and decreased net body weight and net body weight change (subtraction of gravid uterus). Additionally observed at the high-dose were an increase in thyroid weight and a decrease in liver and kidney weight. Related to the affect on thyroid weight was an increase in TSH (thyroid stimulating hormone) and decreases in circulating T_3 and T_4 levels. Evidence of maternal toxicity in the 7 mg/kg dose group was limited to affected thyroid hormone levels: increased TSH levels and decreased T_4 levels. No maternal effects were observed in the 1 mg/kg dose group. There were no test-compound related effects on the gestation index, or any embryologic endpoints: pre/post-implantation loss and resorptions observed in any dose group. There were no statistically significant effects on litter size or the number of fetuses per implantation site. A test compound-related litter finding was observed in the 50 mg/kg dose group: statistically significantly decreased fetal weight (male, female, and combined). Fetal findings noted in the high-dose group included test compound-related fetal malformations and variations, observed during both the external and visceral examinations. External anomalies were observed in all body regions. In contrast, visceral findings were limited to enlarged thyroids and cranial malformations. No effects on fetal external or visceral malformations or variations were observed in the 1 or 7 mg/kg dose groups. A statistically significant increase in fetal skeletal malformations was observed in the 50 mg/kg dose group. Malformations included abnormal radius, lordosis, and fetuses exhibiting multiple skeletal anomalies. The majority of the skeletal variations were statistically significantly increased at the highest dose level, however several findings were also significantly increased in the 1 and 7 mg/kg dose groups. The fetal skeletal variations observed in the 1 mg/kg dose group were not considered test compound-related as they were all within the range of historical controls for the individual findings. In contrast the incidence of many of the skeletal variations observed in the 7 mg/kg dose group fell outside the range of historical controls. As would be expected given the fetal observations, there was a significant increase in both the fetal and litter incidence of total malformations and variations observed at the highest dose level. Also observed at this dose level was a significant difference in the incidence of malformations between males and females. No effects on the incidence of total malformations or variations, or any gender-related differences in fetal effects were observed in the 1 or 7 mg/kg dose groups.

Propylene thiourea, administered as described in this study, produced maternal toxicity at doses of 7 and 50 mg/kg body weight. The 1 mg/kg dose was free of test compound-related maternal effects. Developmental effects were observed in the 7 and 50 mg/kg dose groups. In the 50 mg/kg dose group, developmental effects included reduced fetal weight and increased external, visceral, and skeletal anomalies. In the 7 mg/kg dose group developmental effects were limited to skeletal variations. No test compound-related developmental effects were observed in the 1 mg/kg dose group and no embryotoxicity was observed at any dose level. Both the maternal and developmental no-observed-effect-levels (NOEL) were 1 mg/kg.

MATERIALS

I. The test substance was supplied by the sponsor with the following information:

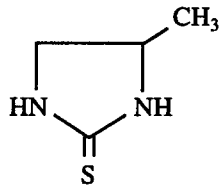
Test Substance:

Identification:	Propylene Thiourea
Physical Appearance:	White powder
Batch No.:	NLL 3790-4
Purity:	99.5% (date of analysis: April 9, 1996) 99.9% (date of analysis: November 11, 1996)
Stability at Storage Conditions:	At least 7 months (based on % purity)

Active Ingredient:

Common Name:	Propylene Thiourea (PTU)
Chemical Name:	4-Methyl-2-imidazolidinethione

Structural Formula:



CAS No.:	2122-19-2
Reference Substance:	same batch as test substance

II. The test substance was stored and will be archived at freezer conditions.

PURPOSE

The purpose of this study was to assess the potential for propylene thiourea, administered by oral gavage to gravid Sprague-Dawley rats on days 6 through 19 of gestation, to promote gestational effects and/or alter the growth and development of the conceptus.

TEST GUIDELINES

This report was prepared in accordance with US EPA FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, November 1984, Guideline 83-3. Also followed were the US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.4900; EU guidelines on Teratogenicity Studies, in the Official Journal of the European Communities, 87/302/EEC, February, 1995; and Japan, Ministry of Agriculture, Forestry, and Fisheries (MAFF), Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January, 1985. These guidelines were followed to the extent that they applied to this study.

METHODS

Animal Information

Source, Number, Age and Test System Rationale

As described in the protocol (Appendix I, page 110), the study design required 120 young adult female (nulliparous and nonpregnant) and 30 sexually mature male Sprague-Dawley rats (Sasco Inc., Kingston, NY). Females and males were not previously treated and were approximately 12-15 weeks of age at the beginning of the study. Rats were used as the test system as they are one of the US EPA, OECD, EU, and Japanese MAFF suggested species for developmental toxicity studies.

Examination and Acclimation

Upon receipt, animals were examined by trained personnel, and those animals considered acceptable were then placed into individual cages and acclimated to their ambient laboratory conditions for at least six days prior to study initiation. For the holding period, animal care personnel observed the animals at least once daily for moribundity and mortality. Moribund animals were sacrificed if their condition dictated. Necropsies were not required on animals that were either found dead or were sacrificed in a moribund condition at any time prior to initiation of the study. With completion of the acclimation period, a veterinarian reviewed the status of the animals prior to their being release for the study.

Care and Housing

Male rats, and females prior to being declared sperm positive, were individually housed in suspended stainless steel cages. Sperm positive females were housed individually in plastic cages with corn cob bedding. The room, stainless steel cages, and cage racks were thoroughly cleaned and disinfected before arrival of the animals. Deotized Animal Cage Board was used in the bedding trays and changed at least three times weekly. The stainless steel cages and racks were replaced at least once every two weeks with clean, disinfected cages and racks. Clean plastic cages were provided every week and bedding was changed at least twice weekly. The room was disinfected at least once every two weeks. Municipal tap water and Purina Mills Rodent Lab Chow 5001-4 was provided for ad libitum consumption. Water and feed are periodically analyzed for possible contaminants and the results are compared to the allowable limits in "Lab Chows Animal Diet Reference Guide" (Publication SP2437M-87010 dated 1987) from Purina Co., St. Louis, Missouri. The animal room was maintained at 18 to 26 ^{o}C with 30 to 70% relative humidity and a 12-hour photoperiod.

Identification

Males were identified by cage card and tail marking. Females prior to being declared sperm positive were identified by cage card and tattoo. Once declared sperm positive, females were additionally identified by tail marking.

Animal Selection

Females were put on study if their body weight was within +/- 20% of the mean body weight for all females.

Rationale for Dose Selection

The doses selected for this study were based on a dose range-finding developmental toxicity study with propylene thiourea in the Sprague-Dawley rat [1]. In this study gravid Sprague Dawley rats were administered nominal doses of 0, 1, 10, 100, or 500 mg of PTU/kg body weight by oral gavage on gestation days 6 through 19. Severe maternal toxicity was demonstrated in both the 100 and 500 mg/kg dose groups. In the 500 mg/kg dose group two dams were found dead, two dams were sacrificed in moribund condition, and two dams were sacrificed prior to the completion of the study. Body weight gain was significantly affected in the dams of the 100 mg/kg dose, decreased 93% relative to control for the dosing period. Dams from the 100 mg/kg dose group also exhibited severe clinical signs, including: hypoactivity, salivation, and oral stain. Necropsy findings in these dams included significantly enlarged thyroids (relative thyroid weight was 3.3-fold greater than control) and an increase in absolute kidney weight (19% greater than control). As expected, given the maternal toxicity demonstrated at this dose level, most of the fetal and litter parameters were also significantly affected. No maternal, fetal, or litter effects were observed in the 1 and 10 mg/kg dose groups.

Based on the findings of this study and collaboration with the Bayer scientists in the toxicology department in Wuppertal, Germany, the dose proposed for the definitive developmental toxicity study were 0, 1, 7, and 50 mg PTU/kg body weight.

Dosage Preparation, Handling, and Analysis

Stock dosing solutions were prepared prior to the first day of dosing by dissolving propylene thiourea in deionized water. Following preparation, the concentration of the test compound at each dose level was determined [2] and the stock solutions refrigerated. On the days of dosing an aliquot of each stock solution was taken, from which the appropriate animals were dosed. Any unused portion of the daily aliquot was discarded. Homogeneity and stability of the test substance in the water vehicle at the storage conditions indicated have been verified [1].

Experimental Design

Route/Dose/Number of Animals

One hundred and twenty female rats were assigned to one of four treatment groups (30 animals/group): 0 (control), 1, 7, and 50 mg PTU/kg. Doses were administered by oral gavage, the suggested route of administration for studies of this type, in deionized water at a dosage volume of 10 ml/kg, on days 6 through 19 of gestation. Dosing volume was adjusted daily, based on dam body weight during the dosing period. On two occasions it was noted that less than 100% of the dose was administered to the animals: dams 62 and 92 on their gestation day 6 and dam 67 on gestation day 13 (see Appendix I, page 110). These deviations are not expected to have significantly affected this study.

Animal Co-Housing

Rats were co-housed with a maximum of two females per male at one time. Following cohabitation, morning vaginal smears were taken and examined for the presence of sperm. Females found to be sperm-positive were randomized into groups as described below. The day on which sperm was observed in the vaginal smear was designated day 0 of gestation for that female.

Randomization Procedure

Females were assigned, using randomization chips, to one of the four groups as they became inseminated. Specifically, females found sperm positive were assigned a numbered chip. Chips were then blindly selected and the corresponding females placed into consecutive treatment groups.

Observations/Body Weight/Food Consumption

Inseminated females were observed for clinical signs twice daily (AM, detailed; and PM, cageside) on gestation days 0-19. Dams were observed once (detailed) prior to termination on day 20. A detailed clinical observation was performed at least once daily on weekends and holidays. The detailed evaluation of clinical signs included both observing the animal in the cage and removing the animal to perform a physical examination. Cageside observations characterized mortality, moribundity, behavioral changes, and overt toxicity by viewing the animal in the cage. In the event a possible clinical sign was observed during the cageside evaluation, the animal may have been removed from the cage and a detailed assessment conducted. Dam body weights were taken on days 0, 2, 4, 6 through 19, and 20 of gestation. Food consumption was recorded on gestation days 2, 4, 6 through 19, and 20.

Clinical Biochemistry

On gestation day 20, prior to termination, blood was collected via the retroorbital sinus from the first ten gravid dams from each dose level. One exception to this collection procedure occurred when it was noticed that the waterer from the level I females animal rack was disconnected (see animal care and environmental conditions discussion in the results section of this report). Three animals were bled that may have been affected by the waterer malfunction. The results from these animals are not included in this study. Three replacement animals were bled and their data are included in the clinical biochemistry results. The blood was collected for the determination of circulating levels of T_3, T_4, and TSH.

Day 20 Termination/Gross Pathology

On day 20 of gestation, the dams were terminated by carbon dioxide asphyxiation and a gross external examination performed. The abdomen and thoracic cavities were opened and a gross internal necropsy performed. The liver, thyroids, and kidneys were excised and weighed. The ovaries were excised, corpora lutea counted, and pregnancy determined. The intact uterus was removed and weighed. The uterus was opened and resorptions, if any, were characterized. Fetuses were removed from the uterine wall and each implant was noted. The placentas were trimmed of extraneous tissue, blotted, and weighed. Fetuses were sacrificed by intraperitoneal injection of 0.01-0.05cc Fatal Plus (Vortech Pharmaceuticals, Dearborn, MI). All fetuses were individually identified, sexed, weighed, and externally examined. Approximately half of all fetuses from each litter were fixed in toto in 70% alcohol, eviscerated, processed, and evaluated for general skeletal development [3]. The remaining fetuses were subjected to a gross visceral examination [4] and placed in Bouin's solution. Prior to fetal cranial examination, the fetuses were transferred to 70% alcohol. Sectioning of the head was performed according to the method of Wilson [5].

Necropsy of Non-Gravid, Moribund, or Dams Found Dead

Dams sacrificed on gestation day 20 and suspected to be not pregnant underwent a gross examination. The abdomen was opened and the uterus was flushed with saline or water to verify the patency of the cervical/uterine os. If the openings were patent the uterus was excised and examined for implantation sites to confirm pregnancy. If the dam was not pregnant no further examinations were performed. Dams

found dead, moribund, or delivering prematurely while on study, were sacrificed if their status dictated and a gross necropsy was performed.

Evaluated Parameters

Reproductive and Dam Assessment included:

- Fertility Index: # pregnant (with implants) / # sperm-positive x 100
- Gestation Index: # with viable fetuses / # pregnant (with implants) x 100
- Mating Index: # sperm-positive / # co-housed x 100
- Body weight gain (corrected for gravid uterine weight)
- Food consumption
- Clinical signs
- Clinical biochemistry: T3, T4, and TSH
- Necropsy findings
- Organ weights: gravid uterus, liver, thyroids, and kidney
- Number of corpora lutea
- Total number of implantations

Litter Assessment included:

- Total number of fetuses
- Number of viable fetuses
- Number of non-viable fetuses
- Fetal sex distribution
- Number/type of resorptions
- Number of affected (i.e., nonviable and malformed) implants
- Number of malformed males or females
- Pre-implantation loss: # corpora lutea - # implants / # corpora lutea x 100
- Post-implantation loss: # implantations - # viable progeny / # implantations x 100
- Number of affected litters

Fetal Assessment included:

- Placental weight
- Fetal weight
- Type and incidence of:
    - external malformations and variations
    - visceral malformations and variations
    - skeletal malformations and variations

External, visceral, and skeletal findings were considered either malformations or variations. Malformations include defective or abnormal development that may be life-threatening or life-limiting. Malformations occur at low frequencies in every population. However, they do not typically occur in several litters within one group (treatment or control), unless induced. Malformations, (particularly those of genetic origin) may be spontaneous in origin, and can occur in one to several individuals within a given litter. In contrast to malformations, variations are alterations in development that are commonly observed in a given strain of animal. These changes are not considered meaningful unless they occur in a

treatment group, in a dose-dependent fashion, and at significantly higher rates than observed in the control [6].

Statistical Analysis

The data was analyzed with the litter as the primary experimental unit, using applications provided by TASC [7], SAS [8], or DATATOX [9]. Parametric data (including dam body weights and food consumption) was analyzed using an Analysis of Variance (ANOVA), and if significant differences were observed, a Dunnett's Test was performed. Fetal and placental weights were specifically analyzed via the Healy's Test if significance was observed in the ANOVA. Nonparametric data (e.g. litter size and number of corpora lutea) were first analyzed by the Kruskal-Wallis test and then subjected to Dunn's Test if significant differences were identified. Nonparametric dichotomous data (e.g. number normal/abnormal) were initially analyzed by the Chi-Square Test and if significance was observed between groups then by the Fisher's Exact Test with the Bonferroni adjustment. Thyroid hormone levels (T3 and T4) were analyzed first via a one-way ANOVA followed by a Dunnett's Test. TSH levels were evaluated using the Kruskal-Wallis ANOVA and a pairwise Mann/Whitney U-test. Differences between the control and test compound-treated groups were considered statistically significant when $p \leq 0.05$.

Archival Procedures

The final report, protocol, raw data, tissues, and a sample of the test substance will be archived at locations specified by Bayer Corporation, Agriculture Division, Toxicology, 17745 South Metcalf, Stilwell, Kansas 66085-9104.

RESULTS AND DISCUSSION

Animal Care and Environmental Conditions

With one exception, there were no deviations from the animal care procedures or the environmental conditions described in the methods section, the study protocol (Appendix I, page 110), or the Animal care Report (Appendix II, page 126). The exception occurred on March 18, 1997 when the waterer to the level I dams was unhooked. Although an immediate effect was noted, decreased body weight in the affected females on the one day, no meaningful impact on the integrity of the study was observed.

Dose Analysis

A summary of the results from the analysis of the dosing solutions are shown in Appendix III (page 129).

Homogeneity and five-week stability of the test substance in the dosing vehicle at the storage conditions previously described were confirmed for concentrations which encompassed the range of dosages used in this study [1]. The actual concentrations of propylene thiourea (PTU) in the nominal 0, 0.1, 0.7, and 5.0 mg/ml dosing solutions were 0, 0.10, 0.70, and 5.14 mg/ml, respectively. Based on a dosage volume of 10 ml/kg, the actual doses were 0, 1, 7, and 51.4 mg PTU/kg body weight. In the interest of clarity and consistency between the text, tables, and appendices, the dose levels will be presented throughout the report as the control, 0; level I, 1; level II, 7; and level III, 50 mg/kg nominal doses.

Clinical Signs

A summary of the clinical signs observed prior to, during, and following PTU treatment are presented in Table 1 (page 28). Individual clinical observations are given in Appendix VI (page 133).

There were no test compound-related clinical signs. Incidental findings included hair thinning and oral and urine stain.

The no-observed-effect-level (NOEL) for maternal clinical signs was 50 mg/kg.

Gestational Body Weight and Food Consumption

Body weight gain is summarized in Table 2 (page 30) and illustrated in Figure 1 (page 106). The individual body weight data is shown in Appendix V (page 142). The summary of food consumption during gestation is given in Table 3 (page 32) with the individual food consumption data in Appendix VI (page 151).

A statistically significant decrease in body weight change was observed in level III during gestation days 6-7. Also observed in this group were statistically significant effects on body weight change during the dosing period (gestation days 6-20), decreased 11%; and over the course of the entire study (gestation days 0-20), decreased 12%, relative to control. No other statistically significant effects on body weight were observed.

Statistically significantly decreased food consumption was observed in the dams of level III during gestation days 7-8 and 17-20. No other statistically significant effects on food consumption were observed.

The NOEL for effects on maternal body weight gain and food consumption was 7 mg/kg.

Maternal Necropsy

Maternal necropsy findings are summarized in Table 4 (page 34), with the individual findings shown in Appendix VII (page 160). A summary of the mean final body weights, liver, kidney, and thyroid weights are given in Table 5 (page 36). Maternal organ weights expressed relative to the final body weight are summarized in Table 6 (page 38). The individual organ weights are shown in Appendix VIII (page 169). Table 7 (page 40) summarizes the gravid uterus weights, the net body weight (day 20 body weight - gravid uterine weight), and the net body weight change from day 0 ([day 20 body weight - weight of gravid uterus] - day 0 body weight) at each level. Individual net body weight data may be found in Appendix IX (page 174).

The only test-compound related necropsy finding was enlarged thyroids, noted in 15 dams of level III. Statistically significant effects on absolute organ weights; decreased liver and kidney, and increased thyroid, were observed in level III. However, the only statistically significant effect on relative organ weight was the increase in thyroid weight observed in level III. No effects on organ weights were noted in any other dose levels. Final body weight was unaffected at all dose levels. A statistically significant effect on net body weight and net body weight change were observed in level III, decreased 5 and 28% relative to control, respectively. No other statistically significant effects were seen on net body weights and there were no effects seen on gravid uterine weight.

The NOEL for findings observed at maternal necropsy, including organ weights and net body weight change, was 7 mg/kg.

Maternal Clinical Biochemistry

The maternal clinical biochemistry results are summarized in Table 8 (page 42). Individual clinical biochemistry data is given in Appendix X (page 179).

The clinical biochemistry parameters measured in this study included the circulating thyroid hormones T_3, T_4, and TSH (thyroid stimulating hormone). All three parameters were statistically significantly affected in level III: TSH was increased 75% relative to control, and T_3 and T_4 were decreased 59 and 83% relative to control, respectively. In level II, T_4 was statistically significantly decreased (32% relative to control) and TSH was statistically significantly increased (36% relative to control). No effects were observed in level I.

The NOEL for clinical biochemistry was 1 mg/kg.

Reproductive Parameters

A summary of the reproduction data is given in Table 9 (page 44) with individual data shown in Appendix XI (page 182). Individual breeding records may be found in Appendix XII (page 187).

The fertility index was 96.7, 93.3, 90.0, and 93.3%, for the control, level I, level II, and level III, respectively. The mating index was 100% for all levels. The results of these two indices indicate that there were an adequate number of litters for evaluation. The gestation index was 100% for all dose groups.

The NOEL for reproductive parameters was 50 mg/kg.

Embryo Implantation/Resorption

Table 9 (page 44) summarizes the implantation results for each dose group. The historical control data for maternal and fetal data at cesarean section is presented in Appendix XIII (page 192).

All gravid dams terminated on day 20 gestation had viable fetuses. No statistically significant differences were seen in the number of corpora lutea or the number of implantation sites. There were no statistically significant effects on resorptions or post-implantation loss between animals of the control and levels I, II, and III. An incidental, albeit statistically significant, decrease in pre-implantation loss was observed in levels II and III.

The NOEL for embryotoxicity was 50 mg/kg.

Litter Effects

The litter data at each dose level are summarized in Table 10 (page 47). Mean fetal body weights are depicted graphically in Figure 2 (page 108). Individual fetal weights are presented in Appendix XIV (page 195). Historical control data for fetal weight is presented in Appendix XV (page 233).

No statistically significant differences in the litter size, the number and proportion of live fetuses/litter, or the median percent of male fetuses were observed between the control and the test substance-treated groups. A statistically significant decrease in the male, female, and combined (male + female + unknown) mean fetal weights were observed in level III. No effect was observed on the mean placental weight at any dose level.

The NOEL for litter effects was 7 mg/kg.

Fetal External Malformations/Variations

A summary of fetal external malformations and variations are given in Table 11 (page 49), with the fetal external findings summarized in Table 12 (page 51). Individual external observations per fetus are shown in Appendix XVI (page 235). The historical control data for fetal external findings may be found in Appendix XVII (page 289).

Statistically significant increases in the fetal and litter incidence of both external malformations and external variations were observed in level III. These anomalies were observed in all body regions, including the head, torso, and appendages. No statistically significant effects on the fetal or litter incidences of external malformations or variations were observed in levels I or II.

The NOEL for fetal external malformations and variations was 7 mg/kg.

Fetal Visceral Malformations/Variations

A summary of fetal visceral malformations and variations are given in Table 13 (page 60), with the fetal visceral findings summarized in Table 14 (page 62). Individual visceral observations per fetus are shown in Appendix XVIII (page 291). The historical control data for fetal visceral findings may be found in Appendix XIX (page 320).

A statistically significant increase in both the fetal and litter incidence of total visceral malformations was observed in level III. Specific visceral findings that were affected included: enlarged thyroids, dilated cerebral ventricles, cleft palate, hydrocephalus, and malformed brain. No statistically significant effects on either the fetal or litter incidences of visceral malformations were observed in levels I or II.

The fetal and litter incidences of total visceral variations were statistically significantly increased in level III. Statistically significant fetal visceral variations observed at this level included: left-sided umbilical artery (increased fetal incidence) and hydroureter (increased fetal and litter incidences). The finding of left-sided umbilical artery observed in level III (fetal incidence, 6.5%) is not considered treatment-related as the incidence rate was within the range of the historical control for this variation (fetal incidence, 0 to 9.0%). No statistically significantly affected visceral findings were observed in levels I and II.

The NOEL for fetal visceral malformations and variations was 7 mg/kg.

Fetal Skeletal Malformations/Variations

Table 15 (page 68) summarizes the fetal skeletal malformations and variations for each dose level, with the fetal skeletal findings summarized in Table 16 (page 70). Individual skeletal findings per fetus are shown in Appendix XX (page 322). The historical control data for fetal skeletal findings may be found in Appendix XXI (page 597).

A statistically significant increase in both the fetal and litter incidence of total skeletal malformations, and the number of fetuses/litter demonstrating fetal skeletal malformations was observed in level III. Specific malformations that statistically significantly increased at this dose level were: abnormal radius, lordosis, and fetuses exhibiting multiple skeletal anomalies. There were no statistically significant effects on either the fetal or litter incidences of skeletal malformations in levels I or II.

There were no statistically significant effects on either the fetal or litter incidences of total skeletal variations. Skeletal variations were observed in virtually all fetuses from all dose levels. A number of the variations were significantly increased only at level III, several others were significantly increased at both levels II and III, and several more were significantly increased at all dose levels. The incidence of the skeletal variations significantly increased in levels II and III, were, in virtually all cases, outside the range of the historical control for the particular variations. In contrast, the incidences for all of the variations observed in level I were always within the range of historical controls for the individual variations. Moreover, for all of these variations, only the fetal incidence was significantly increased, no significant effect on the litter incidences were noted. Previous developmental toxicity studies in the Sprague-Dawley rat have also noted that a variety of fetal skeletal variations, many of which were observed in the current study, can occur spontaneously in this rodent strain [10,11]. Based on these findings, the skeletal variations observed in level I were not considered treatment-related, but within the range of normal variation observed in this test system.

The NOEL for fetal skeletal malformations and variations was 1 mg/kg.

Total Fetal Malformations/Variations

An overall summary of fetal external, visceral, and skeletal malformations and variations is given in Table 17 (page 101).

The summary includes the results from the external examination of all fetuses, the visceral examination of approximately half of each litter, and the skeletal examination of the remaining fetuses from each litter.

As would be expected given the increased incidence in the individual malformation and variation categories previously described, statistically significant increases in the fetal and litter incidences and an increase in the number of affected fetuses/litter for total malformations, total variations, and total affected fetuses (malformed and nonviable), were observed in level III. No other statistically significant effects were observed at any other dose level.

The NOEL for total fetal malformations, variations, and total affected fetuses was 7 mg/kg.

Relationship Between Gender and Malformations

A comparison of the incidences of malformations between male and female fetuses is presented in Table 18 (page 103).

The comparison considered total malformations and individual malformation categories: external, visceral, and skeletal. A statistically significant difference in the incidence of total malformations, and in particular external malformations, was noted between the males and females of level III. However, this effect was only observed using an absolute basis of comparison. No statistically significant differences were observed on the relative incidence rates, namely the mean percent affected per litter. No other gender-related differences in the incidence of total malformations or the incidence of individual malformation categories: external, visceral, or skeletal, were observed.

The NOEL for gender-related effects on malformations was 7 mg/kg.

SUMMARY AND CONCLUSIONS

This study assessed the potential for propylene thiourea (PTU) to promote gestational effects and/or alter the growth and development of the conceptus. Inseminated dams were administered nominal doses of 0, 1, 7, or 50 mg PTU/kg body weight (analytically confirmed doses of 0, 1.0, 7.0, and 51.4 mg PTU/kg, respectively) by oral gavage on days 6 through 19 of gestation. Maternal toxicity, as demonstrated by clinical signs and changes in body weight gain and food consumption during gestation, was characterized. All dams were sacrificed on gestation day 20, at which time gross external and internal necropsies were performed, the uterus was examined, and the fetuses were removed by cesarean section. All fetuses were evaluated for external anomalies. Approximately half of each litter was examined for visceral effects, and the other half underwent a skeletal examination.

Test compound-related maternal effects were observed in the 7 and 50 mg/kg dose groups. Gravid dams in the 50 mg/kg dose group demonstrated decreased body weight gain and food consumption, and decreased net body weight and net body weight change (subtraction of gravid uterus). Additionally observed at the high-dose were an increase in thyroid weight and a decrease in liver and kidney weight. Related to the affect on thyroid weight was an increase in TSH (thyroid stimulating hormone) and decreases in circulating T_3 and T_4 levels. Evidence of maternal toxicity in the 7 mg/kg dose group was limited to affected thyroid hormone levels, specifically, increased TSH levels and decreased T_4 levels. No maternal effects were observed in the 1 mg/kg dose group. There were no test-compound related effects on the gestation index, or any embryologic endpoints: pre/post-implantation loss and resorptions observed in any dose group. There were no statistically significant effects on litter size or the number of fetuses per implantation site. One test compound-related litter finding was observed in the 50 mg/kg dose group: a statistically significant decrease in fetal weight (male, female, and combined). Test compound-related fetal malformations and variations were observed in the 50 mg/kg dose group during both the external and visceral examinations. External anomalies were observed in all body regions. In contrast, visceral findings were limited to enlarged thyroids and cranial malformations. No effects on fetal external or visceral malformations or variations were observed in the 1 or 7 mg/kg dose groups. A statistically significant increase in fetal skeletal malformations was observed in the 50 mg/kg dose group. Malformations included abnormal radius, lordosis, and fetuses exhibiting multiple skeletal anomalies. Fetal skeletal variations were observed at all dose levels. The majority of the variations were statistically significantly increased in the highest dose level, however several findings were also significantly increased in the 1 and 7 mg/kg dose groups. The fetal skeletal variations observed in the 1 mg/kg dose group were not considered test compound-related as they were all within the range of historical controls for the individual findings. In contrast the incidence of many of the skeletal variations observed in the 7 mg/kg dose group fell outside the range of historical controls. As would be expected given the fetal observations, there was a significant increase in both the fetal and litter incidence of total malformations and variations observed at the highest dose. Also observed at this dose level was a significant difference in the incidence of malformations between males and females. No effects on the incidence of total malformations or variations, or any gender-related differences in fetal effects were observed in the 1 or 7 mg/kg dose groups.

Propylene thiourea, administered as described in this study, produced maternal toxicity at doses of 7 and 50 mg/kg body weight. The 1 mg/kg dose was free of test compound-related maternal effects. Developmental effects were observed in the 7 and 50 mg/kg dose groups. In the 50 mg/kg dose group, developmental effects included reduced fetal weight and increased external, visceral, and skeletal anomalies. In the 7 mg/kg dose group developmental effects were limited to skeletal variations. No test compound-related developmental effects were observed in the 1 mg/kg dose group and no embryotoxicity was observed at any dose level. Both the maternal and developmental no-observed-effect-levels (NOEL) were 1 mg/kg.

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TABLE 1

SUMMARY OF GESTATIONAL CLINICAL OBSERVATIONS

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF CLINICAL OBSERVATIONS DURING GESTATION

97-612-KR

	Dose Group			
	CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Number of Dams Evaluated	29	28	27	28
DAY 0 to 5				
NO REMARKABLE CLINICAL OBSERVATIONS	28	28	27	28
LACRIMATION	1	0	0	1
MALOCCLUSION UPPER INCISORS	1	0	0	1
ULCERATED HARD PALATE	1	0	0	0
HAIR THINNING	0	0	1	0
WOUNDS,CUTS,SCRATCHES,LACERAT.	1	0	0	0
URINE STAIN	0	1	0	0
DAY 6 to 20				
NO REMARKABLE CLINICAL OBSERVATIONS	28	28	27	28
NASAL STAIN	0	1	0	0
MALOCCLUSION UPPER INCISORS	1	0	0	1
ULCERATED HARD PALATE	1	0	0	0
HAIR THINNING	0	0	2	1
URINE STAIN	0	1	0	0

Includes only dams found pregnant at termination (day 20)
One animal may exhibit more than one sign.

Agriculture Division
Report Number
108018

TABLE 2

SUMMARY OF MATERNAL BODY WEIGHT CHANGE

24-SEP-1997 14:42

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF BODY WEIGHT CHANGES (GRAMS) DURING GESTATION

97-612-KR

	Dose Group											
	CONTROL 0 MG/KG			LEVEL I 1 MG/KG			LEVEL II 7 MG/KG			LEVEL III 50 MG/KG		
DAY	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N
0 TO 2	10.0	1.84	29	9.3	2.03	28	5.7	2.47	27	7.5	2.11	28
2 TO 4	6.8	1.42	29	7.7	1.86	28	12.0	2.14	27	7.6	1.70	28
4 TO 6	7.0	0.72	29	6.5	2.07	28	5.8	0.62	27	7.2	1.95	28
6 TO 7	1.8	0.62	29	1.6	1.08	28	-0.7	0.88	27	-3.3**	1.19	28
7 TO 8	2.5	0.55	29	1.9	0.82	28	2.4	0.82	27	2.2	0.83	28
8 TO 9	2.8	0.61	29	2.7	0.87	28	2.7	0.87	27	3.1	0.85	28
9 TO 10	4.0	0.80	29	3.9	0.63	28	3.2	1.28	27	5.5	0.74	28
10 TO 11	5.0	0.69	29	5.4	0.72	28	5.6	1.13	27	2.0	1.26	28
11 TO 12	1.7	1.19	29	2.7	0.67	28	3.0	0.77	27	2.9	1.70	28
12 TO 13	3.2	1.10	29	3.0	1.32	28	3.0	0.72	27	5.4	1.65	28
13 TO 14	4.6	1.12	29	2.3	1.53	28	5.8	0.79	27	3.0	0.88	28
14 TO 15	5.8	1.04	29	6.0	1.83	28	4.8	0.63	27	5.8	0.67	28
15 TO 16	8.7	1.79	29	8.9	1.21	28	7.8	0.92	27	10.4	0.87	28
16 TO 17	11.7	0.88	29	10.3	1.57	28	13.2	0.90	27	10.9	1.37	28
17 TO 18	13.7	1.08	29	14.0	1.69	28	13.4	0.85	27	14.4	1.33	28
18 TO 19	14.1	1.08	29	7.3	3.06	28	13.3	1.03	27	11.8	0.97	28
19 TO 20	16.5	0.84	29	15.0	3.63	28	14.2	1.00	27	10.0	1.10	28
0 TO 20	119.9	3.22	29	108.6	4.20	28	115.1	1.85	27	106.6**	2.89	28
6 TO 20	96.1	3.19	29	85.1	4.12	28	91.6	2.23	27	84.2*	3.00	28

Significantly Different from Control: * = $p<0.05$ ** = $p<0.01$
MEAN INCLUDES ONLY DAMS FOUND PREGNANT AT TERMINATION (DAY 20)

TABLE 3

SUMMARY OF FOOD CONSUMPTION DURING GESTATION

24-SEP-1997 14:45

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FOOD CONSUMPTION (GM/KG/DAY) DURING GESTATION

97-612-KR

	Dose Group											
	CONTROL 0 MG/KG			LEVEL I 1 MG/KG			LEVEL II 7 MG/KG			LEVEL III 50 MG/KG		
DAY	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N
0 - 2	75.0	1.81	29	68.6	2.57	28	70.2	2.70	27	71.3	2.45	28
2 - 4	76.4	1.64	29	77.2	2.77	28	80.7	1.54	27	78.0	2.64	28
4 - 6	80.5	1.19	29	78.6	1.96	28	79.4	1.54	27	84.0	2.88	28
6 - 7	77.8	1.43	29	71.6	1.70	28	69.9	2.27	27	76.4	22.02	28
7 - 8	75.9	1.27	29	71.2	1.84	28	71.4	1.99	27	64.4**	2.46	28
8 - 9	74.2	1.22	29	72.0	2.12	28	72.9	1.71	27	72.1	2.46	28
9 - 10	74.1	1.61	29	73.6	1.79	28	72.3	2.15	27	73.9	1.96	28
10 - 11	71.4	0.99	29	70.7	1.84	28	74.3	1.81	27	66.9	2.11	28
11 - 12	73.2	1.92	29	75.6	2.30	28	73.0	1.38	27	72.7	2.55	28
12 - 13	73.7	2.66	29	72.7	2.21	28	71.5	1.75	27	74.6	3.18	28
13 - 14	75.4	2.41	29	72.2	3.49	28	76.3	1.41	27	70.2	2.19	28
14 - 15	71.9	2.81	29	73.0	2.05	28	72.3	1.13	27	68.9	1.74	28
15 - 16	75.0	3.00	29	78.1	1.60	28	76.0	1.39	27	73.6	2.05	28
16 - 17	75.1	2.49	29	76.2	1.72	28	76.6	1.38	27	70.1	2.37	28
17 - 18	76.0	1.98	29	78.7	1.42	28	77.2	1.12	27	67.9**	1.64	28
18 - 19	76.9	1.78	29	69.6	2.96	28	72.7	1.63	27	61.3**	2.09	28
19 - 20	71.8	1.32	29	68.3	2.86	28	67.6	1.45	27	53.0**	2.11	28

Significantly Different from Control: ** = $p<0.01$
MEAN INCLUDES ONLY DAMS FOUND PREGNANT AT TERMINATION (DAY 20)

Bayer Corporation
97-612-KR
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TABLE 4

SUMMARY OF MATERNAL NECROPSY FINDINGS

24-SEP-1997 14:48

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF MATERNAL NECROPSY FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
DAMS	N	29	28	26	27
ESOPHAGUS	N	1	0	0	1
PERFORATION/WOUND	N	1	0	0	1
	%	3.4	0.0	0.0	3.7
THYROIDS	N	0	0	0	15
ENLARGED	N	0	0	0	15**
	%	0.0	0.0	0.0	55.6

Significantly Different from Control: ** = $p \leq 0.01$

TABLE 5

SUMMARY OF MATERNAL ORGAN WEIGHTS

13-OCT-1997 07:27

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF MATERNAL ORGAN WEIGHTS

97-612-KR

ORGAN WEIGHTS IN GRAMS

	Dose Group											
	CONTROL 0 MG/KG			LEVEL I 1 MG/KG			LEVEL II 7 MG/KG			LEVEL III 50 MG/KG		
	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N
FINAL BODY WEIGHT g	349	4.2	29	339	5.5	28	344	3.7	27	335	4.1	28
LIVER	13.564	0.2214	29	13.161	0.2824	28	13.033	0.1984	27	12.437**	0.2724	28
KIDNEYS	1.814	0.0340	29	1.773	0.0296	28	1.778	0.0291	27	1.654**	0.0264	28
THYROID	0.017	0.0005	29	0.017	0.0006	27	0.018	0.0006	27	0.028**	0.0010	28

Significantly Different from Control: ** = $p<0.01$
MEAN INCLUDES ONLY DAMS FOUND PREGNANT AT TERMINATION (DAY 20)

TABLE 6

SUMMARY OF MATERNAL ORGAN/BODY WEIGHT RATIOS

13-OCT-1997 07:27

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF MATERNAL ORGAN WEIGHT TO BODY WEIGHT RATIOS

97-612-KR

ORGAN WEIGHT TO BODY WEIGHT RATIO

	Dose Group											
	CONTROL 0 MG/KG			LEVEL I 1 MG/KG			LEVEL II 7 MG/KG			LEVEL III 50 MG/KG		
	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N	MEAN	S.E.	N
FINAL BODY WEIGHT g	349	4.2	29	339	5.5	28	344	3.7	27	335	4.1	28
LIVER	3.893	0.0558	29	3.878	0.0523	28	3.789	0.0563	27	3.708	0.0577	28
KIDNEYS	0.521	0.0097	29	0.524	0.0085	28	0.517	0.0073	27	0.494	0.0065	28
THYROID	0.005	0.0002	29	0.005	0.0002	27	0.005	0.0002	27	0.008**	0.0003	28

Significantly Different from Control: ** = $p<0.01$
MEAN INCLUDES ONLY DAMS FOUND PREGNANT AT TERMINATION (DAY 20)

TABLE 7

SUMMARY OF UTERINE AND NET BODY WEIGHTS

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF UTERINE AND NET BODY WEIGHTS (GRAMS)

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
GRAVID UTERUS	Mean	71.6	64.5	69.6	71.6
	S.E.	2.84	2.14	1.92	2.44
	N	29	28	27	28
NET WEIGHT	Mean	277.3	274.9	274.8	263.4**
	S.E.	2.73	4.64	2.50	2.86
	N	29	28	27	28
NET WEIGHT CHANGE FROM DAY 0	Mean	48.3	44.2	45.5	35.0**
	S.E.	1.99	3.17	1.22	2.48
	N	29	28	27	28

Significantly Different from Control: ** = $p \leq 0.01$

NET WEIGHT = DAY 20 BODY WEIGHT MINUS UTERINE WEIGHT
NET WEIGHT CHANGE FROM DAY 0 = NET WEIGHT MINUS DAY 0 BODY WEIGHT

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TABLE 8

SUMMARY OF
MATERNAL CLINICAL BIOCHEMISTRY DATA

SUMMARY OF MATERNAL CLINICAL BIOCHEMISTRY DATA

Group Means

		T3 ug/dl	T4 ng/ml	TSH ng/ml
CONTROL	Mean	0.49	1.48	11.08
	SD	0.15	0.37	3.14
	n	10	10	10
LEVEL I	Mean	0.50	1.31	11.71
	SD	0.08	0.29	2.27
	n	10	10	10
LEVEL II	Mean	0.51	1.01*	17.25$
	SD	0.11	0.27	5.63
	n	10	10	10
LEVEL III	Mean	0.20*	0.25*	43.49$
	SD	0.08	0.18	9.11
	n	10	10	10

Means include only dams found pregnant at termination.
Statistics: * = ANOVA + Dunnetts tests, two-sided ($p \leq 0.05$)
$ = Kruskal-Wallis ANOVA + Mann-Whitney U-Tests, two-sided ($p \leq 0.05$)

TABLE 9

SUMMARY OF REPRODUCTION/IMPLANTATION AND RESORPTION DATA

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF REPRODUCTION/IMPLANTATION/RESORPTION DATA

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Fertility Index		96.7	93.3	90.0	93.3
Gestation Index		100.0	100.0	100.0	100.0
Mating Index		100.0	100.0	100.0	100.0
Dams with Resorption Sites only		0	0	0	0
Dams with Viable Fetuses		29	28	27	28
Dams with Nonviable Fetuses		0	0	0	0
No. of Dams Found Dead		0	0	0	0
No. of Dams Sacrificed Moribund		0	0	0	0
No. of Dams which Aborted		0	0	0	0
Total No. of Corpora Lutea		418	389	377	392
	Mean	14.4	13.9	14.0	14.0
	S.E.	0.35	0.41	0.36	0.51
	Median	15	14	14	14
	Range	10-18	9-20	10-19	9-25
Total No. of Implantations		374	343	363	368
	Mean	12.9	12.3	13.4	13.1
	S.E.	0.39	0.39	0.33	0.49
	Median	13	13	14	13
	Range	8-18	7-14	10-18	9-23
Pre-implantation Loss	Total	44	46	16	24
No. per animal	Mean	1.5	1.6	0.6**	0.9*
	S.E.	0.24	0.49	0.18	0.24
% per animal	Mean	10.5	10.6	4.1	5.8
	S.E.	1.71	2.72	1.26	1.68
	Median	7	7	0*	0
	Range	0-33	0-60	0-23	0-36

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
Mating index = No. of animals sperm positive/No. of animals co-housed x 100
Fertility Index = No. of animals pregnant (with implants)/No. of animals sperm positive x 100
Gestation Index = No. of animals with viable progeny at termination (day 20)/No. of pregnant animals x 100
% Pre-implantation Loss = No. of corpora lutea minus no. of implantations/No. of corpora lutea x 100

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Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF REPRODUCTION/IMPLANTATION/RESORPTION DATA

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Post-implantation Loss	Total	21	25	27	20
No. per animal	Mean	0.7	0.9	1.0	0.7
	S.E.	0.19	0.18	0.18	0.16
% per animal	Mean%	6.4	7.2	7.5	5.1
	S.E.	2.20	1.36	1.44	1.08
	Median	7	8	7	4
	Range	0-63	0-29	0-25	0-17
Nonviable Fetuses	Total	0	0	0	0
No. per animal	Mean	0.0	0.0	0.0	0.0
	S.E.	0.00	0.00	0.00	0.00
% per animal	Mean%	0.0	0.0	0.0	0.0
	S.E.	0.00	0.00	0.00	0.00
Resorptions: Early+Late	Total	21	25	27	20
No. per animal	Mean	0.7	0.9	1.0	0.7
	S.E.	0.19	0.18	0.18	0.16
	Median	1	1	1	1
	Range	0-5	0-4	0-3	0-3
% per animal	Mean%	6.4	7.2	7.5	5.1
	S.E.	2.20	1.36	1.44	1.08
Resorptions: Early	Total	21	25	27	20
No. per animal	Mean	0.7	0.9	1.0	0.7
	S.E.	0.19	0.18	0.18	0.16
% per animal	Mean%	6.4	7.2	7.5	5.1
	S.E.	2.20	1.36	1.44	1.08
Resorptions: Late	Total	0	0	0	0
No. per animal	Mean	0.0	0.0	0.0	0.0
	S.E.	0.00	0.00	0.00	0.00
% per animal	Mean%	0.0	0.0	0.0	0.0
	S.E.	0.00	0.00	0.00	0.00

% Post-implantation Loss = No. of implantations minus no. of viable progeny/No. of implantations x 100

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TABLE 10

SUMMARY OF LITTER DATA

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF LITTER DATA

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
No. of Litters		29	28	27	28
Litter Size	Mean	12.2	11.4	12.4	12.4
	S.E.	0.49	0.38	0.36	0.43
	Median	12	12	13	12
	Range	3-18	6-14	9-16	9-20
Viable Fetuses	Total	353	318	336	348
No. per animal	Mean	12.2	11.4	12.4	12.4
	S.E.	0.49	0.38	0.36	0.43
#fetuses/#implants	Mean%	93.6	92.8	92.5	94.9
	S.E.	2.20	1.36	1.44	1.08
Males viable+nonviable	Total	187	154	165	162
No. per animal	Mean	6.4	5.5	6.1	5.8
	S.E.	0.45	0.43	0.34	0.35
#males/#implants	Mean%	49.4	44.5	45.8	44.5
	S.E.	2.80	2.98	2.52	2.69
Females viable+nonviable	Total	166	164	171	186
No. per animal	Mean	5.7	5.9	6.3	6.6
	S.E.	0.46	0.39	0.42	0.44
#females/#implants	Mean%	44.2	48.3	46.7	50.4
	S.E.	3.23	2.97	2.66	2.74
Total No. of Fetuses		353	318	336	348
No. of Viable Fetuses		353	318	336	348
% Viable		100	100	100	100
No. of Nonviable Fetuses		0	0	0	0
% Nonviable		0	0	0	0
Median Percent Male Fetuses		54	50	50	48
Mean Weight Fetuses (gm) (Male)		4.0	4.0	4.0	3.6**
	S.E.	0.05	0.06	0.04	0.07
(Female)		3.8	3.8	3.7	3.4**
	S.E.	0.05	0.07	0.03	0.06
(Combined)		3.9	3.9	3.9	3.5**
	S.E.	0.05	0.06	0.02	0.06
Wt. of Placentas (gm)	Mean	0.56	0.57	0.56	0.54
	S.E.	0.008	0.012	0.011	0.010

Significantly Different from Control: ** = $p \leq 0.01$

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TABLE 11

SUMMARY OF FETAL EXTERNAL MALFORMATIONS AND VARIATIONS

2-OCT-1997 07:14

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF EXTERNAL MALFORMATIONS AND VARIATIONS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
MALFORMATIONS					
Fetal Incidence	N	1	1	2	262**
	%	0.3	0.3	0.6	75.3
Litter Incidence	N	1	1	2	26**
	%	3.4	3.6	7.4	92.9
Fetuses/Litter	Mean%	0.29	0.45	0.54	76.10**
	S.E.	0.287	0.446	0.379	5.860
VARIATIONS					
Fetal Incidence	N	0	0	0	45**
	%	0.0	0.0	0.0	12.9
Litter Incidence	N	0	0	0	16**
	%	0.0	0.0	0.0	57.1
Fetuses/Litter	Mean%	0.00	0.00	0.00	12.38**
	S.E.	0.000	0.000	0.000	3.239

Significantly Different from Control: ** = $p \leq 0.01$

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TABLE 12

SUMMARY OF FETAL EXTERNAL FINDINGS

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
GROSS EXAM					
Litter Incidence	N	0	0	0	1
Fetal Incidence	N	0	0	0	12
M HYDROPS AMNII					
Fetal Incidence	N	0	0	0	12**
	%	0.0	0.0	0.0	3.4
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
HEAD/BRAIN/SKULL					
Litter Incidence	N	1	0	0	26
Fetal Incidence	N	1	0	0	193
M MENINGOCELE					
Fetal Incidence	N	0	0	0	63**
	%	0.0	0.0	0.0	18.1
Litter Incidence	N	0	0	0	11**
	%	0.0	0.0	0.0	39.3
V HEMATOMA					
Fetal Incidence	N	0	0	0	45**
	%	0.0	0.0	0.0	12.9
Litter Incidence	N	0	0	0	16**
	%	0.0	0.0	0.0	57.1

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

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2-OCT-1997 07:37

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M DOMED HEAD					
Fetal Incidence	N	1	0	0	99**
	%	0.3	0.0	0.0	28.4
Litter Incidence	N	1	0	0	24**
	%	3.4	0.0	0.0	85.7
M EXENCEPHALY					
Fetal Incidence	N	0	0	0	20**
	%	0.0	0.0	0.0	5.7
Litter Incidence	N	0	0	0	3
	%	0.0	0.0	0.0	10.7
M MISSHAPEN					
Fetal Incidence	N	0	0	0	8*
	%	0.0	0.0	0.0	2.3
Litter Incidence	N	0	0	0	3
	%	0.0	0.0	0.0	10.7
EYES					
Litter Incidence	N	0	0	0	4
Fetal Incidence	N	0	0	0	5

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

2-OCT-1997 07:37

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M NO EYE BULGE					
Fetal Incidence	N	0	0	0	5
	%	0.0	0.0	0.0	1.4
Litter Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	14.3
MOUTH/JAW/PALATE					
Litter Incidence	N	1	0	1	6
Fetal Incidence	N	1	0	1	26
M PROTRUDING TONGUE					
Fetal Incidence	N	1	0	0	10*
	%	0.3	0.0	0.0	2.9
Litter Incidence	N	1	0	0	4
	%	3.4	0.0	0.0	14.3
M CLEFT PALATE					
Fetal Incidence	N	0	0	0	21**
	%	0.0	0.0	0.0	6.0
Litter Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	14.3

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

2-OCT-1997 07:37

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M MICROGNATHIA					
Fetal Incidence	N	0	0	1	16**
	%	0.0	0.0	0.3	4.6
Litter Incidence	N	0	0	1	3
	%	0.0	0.0	3.7	10.7
TORSO					
Litter Incidence	N	0	0	0	11
Fetal Incidence	N	0	0	0	83
M ANASARCA					
Fetal Incidence	N	0	0	0	64**
	%	0.0	0.0	0.0	18.4
Litter Incidence	N	0	0	0	9**
	%	0.0	0.0	0.0	32.1
M ANAL IMPERFORATE					
Fetal Incidence	N	0	0	0	14**
	%	0.0	0.0	0.0	4.0
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

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Bayer Corporation
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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M ABSENCE OF ABDOM. MUSCULATURE NEAR UMBILICUS					
Fetal Incidence	N	0	0	0	19**
	%	0.0	0.0	0.0	5.5
Litter Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	14.3
APPENDAGES					
Litter Incidence	N	0	1	0	10
Fetal Incidence	N	0	1	0	57
M MALROTATION					
Fetal Incidence	N	0	0	0	57**
	%	0.0	0.0	0.0	16.4
Litter Incidence	N	0	0	0	10**
	%	0.0	0.0	0.0	35.7
M ADACTYLY					
Fetal Incidence	N	0	0	0	14**
	%	0.0	0.0	0.0	4.0
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M MALFORMED					
Fetal Incidence	N	0	0	0	5
	%	0.0	0.0	0.0	1.4
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1
M MICROMELIA					
Fetal Incidence	N	0	1	0	0
	%	0.0	0.3	0.0	0.0
Litter Incidence	N	0	1	0	0
	%	0.0	3.6	0.0	0.0
M SHORTENED DIGIT					
Fetal Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1
TAIL					
Litter Incidence	N	0	0	1	25
Fetal Incidence	N	0	0	1	211

FINDING CODE: M-MALFORMATION V-VARIATION

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Bayer Corporation
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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M KINKED					
Fetal Incidence	N	0	0	0	134**
	%	0.0	0.0	0.0	38.5
Litter Incidence	N	0	0	0	25**
	%	0.0	0.0	0.0	89.3
M CURLY					
Fetal Incidence	N	0	0	1	20**
	%	0.0	0.0	0.3	5.7
Litter Incidence	N	0	0	1	12**
	%	0.0	0.0	3.7	42.9
M SHORTENED					
Fetal Incidence	N	0	0	0	86**
	%	0.0	0.0	0.0	24.7
Litter Incidence	N	0	0	0	16**
	%	0.0	0.0	0.0	57.1
M ACAUDATE					
Fetal Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	1.1
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
Report Number
108018

2-OCT-1997 07:37

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL EXTERNAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
M CONSTRICTED					
Fetal Incidence	N	0	0	0	7*
	%	0.0	0.0	0.0	2.0
Litter Incidence	N	0	0	0	3
	%	0.0	0.0	0.0	10.7

Significantly Different from Control: * = $p \leq 0.05$
FINDING CODE: M-MALFORMATION V-VARIATION

TABLE 13

SUMMARY OF FETAL VISCERAL MALFORMATIONS AND VARIATIONS

13-OCT-1997 10:38

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF VISCERAL MALFORMATIONS AND VARIATIONS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	170	155	163	168
MALFORMATIONS					
Fetal Incidence	N	2	1	1	165**
	%	1.2	0.6	0.6	98.2
Litter Incidence	N	2	1	1	28**
	%	6.9	3.6	3.7	100.0
Fetuses/Litter	Mean%	1.26	0.60	0.62	98.21**
	S.E.	0.882	0.595	0.617	1.786
VARIATIONS					
Fetal Incidence	N	20	13	12	54**
	%	11.8	8.4	7.4	32.1
Litter Incidence	N	10	9	9	22**
	%	34.5	32.1	33.3	78.6
Fetuses/Litter	Mean%	10.96	8.25	6.72	30.37**
	S.E.	3.383	2.759	2.041	4.548

Significantly Different from Control: ** = $p \leq 0.01$

Bayer Corporation
97-612-KR

Agriculture Division
Report Number
108018

TABLE 14

SUMMARY OF FETAL VISCERAL FINDINGS

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL VISCERAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	170	155	163	168
NECK					
Litter Incidence	N	0	0	0	11
Fetal Incidence	N	0	0	0	18
M THYROID, ENLARGED					
Fetal Incidence	N	0	0	0	18**
	%	0.0	0.0	0.0	10.7
Litter Incidence	N	0	0	0	11**
	%	0.0	0.0	0.0	39.3
MAJOR VESSELS					
Litter Incidence	N	3	0	2	9
Fetal Incidence	N	3	0	2	11
V LEFT SIDED UMBILICAL ARTERY					
Fetal Incidence	N	2	0	2	11*
	%	1.2	0.0	1.2	6.5
Litter Incidence	N	2	0	2	9
	%	6.9	0.0	7.4	32.1
M MAJOR VESSELS, TRUNCUS ARTERIOSUS					
Fetal Incidence	N	1	0	0	0
	%	0.6	0.0	0.0	0.0
Litter Incidence	N	1	0	0	0
	%	3.4	0.0	0.0	0.0

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
Report Number
108018

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL VISCERAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	170	155	163	168
HEART					
Litter Incidence	N	2	1	0	2
Fetal Incidence	N	3	1	0	3
M VENTRICLE, SMALL					
Fetal Incidence	N	1	0	0	0
	%	0.6	0.0	0.0	0.0
Litter Incidence	N	1	0	0	0
	%	3.4	0.0	0.0	0.0
V SMALL					
Fetal Incidence	N	2	0	0	3
	%	1.2	0.0	0.0	1.8
Litter Incidence	N	1	0	0	2
	%	3.4	0.0	0.0	7.1
M ENLARGED AURICULAR APPENDAGE					
Fetal Incidence	N	0	1	0	0
	%	0.0	0.6	0.0	0.0
Litter Incidence	N	0	1	0	0
	%	0.0	3.6	0.0	0.0

FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
Report Number
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Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL VISCERAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	170	155	163	168
ABDOMEN					
Litter Incidence	N	1	0	0	0
Fetal Incidence	N	1	0	0	0
V LIVER, MOTTLED					
Fetal Incidence	N	1	0	0	0
	%	0.6	0.0	0.0	0.0
Litter Incidence	N	1	0	0	0
	%	3.4	0.0	0.0	0.0
URINARY					
Litter Incidence	N	9	9	7	23
Fetal Incidence	N	16	13	10	52
V HYDROURETER					
Fetal Incidence	N	16	13	10	46**
	%	9.4	8.4	6.1	27.4
Litter Incidence	N	9	9	7	21**
	%	31.0	32.1	25.9	75.0
V KIDNEY, DILATED PELVIS (PELVES)					
Fetal Incidence	N	2	1	0	8
	%	1.2	0.6	0.0	4.8
Litter Incidence	N	2	1	0	5
	%	6.9	3.6	0.0	17.9

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
Report Number
108018

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL VISCERAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	170	155	163	168
M URETER, AGENESIS					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
M KIDNEY, AGENESIS					
Fetal Incidence	N	0	0	0	5
	%	0.0	0.0	0.0	3.0
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1
M DUPLICATION, KIDNEY					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
WILSON TECHNIQUE					
Litter Incidence	N	0	0	1	28
Fetal Incidence	N	0	0	1	165

FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
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13-OCT-1997 10:38

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL VISCERAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	170	155	163	168
M BRAIN, DILATED VENTRICLES					
Fetal Incidence	N	0	0	0	151**
	%	0.0	0.0	0.0	89.9
Litter Incidence	N	0	0	0	26**
	%	0.0	0.0	0.0	92.9
M CLEFT PALATE					
Fetal Incidence	N	0	0	1	13**
	%	0.0	0.0	0.6	7.7
Litter Incidence	N	0	0	1	4
	%	0.0	0.0	3.7	14.3
M HYDROCEPHALUS					
Fetal Incidence	N	0	0	0	9**
	%	0.0	0.0	0.0	5.4
Litter Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	14.3
M MALFORMED BRAIN					
Fetal Incidence	N	0	0	0	28**
	%	0.0	0.0	0.0	16.7
Litter Incidence	N	0	0	0	7*
	%	0.0	0.0	0.0	25.0

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

TABLE 15

SUMMARY OF FETAL SKELETAL MALFORMATIONS AND VARIATIONS

13-OCT-1997 07:17

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF SKELETAL MALFORMATIONS AND VARIATIONS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
MALFORMATIONS					
Fetal Incidence	N	0	1	1	36**
	%	0.0	0.6	0.6	20.0
Litter Incidence	N	0	1	1	9**
	%	0.0	3.6	3.7	32.1
Fetuses/Litter	Mean%	0.00	0.71	0.62	20.03**
	S.E.	0.000	0.714	0.617	6.513
VARIATIONS					
Fetal Incidence	N	182	163	173	180
	%	99.5	100.0	100.0	100.0
Litter Incidence	N	29	28	27	28
	%	100.0	100.0	100.0	100.0
Fetuses/Litter	Mean%	99.43	100.00	100.00	100.00
	S.E.	0.575	0.000	0.000	0.000

Significantly Different from Control: ** = $p \leq 0.01$

Bayer Corporation
97-612-KR

Agriculture Division
Report Number
108018

TABLE 16

SUMMARY OF FETAL SKELETAL FINDINGS

13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
NASAL					
Litter Incidence	N	0	2	2	5
Fetal Incidence	N	0	2	2	6
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	2	2	6*
	%	0.0	1.2	1.2	3.3
Litter Incidence	N	0	2	2	5
	%	0.0	7.1	7.4	17.9
FRONTAL					
Litter Incidence	N	13	12	14	26
Fetal Incidence	N	18	17	20	105
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	18	17	20	105**
	%	9.8	10.4	11.6	58.3
Litter Incidence	N	13	12	14	26**
	%	44.8	42.9	51.9	92.9
PARIETAL					
Litter Incidence	N	6	13	17	27
Fetal Incidence	N	11	27	45	104

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	11	27**	45**	104**
	%	6.0	16.6	26.0	57.8
Litter Incidence	N	6	13	17**	27**
	%	20.7	46.4	63.0	96.4
INTERPARIETAL					
Litter Incidence	N	18	24	26	27
Fetal Incidence	N	50	96	125	139
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	50	96**	125**	139**
	%	27.3	58.9	72.3	77.2
Litter Incidence	N	18	24	26**	27**
	%	62.1	85.7	96.3	96.4
SUPRAOCCIPITAL					
Litter Incidence	N	15	23	21	27
Fetal Incidence	N	34	59	71	168
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	34	59**	71**	157**
	%	18.6	36.2	41.0	87.2
Litter Incidence	N	15	23	21	27**
	%	51.7	82.1	77.8	96.4

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
Report Number
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13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	0	0	11**
	%	0.0	0.0	0.0	6.1
Litter Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	14.3
TYMPANIC					
Litter Incidence	N	0	1	0	0
Fetal Incidence	N	0	1	0	0
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	1	0	0
	%	0.0	0.6	0.0	0.0
Litter Incidence	N	0	1	0	0
	%	0.0	3.6	0.0	0.0
SQUAMOSAL					
Litter Incidence	N	7	19	16	6
Fetal Incidence	N	11	27	44	6
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	11	27**	44**	6
	%	6.0	16.6	25.4	3.3
Litter Incidence	N	7	19**	16*	6
	%	24.1	67.9	59.3	21.4

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
ZYGOMA					
Litter Incidence	N	1	5	7	0
Fetal Incidence	N	2	6	13	0
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	2	6	13**	0
	%	1.1	3.7	7.5	0.0
Litter Incidence	N	1	5	7	0
	%	3.4	17.9	25.9	0.0
MAXILLA					
Litter Incidence	N	2	6	9	0
Fetal Incidence	N	2	7	15	0
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	2	7	15**	0
	%	1.1	4.3	8.7	0.0
Litter Incidence	N	2	6	9	0
	%	6.9	21.4	33.3	0.0
PREMAXILLA					
Litter Incidence	N	0	1	1	0
Fetal Incidence	N	0	1	1	0

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	1	1	0
	%	0.0	0.6	0.6	0.0
Litter Incidence	N	0	1	1	0
	%	0.0	3.6	3.7	0.0
MANDIBLE					
Litter Incidence	N	0	0	0	1
Fetal Incidence	N	0	0	0	2
M SHORTENED					
Fetal Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	1.1
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
HYOID BODY					
Litter Incidence	N	5	10	8	19
Fetal Incidence	N	8	19	16	42
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	8	14	12	31**
	%	4.4	8.6	6.9	17.2
Litter Incidence	N	5	9	7	17**
	%	17.2	32.1	25.9	60.7

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	5	4	11**
	%	0.0	3.1	2.3	6.1
Litter Incidence	N	0	3	2	8**
	%	0.0	10.7	7.4	28.6
PALATE					
Litter Incidence	N	0	0	0	1
Fetal Incidence	N	0	0	0	1
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
FRONTAL SUTURE					
Litter Incidence	N	1	1	2	1
Fetal Incidence	N	1	1	2	1
V ENLARGED					
Fetal Incidence	N	1	1	2	1
	%	0.5	0.6	1.2	0.6
Litter Incidence	N	1	1	2	1
	%	3.4	3.6	7.4	3.6

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
SAGITTAL SUTURE					
Litter Incidence	N	3	10	13	24
Fetal Incidence	N	4	16	28	117
V ENLARGED					
Fetal Incidence	N	4	16**	28**	117**
	%	2.2	9.8	16.2	65.0
Litter Incidence	N	3	10	13**	24**
	%	10.3	35.7	48.1	85.7
CORONAL SUTURE					
Litter Incidence	N	0	0	1	0
Fetal Incidence	N	0	0	1	0
V ENLARGED					
Fetal Incidence	N	0	0	1	0
	%	0.0	0.0	0.6	0.0
Litter Incidence	N	0	0	1	0
	%	0.0	0.0	3.7	0.0
ANTERIOR FONT					
Litter Incidence	N	13	14	17	26
Fetal Incidence	N	18	24	34	109

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V ENLARGED					
Fetal Incidence	N	18	24	34*	109**
	%	9.8	14.7	19.7	60.6
Litter Incidence	N	13	14	17	26**
	%	44.8	50.0	63.0	92.9
POSTERIOR FONT					
Litter Incidence	N	4	11	15	23
Fetal Incidence	N	7	20	36	100
V ENLARGED					
Fetal Incidence	N	7	20*	36**	100**
	%	3.8	12.3	20.8	55.6
Litter Incidence	N	4	11	15**	23**
	%	13.8	39.3	55.6	82.1
RIBS					
Litter Incidence	N	13	13	20	18
Fetal Incidence	N	26	21	37	46
V WAVY/CURVED					
Fetal Incidence	N	3	5	10	13*
	%	1.6	3.1	5.8	7.2
Litter Incidence	N	2	4	7	8
	%	6.9	14.3	25.9	28.6

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
Report Number
108018

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V THICKENED					
Fetal Incidence	N	0	1	0	2
	%	0.0	0.6	0.0	1.1
Litter Incidence	N	0	1	0	2
	%	0.0	3.6	0.0	7.1
V SMALL					
Fetal Incidence	N	0	0	2	11**
	%	0.0	0.0	1.2	6.1
Litter Incidence	N	0	0	2	6*
	%	0.0	0.0	7.4	21.4
V OSSIFICATION CENTER					
Fetal Incidence	N	20	15	26	27
	%	10.9	9.2	15.0	15.0
Litter Incidence	N	11	11	16	11
	%	37.9	39.3	59.3	39.3
V EXTRA					
Fetal Incidence	N	0	0	1	1
	%	0.0	0.0	0.6	0.6
Litter Incidence	N	0	0	1	1
	%	0.0	0.0	3.7	3.6

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
M FUSED					
Fetal Incidence	N	0	0	0	5
	%	0.0	0.0	0.0	2.8
Litter Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	14.3
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	2	3	3
	%	0.0	1.2	1.7	1.7
Litter Incidence	N	0	2	2	3
	%	0.0	7.1	7.4	10.7
V RUDIMENTARY					
Fetal Incidence	N	5	2	3	4
	%	2.7	1.2	1.7	2.2
Litter Incidence	N	3	2	3	3
	%	10.3	7.1	11.1	10.7
M MISSING					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6

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Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

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		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
THORACIC ARCHES					
Litter Incidence	N	0	0	1	1
Fetal Incidence	N	0	0	1	1
M EXTRA					
Fetal Incidence	N	0	0	1	0
	%	0.0	0.0	0.6	0.0
Litter Incidence	N	0	0	1	0
	%	0.0	0.0	3.7	0.0
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6

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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
THORACIC CENTRA					
Litter Incidence	N	24	26	26	27
Fetal Incidence	N	67	80	100	166
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	65	77	98**	164**
	%	35.5	47.2	56.6	91.1
Litter Incidence	N	24	26	26	27
	%	82.8	92.9	96.3	96.4
V BIPARTITE					
Fetal Incidence	N	2	8	13**	65**
	%	1.1	4.9	7.5	36.1
Litter Incidence	N	2	6	10*	23**
	%	6.9	21.4	37.0	82.1
M EXTRA					
Fetal Incidence	N	0	0	1	0
	%	0.0	0.0	0.6	0.0
Litter Incidence	N	0	0	1	0
	%	0.0	0.0	3.7	0.0

Significantly Different from Control: * = $p \leq 0.05$ ** = $p \leq 0.01$
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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	1	0	1
	%	0.0	0.6	0.0	0.6
Litter Incidence	N	0	1	0	1
	%	0.0	3.6	0.0	3.6
LUMBAR ARCHES					
Litter Incidence	N	1	3	0	15
Fetal Incidence	N	1	3	0	51
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	1	2	0	51**
	%	0.5	1.2	0.0	28.3
Litter Incidence	N	1	2	0	15**
	%	3.4	7.1	0.0	53.6
V UNOSSIFIED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6

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A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

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		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
M UNALIGNED					
Fetal Incidence	N	0	1	0	0
	%	0.0	0.6	0.0	0.0
Litter Incidence	N	0	1	0	0
	%	0.0	3.6	0.0	0.0
LUMBAR CENTRA					
Litter Incidence	N	1	4	7	21
Fetal Incidence	N	1	4	11	67
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	1	4	10*	66**
	%	0.5	2.5	5.8	36.7
Litter Incidence	N	1	4	7	21**
	%	3.4	14.3	25.9	75.0
V BIPARTITE					
Fetal Incidence	N	0	0	1	9**
	%	0.0	0.0	0.6	5.0
Litter Incidence	N	0	0	1	6*
	%	0.0	0.0	3.7	21.4

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
M FUSED					
Fetal Incidence	N	0	0	0	4
	%	0.0	0.0	0.0	2.2
Litter Incidence	N	0	0	0	3
	%	0.0	0.0	0.0	10.7
V UNOSSIFIED					
Fetal Incidence	N	0	2	0	3
	%	0.0	1.2	0.0	1.7
Litter Incidence	N	0	2	0	2
	%	0.0	7.1	0.0	7.1
SACRAL ARCHES					
Litter Incidence	N	28	25	25	27
Fetal Incidence	N	116	92	86	156
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	116	92	86*	156**
	%	63.4	56.4	49.7	86.7
Litter Incidence	N	28	25	25	27
	%	96.6	89.3	92.6	96.4

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Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

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		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	1	0	5
	%	0.0	0.6	0.0	2.8
Litter Incidence	N	0	1	0	4
	%	0.0	3.6	0.0	14.3
M UNALIGNED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
SACRAL CENTRA					
Litter Incidence	N	0	2	1	15
Fetal Incidence	N	0	2	1	54
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	1	1	49**
	%	0.0	0.6	0.6	27.2
Litter Incidence	N	0	1	1	15**
	%	0.0	3.6	3.7	53.6

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		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	2	0	26**
	%	0.0	1.2	0.0	14.4
Litter Incidence	N	0	2	0	9**
	%	0.0	7.1	0.0	32.1
CAUDAL ARCHES					
Litter Incidence	N	29	27	27	27
Fetal Incidence	N	118	114	126	164
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	94	101	106	84
	%	51.4	62.0	61.3	46.7
Litter Incidence	N	29	27	27	26
	%	100.0	96.4	100.0	92.9
V UNOSSIFIED					
Fetal Incidence	N	43	37	37	149**
	%	23.5	22.7	21.4	82.8
Litter Incidence	N	17	19	20	27**
	%	58.6	67.9	74.1	96.4

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SUMMARY OF FETAL SKELETAL FINDINGS

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		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
CAUDAL CENTRA					
Litter Incidence	N	0	2	1	24
Fetal Incidence	N	0	2	1	124
V UNOSSIFIED					
Fetal Incidence	N	0	2	1	111**
	%	0.0	1.2	0.6	61.7
Litter Incidence	N	0	2	1	22**
	%	0.0	7.1	3.7	78.6
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	0	1	27**
	%	0.0	0.0	0.6	15.0
Litter Incidence	N	0	0	1	12**
	%	0.0	0.0	3.7	42.9
ISCHIUMS					
Litter Incidence	N	0	1	0	2
Fetal Incidence	N	0	1	0	2
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	1	0	2
	%	0.0	0.6	0.0	1.1
Litter Incidence	N	0	1	0	2
	%	0.0	3.6	0.0	7.1

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
PUBIS					
Litter Incidence	N	1	1	0	14
Fetal Incidence	N	1	1	0	41
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	1	1	0	41**
	%	0.5	0.6	0.0	22.8
Litter Incidence	N	1	1	0	14**
	%	3.4	3.6	0.0	50.0
RADIUS					
Litter Incidence	N	0	0	0	2
Fetal Incidence	N	0	0	0	6
M ABNORMAL					
Fetal Incidence	N	0	0	0	6*
	%	0.0	0.0	0.0	3.3
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1
METACARPALS					
Litter Incidence	N	14	16	15	27
Fetal Incidence	N	32	36	37	163

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SUMMARY OF FETAL SKELETAL FINDINGS

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		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	31	36	37	163**
	%	16.9	22.1	21.4	90.6
Litter Incidence	N	13	16	15	27**
	%	44.8	57.1	55.6	96.4
V UNOSSIFIED					
Fetal Incidence	N	1	2	1	9*
	%	0.5	1.2	0.6	5.0
Litter Incidence	N	1	2	1	4
	%	3.4	7.1	3.7	14.3
M FUSED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
ANT. PHALANGES					
Litter Incidence	N	0	0	0	1
Fetal Incidence	N	0	0	0	1

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	0.6
Litter Incidence	N	0	0	0	1
	%	0.0	0.0	0.0	3.6
FEMUR					
Litter Incidence	N	0	0	0	5
Fetal Incidence	N	0	0	0	16
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	0	0	0	16**
	%	0.0	0.0	0.0	8.9
Litter Incidence	N	0	0	0	5
	%	0.0	0.0	0.0	17.9
METATARSALS					
Litter Incidence	N	1	1	1	4
Fetal Incidence	N	1	1	1	16
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	1	1	1	16**
	%	0.5	0.6	0.6	8.9
Litter Incidence	N	1	1	1	4
	%	3.4	3.6	3.7	14.3

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
MANUBRIUM					
Litter Incidence	N	12	11	16	27
Fetal Incidence	N	27	21	30	152
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	27	20	30	149**
	%	14.8	12.3	17.3	82.8
Litter Incidence	N	12	10	16	27**
	%	41.4	35.7	59.3	96.4
V BIPARTITE					
Fetal Incidence	N	0	1	1	0
	%	0.0	0.6	0.6	0.0
Litter Incidence	N	0	1	1	0
	%	0.0	3.6	3.7	0.0
V UNOSSIFIED					
Fetal Incidence	N	0	1	0	3
	%	0.0	0.6	0.0	1.7
Litter Incidence	N	0	1	0	3
	%	0.0	3.6	0.0	10.7

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
STERNEBRAE-SEG 2					
Litter Incidence	N	19	22	22	27
Fetal Incidence	N	44	53	63	162
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	43	51	62*	136**
	%	23.5	31.3	35.8	75.6
Litter Incidence	N	19	20	22	27*
	%	65.5	71.4	81.5	96.4
V UNOSSIFIED					
Fetal Incidence	N	1	2	1	26**
	%	0.5	1.2	0.6	14.4
Litter Incidence	N	1	2	1	17**
	%	3.4	7.1	3.7	60.7
V ASYMMETRICAL					
Fetal Incidence	N	0	1	0	0
	%	0.0	0.6	0.0	0.0
Litter Incidence	N	0	1	0	0
	%	0.0	3.6	0.0	0.0

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
STERNEBRAE-SEG 3					
Litter Incidence	N	19	21	21	26
Fetal Incidence	N	39	34	44	149
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	39	33	44	148**
	%	21.3	20.2	25.4	82.2
Litter Incidence	N	19	20	21	26
	%	65.5	71.4	77.8	92.9
V ASYMMETRICAL					
Fetal Incidence	N	1	2	0	4
	%	0.5	1.2	0.0	2.2
Litter Incidence	N	1	2	0	4
	%	3.4	7.1	0.0	14.3
V BIPARTITE					
Fetal Incidence	N	0	1	0	3
	%	0.0	0.6	0.0	1.7
Litter Incidence	N	0	1	0	3
	%	0.0	3.6	0.0	10.7

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	0	1	0	0
	%	0.0	0.6	0.0	0.0
Litter Incidence	N	0	1	0	0
	%	0.0	3.6	0.0	0.0
STERNEBRAE-SEG 4					
Litter Incidence	N	24	26	23	27
Fetal Incidence	N	67	66	69	154
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	65	65	68	151**
	%	35.5	39.9	39.3	83.9
Litter Incidence	N	24	25	23	27
	%	82.8	89.3	85.2	96.4
V UNOSSIFIED					
Fetal Incidence	N	1	1	1	1
	%	0.5	0.6	0.6	0.6
Litter Incidence	N	1	1	1	1
	%	3.4	3.6	3.7	3.6

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SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V ASYMMETRICAL					
Fetal Incidence	N	1	3	2	7
	%	0.5	1.8	1.2	3.9
Litter Incidence	N	1	3	2	5
	%	3.4	10.7	7.4	17.9
V BIPARTITE					
Fetal Incidence	N	1	2	0	5
	%	0.5	1.2	0.0	2.8
Litter Incidence	N	1	2	0	4
	%	3.4	7.1	0.0	14.3
STERNEBRAE-SEG 5					
Litter Incidence	N	29	28	27	27
Fetal Incidence	N	174	160	160	169
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	153	144	146	156
	%	83.6	88.3	84.4	86.7
Litter Incidence	N	28	28	27	27
	%	96.6	100.0	100.0	96.4

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97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V UNOSSIFIED					
Fetal Incidence	N	21	16	14	12
	%	11.5	9.8	8.1	6.7
Litter Incidence	N	13	12	7	7
	%	44.8	42.9	25.9	25.0
V ASYMMETRICAL					
Fetal Incidence	N	0	1	1	2
	%	0.0	0.6	0.6	1.1
Litter Incidence	N	0	1	1	2
	%	0.0	3.6	3.7	7.1
V BIPARTITE					
Fetal Incidence	N	0	0	1	5
	%	0.0	0.0	0.6	2.8
Litter Incidence	N	0	0	1	4
	%	0.0	0.0	3.7	14.3
XIPHOID					
Litter Incidence	N	29	27	27	27
Fetal Incidence	N	105	107	113	157

FINDING CODE: M-MALFORMATION V-VARIATION

Agriculture Division
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13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
V INCOMPLETELY OSSIFIED					
Fetal Incidence	N	102	104	109	155**
	%	55.7	63.8	63.0	86.1
Litter Incidence	N	29	27	27	27
	%	100.0	96.4	100.0	96.4
V UNOSSIFIED					
Fetal Incidence	N	3	3	4	2
	%	1.6	1.8	2.3	1.1
Litter Incidence	N	3	3	3	1
	%	10.3	10.7	11.1	3.6
GENERAL					
Litter Incidence	N	0	0	0	7
Fetal Incidence	N	0	0	0	25
M LORDOSIS					
Fetal Incidence	N	0	0	0	15**
	%	0.0	0.0	0.0	8.3
Litter Incidence	N	0	0	0	5
	%	0.0	0.0	0.0	17.9

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
M MULTIPLE MALFORMATIONS					
Fetal Incidence	N	0	0	0	10**
	%	0.0	0.0	0.0	5.6
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1
V MULTIPLE VARIATIONS					
Fetal Incidence	N	0	0	0	10**
	%	0.0	0.0	0.0	5.6
Litter Incidence	N	0	0	0	2
	%	0.0	0.0	0.0	7.1
LAMBOIDAL SUTURE					
Litter Incidence	N	0	0	1	1
Fetal Incidence	N	0	0	1	2
V ENLARGED					
Fetal Incidence	N	0	0	1	2
	%	0.0	0.0	0.6	1.1
Litter Incidence	N	0	0	1	1
	%	0.0	0.0	3.7	3.6

Significantly Different from Control: ** = $p \leq 0.01$
FINDING CODE: M-MALFORMATION V-VARIATION

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13-OCT-1997 07:16

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF FETAL SKELETAL FINDINGS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	183	163	173	180
SQUAMOSAL SUTURE					
Litter Incidence	N	2	5	6	0
Fetal Incidence	N	4	6	16	0
V ENLARGED					
Fetal Incidence	N	4	6	16*	0
	%	2.2	3.7	9.2	0.0
Litter Incidence	N	2	5	6	0
	%	6.9	17.9	22.2	0.0

Significantly Different from Control: * = $p \leq 0.05$
FINDING CODE: M-MALFORMATION V-VARIATION

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TABLE 17

SUMMARY OF FETAL EXTERNAL, VISCERAL AND SKELETAL MALFORMATIONS AND VARIATIONS

13-OCT-1997 10:39

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF EXTERNAL, VISCERAL AND SKELETAL MALFORMATIONS AND VARIATIONS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Viable Fetuses					
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
MALFORMATIONS					
Fetal Incidence	N	3	3	3	301**
	%	0.8	0.9	0.9	86.5
Litter Incidence	N	3	3	2	28**
	%	10.3	10.7	7.4	100.0
Fetuses/Litter	Mean%	0.90	1.10	0.85	86.74**
	S.E.	0.503	0.621	0.651	3.663
VARIATIONS					
Fetal Incidence	N	202	176	185	251**
	%	57.2	55.3	55.1	72.1
Litter Incidence	N	29	28	27	28
	%	100.0	100.0	100.0	100.0
Fetuses/Litter	Mean%	57.21	55.24	54.96	71.33**
	S.E.	1.566	1.431	0.980	2.561
Malformed and Nonviable Fetuses					
Litters Evaluated	N	29	28	27	28
Fetuses Evaluated	N	353	318	336	348
TOTAL AFFECTED FETUSES					
Fetal Incidence	N	3	3	3	301**
	%	0.8	0.9	0.9	86.5
Litter Incidence	N	3	3	2	28**
	%	10.3	10.7	7.4	100.0
Fetuses/Litter	Mean%	0.90	1.10	0.85	86.74**
	S.E.	0.503	0.621	0.651	3.663

Significantly Different from Control: ** = $p \leq 0.01$

TABLE 18

SUMMARY OF MALE/FEMALE MALFORMATIONS

13-OCT-1997 10:37

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF MALE/FEMALE MALFORMATIONS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Males Evaluated	N	187	154	165	162
Females Evaluated	N	166	164	171	186
TOTAL MALFORMATIONS					
Male Incidence	N	2	0	0	131*
	%	1.1	0.0	0.0	80.9
Female Incidence	N	1	3	3	170
	%	0.6	1.8	1.8	91.4
Affected Males/Litter(a)	Mean%	1.15	0.00	0.00	83.45
	S.E.	0.798	0.000	0.000	4.459
Affected Females/Litter(a)	Mean%	0.43	2.12	1.89	91.00
	S.E.	0.431	1.208	1.522	3.155
TOTAL EXTERNAL MALFORMATIONS					
Male Incidence	N	1	0	0	110*
	%	0.5	0.0	0.0	67.9
Female Incidence	N	0	1	2	152
	%	0.0	0.6	1.2	81.7
Affected Males/Litter(a)	Mean%	0.57	0.00	0.00	71.90
	S.E.	0.575	0.000	0.000	6.480
Affected Females/Litter(a)	Mean%	0.00	0.89	1.15	81.24
	S.E.	0.000	0.893	0.833	5.524

Significantly Different from Female Incidence: $p<0.05$
(a) = Affected Males or Females/ # Males or Females Examined/ Litter
TABLE INCLUDES ONLY DATA FROM VIABLE FETUSES

Bayer Corporation
97-612-KR

A Developmental Toxicity Study with Propylene Thiourea in the
Sprague-Dawley Rat
SUMMARY OF MALE/FEMALE MALFORMATIONS

97-612-KR

		Dose Group			
		CONTROL 0 MG/KG	LEVEL I 1 MG/KG	LEVEL II 7 MG/KG	LEVEL III 50 MG/KG
Litters Evaluated	N	29	28	27	28
Males Evaluated	N	90	80	82	75
Females Evaluated	N	80	75	81	93
TOTAL VISCERAL MALFORMATIONS					
Male Incidence	N	1	0	0	73
	%	1.1	0.0	0.0	97.3
Female Incidence	N	1	1	1	92
	%	1.3	1.3	1.2	98.9
Affected Males/Litter(a)	Mean%	1.23	0.00	0.00	96.15
	S.E.	1.235	0.000	0.000	3.846
Affected Females/Litter(a)	Mean%	0.93	0.60	1.85	99.11
	S.E.	0.926	0.595	1.852	0.893
Litters Evaluated	N	29	28	27	28
Males Evaluated	N	97	74	83	87
Females Evaluated	N	86	89	90	93
TOTAL SKELETAL MALFORMATIONS					
Male Incidence	N	0	0	0	15
	%	0.0	0.0	0.0	17.2
Female Incidence	N	0	1	1	21
	%	0.0	1.1	1.1	22.6
Affected Males/Litter(a)	Mean%	0.00	0.00	0.00	21.43
	S.E.	0.000	0.000	0.000	6.632
Affected Females/Litter(a)	Mean%	0.00	0.89	1.28	20.31
	S.E.	0.000	0.893	1.282	7.280

TABLE INCLUDES ONLY DATA FROM VIABLE FETUSES

(a)=Affected Males or Females/ # Males or Females Examined/ Litter

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FIGURE 1

COMPARISON OF THE MEAN GESTATIONAL BODY WEIGHT BETWEEN DOSAGE GROUPS

FIGURE 2

COMPARISON OF THE MALE, FEMALE, AND COMBINED MEAN FETAL BODY WEIGHT BETWEEN DOSAGE GROUPS