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December 22, 1993

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OFFICE OF POLLUTION
PREVENTION AND TOXICS
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Attention: Section 8(e) Coordinator

Dear Sir/Madam:

Enclosed you will find a final report of a rat teratology study with Santovar A Antioxidant - 2,5-di(tert-amyl) hydroquinone (CAS Nc. 79-74-3). I sent a copy of the draft report for this study on December 7, 1992.

The assigned 8(e) Docket Number is 8E HQ-92-8589 and the Reference Number is TS-9252.

Although these findings are not considered to be indicative of substantial risk, we are providing the results in order to satisfy any reporting obligations that the Agency may consider necessary.

Sincerely,

Ronald D. Hogue, Ph.D.
Manager, Product Safety

Enclosure

325 pgs.

0003

Springborn Laboratories, Inc.
Life Sciences Division

SB-91-433

553 North Broadway • Spencerville, Ohio 45887 • (419) 647-4196 • Telex 4430041 • Facsimile 419-647-0580

ASTER FILE
PROJECT NO.

SB-91-433

TERATOLOGY STUDY IN RATS
WITH SANTOVAR A

FINAL REPORT

Author

Dean E. Rodwell, M.S.

Study Completed on

December 18, 1992

Performing Laboratory

Springborn Laboratories, Inc. (SLS)
Life Sciences Division
553 North Broadway
Spencerville, OH 45887

SLS Study No.

3044.230

Client Study No.

SB-91-433

Submitted to:

Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63167

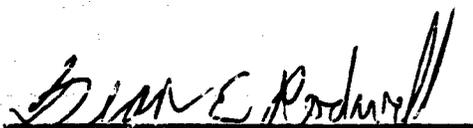
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SLS Study No. 3044.230
Monanto Study No. SB-91-433

(2)

COMPLIANCE STATEMENT

This study was conducted in compliance with the Environmental Protection Agency Good Laboratory Practice regulations (40 CFR Part 792) and SLS's Standard Operating Procedures.



Dean E. Rodwell, M.S.
Study Director/Author
Springborn Laboratories, Inc.

Date

12/18/92

SLS Study No. 3044.230
Monsanto Study No. SB-91-433

(3)

QUALITY ASSURANCE STATEMENT

This study was inspected by the Quality Assurance Unit and reports were submitted to management and the study director in accordance with SLS's Standard Operating Procedures as follows:

<u>Phase</u>	<u>Date</u>
Animal Receipt	10/31/91
Mating/Pairing	11/11/91
Evidence of Mating and Group Assignment	11/12/91
Dose Preparation	11/18/91
Dose Concentration Analysis	11/18/91
Dosing	11/18/91
Cesarean Section	12/02/91
Food Consumption	12/04/91
Body Weights	12/04/91
Fetal Skeletal Examinations	02/27/92
Fetal Visceral Examinations	02/27/92
Data Audits	03/27/92, 03/30/92, 03/31/92, 04/01/92, 04/10/92, 04/13/92
Draft Report Review	11/19/92
Final Report Review	12/18/92
Reports Submitted to Study Director and Management	11/12/91, 11/18/91, 02/03/92, 03/26/92, 06/01/92, 11/17/92, 11/19/92, 12/18/92

This study was conducted in compliance with Good Laboratory Practice regulations as described by the EPA (40 CFR Part 792) and SLS's Standard Operating Procedures.

Anita M. Bosau
Anita M. Bosau, Director
Quality Assurance Unit

Date 12/18/92

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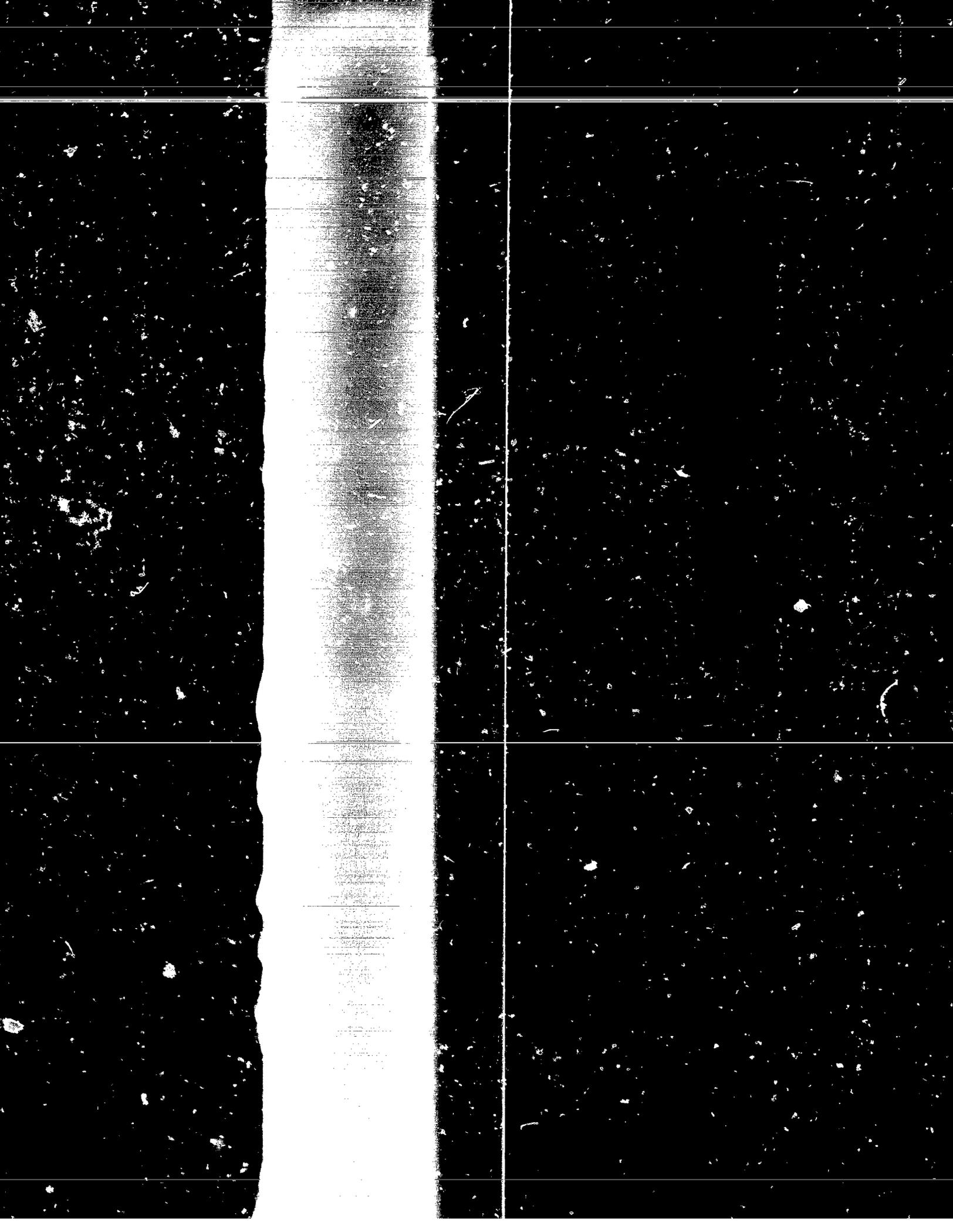
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SUMMARY

This study was performed to detect and evaluate the potential embryotoxic or teratogenic effects of Santovar A when administered orally to pregnant rats during the period of major organogenesis. The study design consisted of a vehicle control and three treatment groups. Each group contained twenty-five mated female Sprague-Dawley rats. The test article was mixed with corn oil and administered at dosage levels of 20.0, 70.0 and 175.0 mg/kg/day from gestation day 6 through gestation day 15. All doses were given at a constant volume of 5 ml/kg. Control animals were administered corn oil under the same experimental conditions and at an equivalent dose volume. The animals were observed daily for clinical signs of toxicity. Body weights and food consumption were measured on gestation days 0, 6, 9, 12, 16 and 20. All females were euthanized on gestation day 20 and subjected to cesarean section. Fetuses were individually weighed, sexed and examined for external, visceral and skeletal abnormalities.

Oral administration of Santovar A produced slight maternal toxicity at the 70.0 mg/kg/day level and substantial maternal toxicity at the 175.0 mg/kg/day level. The toxicity was characterized by an increase in the incidence of reddish colored vaginal discharge and post-dose salivation at the 70.0 mg/kg/day level and more frequent and severe clinical signs, body weight loss and reduced food consumption at the 175.0 mg/kg/day level. No adverse clinical signs were observed in the 20.0 mg/kg/day group. Similarly, no treatment-related differences in mean body weights, body weight gain or food consumption were observed at the 20.0 or 70.0 mg/kg/day levels. Mean fetal body weight was slightly, but statistically reduced at the 175.0 mg/kg/day level when compared to the control group. All other cesarean section parameters were comparable among the groups. No apparent treatment-related malformations or developmental variations were observed at the 20.0 or 70.0 mg/kg/day levels. Slight, nonstatistical increases in the incidence of skull anomalies and 7th cervical ribs were observed in the 175.0 mg/kg/day group. The number of litters with sternbrae #5 and/or #6 unossified was also statistically increased at this level when compared to the control group. The number of litters in the control group with unossified sternbrae in this study is unusually low when compared to SLS historical control data. Therefore, it is not clear if the increase in the number of litters with sternbrae #5 and/or #6 unossified at the 175.0 mg/kg/day level in this study was spontaneous or associated with the reduced fetal body weights observed at this level.

Based on the results of this study, a dosage level of 20.0 mg/kg/day was considered a no-observed-effect level (NOEL) for maternal toxicity and a dosage level of 70.0 mg/kg/day was considered a NOEL for developmental toxicity. Santovar A at a dosage level of 175.0 mg/kg/day produced substantial maternal toxicity with minimal developmental toxicity.



I. INTRODUCTION

This report details experimental procedures and results of a teratology study in rats treated with Santovar A. This study was performed to detect and evaluate the potential embryotoxic or teratogenic effects of the test article when administered orally to pregnant rats during the period of major organogenesis. The study was authorized by Monsanto Company, St. Louis, MO, and was conducted at the facilities of Springborn Laboratories, Inc. (SLS), Spencerville, OH. The Sprague-Dawley rat was selected as the animal model for this study based on its susceptibility to teratogens, availability of historical control data, and recommendation by the regulatory agencies. The in-life phase of the study was initiated with the assignment of mated female rats to study groups on November 12, 1991 (gestation day 0) and concluded with terminal sacrifice on December 5, 1991 (gestation day 20).

II. MATERIALS AND METHODS

A. Experimental Protocol

The study protocol and protocol amendments are presented in Appendix A.

B. Test and Control Articles

1. Test Article Receipt, Identification and Storage

The test article was received from the Sponsor and identified as follows:

<u>Sponsor's ID</u>	<u>Assigned SLS ID</u>	<u>Physical Description</u>	<u>Receipt Date</u>	<u>Expiration Date</u>
Santovar A Milled#1 Lot No. NOA027	S91.022.3044	White Powder	8/09/91	6/92

A reserve 1 g sample of the test article was taken and stored at SLS. The reserve sample and bulk compound were stored at room temperature. The purity of the test article was 98%. Documentation concerning chemical identification, purity, strength, stability and test article characterization was the responsibility of the Sponsor.

2. Test Control (Vehicle) Receipt and Identification

The control article used in the preparation of dosing mixtures and for administration to control animals was Mazola® corn oil. The corn oil was used as received from Best Foods, Englewood Cliffs, NJ, and identified as follows:

<u>Lot Number</u>	<u>Assigned SLS ID</u>	<u>Receipt Date</u>	<u>Expiration Date</u>
JUL1592A	V91.026	8/22/91	7/15/92

3. Preparation of Dosing Mixtures

A specified amount of the test article for each dose group was weighed into a calibrated beaker. A sufficient amount of corn oil was added to each beaker to achieve the desired concentration and the mixtures were stirred for 45 minutes. The test article was not adjusted for purity. The mixtures were prepared fresh weekly, dispensed into daily aliquots and stored refrigerated. During each weekly preparation, an appropriate amount of corn oil was also dispensed into daily aliquots for administration to control animals and stored refrigerated. Daily aliquots were stirred for 10 minutes prior to dispensation and continuously during dosing.

4. Stability, Homogeneity and Concentration Analyses

Prior to study initiation, a modified version of the analytical method provided by the Sponsor was validated at SLS. Prestudy homogeneity and stability analyses were performed on concentrations of the test article which encompassed those used in this study. In addition, each fresh preparation of the dosing mixtures was analyzed for verification of test article concentration. Analytical methodology is described in detail in the Analytical Chemistry Report which is presented in Appendix B.

C. Animals and Animal Husbandry

Animal housing and care were based on the standards established by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and the guidelines set forth in the Guide for the Care and Use of Laboratory Animals, NIH Publication No. 86-23, 1985.

1. Animal Receipt, Identification and Housing

One hundred and thirty-two female Sprague-Dawley CrI:CD® BR VAF/Plus® rats were received at SLS on October 31, 1991, from Charles River Laboratories, Inc., Portage, MI. At the time of receipt, each rat was identified with a metal ear tag

displaying a unique number. Animals were housed individually during acclimation and while on study (except during cohabitation) in suspended stainless steel cages.

2. Acclimation

Animals were examined upon receipt and daily thereafter during acclimation for signs of physical or behavioral abnormalities. Only healthy animals were maintained for possible assignment to the study. Mortality checks were performed twice daily, in the morning and afternoon. Individual body weights were measured on the day following receipt and just prior to cohabitation for mating. The females were acclimated to the laboratory environment for a period of 11 days prior to cohabitation.

3. Diet and Drinking Water

Purina Certified Rodent Meal #5002 and municipal tap water were provided to each animal ad libitum. The feed was analyzed by the supplier for nutritional components and environmental contaminants. The lot number and expiration date of each batch of food used during the study was recorded. The tap water was purified by reverse osmosis or deionization (backup purification system) and supplied to the animals by an automatic watering system. Water supplying the facility is analyzed on an annual basis for contaminants according to SLS Standard Operating Procedures. The results of the food and water analyses are maintained at SLS.

4. Environmental Conditions

Animals were housed throughout the study in an environment-controlled room with a 12-hour light/12-hour dark cycle. The controls were set to maintain a room temperature of 64-79°F and a relative humidity of 40-70%. The animal room temperature and relative humidity were measured and recorded a minimum of once daily. On one occasion, the animal room relative humidity was outside the specified range by -4%. This occurrence was not considered to have had an impact on the outcome of the study.

D. Experimental Design

1. Mating and Group Assignment

At the conclusion of the acclimation period, the animals were weighed and examined. Females determined to be suitable test subjects, based on age, healthy appearance, and body weight, were cohabitated with resident Sprague-Dawley

Crl:CD® BR VAF/Plus® male rats. At the initiation of breeding, all females were approximately 12 weeks of age with body weights ranging from 227-271 g. Evidence of mating was determined by the presence of a copulatory plug in the vagina or a sperm positive vaginal smear. The day evidence of copulation was confirmed was designated as day 0 of gestation. At that time, the female rats were assigned consecutively, in a block design, to study groups.

2. Study Group Design

The following table presents the study group design and dosage levels tested:

Group	Number of Females	Dosage Material	Dosage Level (mg/kg/day)	Dosage Conc. (mg/ml)	Dosage Volume (ml/kg)
1	25	Corn Oil	0.0	0.0	5
2	25	Santovar A	20.0	4.0	5
3	25	Santovar A	70.0	14.0	5
4	25	Santovar A	175.0	35.0	5

3. Treatment

Dosing preparations were administered orally, by gavage, as a single dose daily from gestation day 6 through gestation day 15. Individual doses were calculated using the most recent body weight data. Oral administration of the test article was selected since this is a potential route of human exposure.

E. Parameters Evaluated

1. Clinical Observations

During the experimental period, all animals were observed daily for clinical signs of toxicity, including physical or behavioral abnormalities. Mortality checks were performed twice daily, in the morning and afternoon. In addition, during the treatment period, the rats were observed for toxic effects between one-half hour and two hours following dosing.

2. Body Weights

Individual body weights were measured on gestation days 0, 6, 9, 12, 16, and 20. Body weight changes were calculated for the following gestation intervals: 0-6, 6-9, 9-12, 12-16, 16-20, 6-16, and 0-20.

3. Food Consumption

Individual food consumption was measured during gestation days 0-6, 6-9, 0-12, 12-16 and 16-20. Food consumption was calculated and reported as grams/animal/day and grams/kg/day.

4. Scheduled Euthanasia and Cesarean Section

All females were euthanized on gestation day 20 by carbon dioxide inhalation and subjected to a morphological examination. The thoracic, abdominal and pelvic cavities were opened and the viscera examined. Abnormalities were recorded and representative tissue samples from internal lesions were preserved in 10% neutral buffered formalin for possible histological examination.

The uterus was removed from the body, examined externally, weighed and then opened for an internal examination. The number of viable and nonviable fetuses and early and late resorptions was recorded beginning with the left distal uterine horn, noting the position of the cervix, and continuing with the right uterine horn. Corpora lutea were counted and recorded for each ovary. Uteri with no macroscopic evidence of implantation were opened and placed in 10% aqueous ammonium sulfide solution for detection of early embryoletality as described by Salowski [1].

5. Fetal Morphological Observations

Fetuses were examined for external, internal (visceral) and skeletal abnormalities. Findings were classified based upon the severity of the anatomical change(s) and their potential for interference with organ and/or body function(s).

a. External Examination

Each fetus was examined for the occurrence of external abnormalities. The sex of each fetus was determined. The fetuses were then weighed and tagged individually. The tags displayed the study, dam and fetus numbers, as well as the fixative designation. The crown-rump length of each late resorption (evidence of autolysis) was measured and the tissue was discarded.

b. Visceral Examination

Approximately one-half of the fetuses were fixed in Bouin's solution for subsequent examination of visceral abnormalities using a technique described by Wilson [2]. The examination was performed using a low power microscope.

c. Skeletal Examination

Approximately one-half of the fetuses were fixed in 95% isopropyl alcohol. Following fixation, the fetuses were macerated in 1-2% aqueous potassium hydroxide solution, stained with Alizarin Red S, and cleared in glycerin [3]. Subsequent skeletal examination was performed using a low power microscope.

III. STATISTICAL ANALYSES

Continuous maternal and fetal data, including body weights, body weight gain, food consumption, number of fetuses, implantation sites and corpora lutea, were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's test [4]. The Mann-Whitney U test was used to compare post-implantation loss and resorptions [5]. Fetal sex ratios were analyzed using the Chi-Square test [6]. Fisher's Exact test was used to analyze the incidence and number of fetal malformations and variations utilizing the dam (litter) as the experimental unit [7]. All analyses were two-tailed with a minimum significance level of 5%.

IV. MAINTENANCE OF RAW DATA, RECORDS AND SPECIMENS

Following completion of the in-life phase of the study, the remaining test article(s) were returned to the Sponsor. All original paper data, the final report, magnetically encoded records, wet tissues and fetal specimens will be stored in the SLS archives. The Sponsor will be consulted prior to final disposition of these items.

V. RESULTS

A. Analytical Chemistry Evaluations

Appendix B (Analytical Chemistry Report)

Prestudy analytical chemistry evaluations indicated that Santovar A was homogeneous and stable in corn oil for up to eight days when stored refrigerated. Analysis of dosing preparations resulted in average test article recoveries ranging from 99.2 to 103.0% indicating that the mixtures were accurately prepared.

SLS Study No. 3044.230 (15)
Monsanto Study No. SB-91-433

B. Maternal Survival and Pregnancy Status

Table 1 (Summary Data)

All females in the control and Sartovar A treatment groups survived to scheduled euthanasia on gestation day 20. The pregnancy rate was 92% in the control and 175.0 mg/kg/day groups, and 96% in the 20.0 and 70.0 mg/kg/day groups.

C. Clinical Observations

**Table 2 (Summary Data)
Appendix C (Individual Data)**

No adverse clinical signs of toxicity were observed at the 20.0 mg/kg/day level. A low incidence of scabbing, hairloss, reddish colored vaginal discharge, and dark material was noted at the 20.0 mg/kg/day level, however, similar findings were observed in the control group. At the 70.0 mg/kg/day level, an increased incidence of reddish colored vaginal discharge and post-dose salivation were observed. More frequent and severe clinical signs were observed at the 175.0 mg/kg/day level. These findings included mucoid stools, soft stools, few feces, fecal stain, urine stain, rough coat, unkempt appearance, lacrimation, ocular discharge, dark material around the eyes, nose and/or mouth, wobbly gait, tail discoloration, tail necrosis, and post-dose salivation.

D. Body Weights and Weight Gain

**Tables 3 and 4 (Summary Data)
Appendices D and E (Individual Data)**

With the exception of an incidental statistical increase in mean body weight at the 70.0 mg/kg/day level on gestation day 9, mean maternal body weights and body weight gain were comparable between the control, 20.0 and 70.0 mg/kg/day groups throughout the study. At the 175.0 mg/kg/day level, statistically significant body weight loss occurred during gestation days 6-9 and reduced body weight gain was observed during gestation days 12-16, 6-16 and 0-20. The body weight loss at the 175.0 mg/kg/day level during gestation days 6-9 resulted in a statistically lower group mean body weight on gestation day 9 when compared to the control group. Subsequent mean body weights at the 175.0 mg/kg/day level were, however, comparable to the control group on gestation days 12, 16 and 20 due to a significant increase in body weight gain during gestation days 9-12.

Net maternal body weights and body weight gain (adjusted for gravid uterus weight) were comparable between the control, 20.0 and 70.0 mg/kg/day groups and statistically reduced at the 175.0 mg/kg/day level when compared to the control group.

E. Food Consumption

Tables 5 and 6 (Summary Data)
Appendices F and G (Individual Data)

Food consumption was similar between the control, 20.0 and 70.0 mg/kg/day groups throughout the study, with the following exceptions. Incidental statistical increases in food consumption occurred at the 70.0 mg/kg/day level during gestation days 16-20 and 0-20 when calculated as grams/animal/day and during gestation days 16-20 when calculated as grams/kg/day.

Food consumption calculated as grams/animal/day and grams/kg/day was statistically lower than the control group at the 175.0 mg/kg/day level during gestation days 6-9, 12-16, 6-16 and 0-20. Following the cessation of dosing (gestation days 16-20), food consumption at the 175.0 mg/kg/day level was statistically increased when compared to the control group.

F. Maternal Necropsy Observations

Table 7 (Summary Data)
Appendix H (Individual Data)

No remarkable internal gross abnormalities were observed at necropsy. Tail necrosis was observed externally in two females of the 175.0 mg/kg/day group.

G. Cesarean Section Observations

Table 8 (Summary Data)
Appendices I, J and K (Individual Data)

Mean fetal body weight was slightly, but statistically decreased at the 175.0 mg/kg/day level when compared to the control group. All other cesarean section parameters, including the mean number of corpora lutea, implantation sites, viable fetuses, early resorptions, post-implantation loss, fetal sex ratios and gravid uterus weights, were comparable between the control and Santovar A treatment groups.

II. Fetal Morphological Observations

Tables 9 and 10 (Summary Data)
Appendices L, M and N (Individual Data)
Appendix O (Historical Control Data)

The total number of litters with malformations were comparable among the groups and the observed malformations were generally dissimilar between the groups. The total number of fetuses with malformations, however, was increased at the 70.0 mg/kg/day level due to one litter (#1160) in which 7/15 fetuses were observed to have multiple head anomalies (exencephaly with open eyelids, absent cranium, micrognathia and facial cleft). Since these malformations occurred in only one litter and similar changes were not observed at the 175.0 mg/kg/day level, the occurrence was not considered to be indicative of a treatment-related response. At the 175.0 mg/kg/day level, 4/185 fetuses (3 fetuses from dam #1037 and one fetus from dam #1055) were observed to have skull anomalies (involving the exoccipital) during skeletal examinations.

An increase in the number of fetuses/litters with 7th cervical ribs occurred at the 175.0 mg/kg/day level. In addition, a statistically significant increase in the number of litters with sternbra(e) #5 and/or #6 unossified was observed at the 175.0 mg/kg/day level. The increase in unossified sternbrae corresponded to a decrease in fetal body weights at this level. The incidence of other developmental variations was comparable among the groups.

VI. DISCUSSION

The potential embryotoxic and teratogenic effects of Santovar A were evaluated in this definitive teratology study in rats at dosage levels of 20.0, 70.0 and 175.0 mg/kg/day.

No mortality occurred during the study. Oral administration of Santovar A did, however, produce slight maternal toxicity at the 70.0 mg/kg/day level and substantial maternal toxicity at the 175.0 mg/kg/day level. The toxicity was characterized by an increase in the incidence of reddish colored vaginal discharge and post-dose salivation at the 70.0 mg/kg/day level and more frequent and severe clinical signs, body weight loss and reduced food consumption at the 175.0 mg/kg/day level. No adverse clinical signs were observed in the 20.0 mg/kg/day group. Similarly, no treatment-related differences in mean body weights, body weight gain or food consumption were observed at the 20.0 or 70.0 mg/kg/day levels. Mean fetal body weight was slightly, but statistically

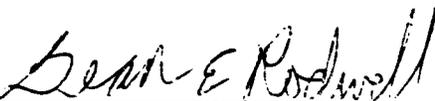
SLS Study No. 3044.230
Monsanto Study No. SB-91-433

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reduced at the 175.0 mg/kg/day level when compared to the control group. All other cesarean section parameters were comparable among the groups. No apparent treatment-related malformations or developmental variations were observed at the 20.0 or 70.0 mg/kg/day levels. The total number of fetuses with malformations was increased at the 70.0 mg/kg/day level due to one litter in which 7/15 fetuses were observed to have multiple head anomalies. This occurrence was not considered to be treatment related since the malformations were observed in only one litter and a similar change was not observed at the 175.0 mg/kg/day level. Slight, nonstatistical increases in the incidence of skull anomalies and 7th cervical ribs were observed in the 175.0 mg/kg/day group. The number of litters with sternbra(e) #5 and/or #6 unossified was also statistically increased at this level when compared to the control group. The number of litters in the control group with unossified sternbrae in this study is unusually low when compared to SLS historical control data. Therefore, it is not clear if the increase in the number of litters with sternbra(e) #5 and/or #6 unossified at the 175.0 mg/kg/day level in this study was spontaneous or associated with the reduced fetal body weights observed at this level.

VII. CONCLUSION

Based on the results of this study, a dosage level of 20.0 mg/kg/day was considered a no-observed-effect level (NOEL) for maternal toxicity and a dosage level of 70.0 mg/kg/day was considered a NOEL for developmental toxicity. Santovar A at a dosage level of 175.0 mg/kg/day produced substantial maternal toxicity with minimal developmental toxicity.



Dean E. Rodwell, M.S.
Study Director

Date

12/18/92

SLS Study No. 3044.230
Monsanto Study No. SB-91-433

(19)

VIII. REPORT REVIEW

Michael D. Mercieca

Michael D. Mercieca, B.S.
Toxicologist

Date 12/18/92

Joseph C. Siglin

Joseph C. Siglin, M.S., DABT
Associate Director of Toxicology

Date 12/18/92

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TABLE 1
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF SURVIVAL AND PREGNANCY

SLS STUDY NO.: 3044 230
 CLIENT: MORISANTO
 CLIENT NO.: SB-91-433

GROUP : LEVEL :	1 0.0 MG/KG/DAY		2 20.0 MG/KG/DAY		3 70.0 MG/KG/DAY		4 175.0 MG/KG/DAY	
	NO.	%	NO.	%	NO.	%	NO.	%
FEMALES ON STUDY	25		25		25		25	
FEMALES EXAMINED AT SCHEDULED NECROPSY	25	100.0	25	100.0	25	100.0	25	100.0
NONGRAVID	2	8.0	1	4.0	1	4.0	2	8.0
GRAVID	23	92.0	24	96.0	24	96.0	23	92.0
WITH RESORPTIONS ONLY	0	0.0	0	0.0	0	0.0	0	0.0
WITH VIABLE FETUSES	23	100.0	24	100.0	24	100.0	23	100.0
TOTAL FEMALES GRAVID	23	92.0	24	96.0	24	96.0	23	92.0

(21)

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 2
 REPRODUCTION STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF CLINICAL OBSERVATIONS (OCCURRENCE/ANIMALS AFFECTED)

----- F E M A L E -----

	TABLE RANGE:			
	GROUP:	GESTATION DAYS	0 - 20	
LEVEL (MG/KG/DAY):	1	2	3	4
	0.0	20.0	70.0	175.0
NORMAL				
-NO CLINICAL SIGNS	441/ 25	459/ 25	465/ 25	228/ 25
DEAD				
-SCHEDULED EUTHANASIA	25/ 25	25/ 25	25/ 25	25/ 25
ACTIVITY				
-WOBBLY GAIT	0/ 0	0/ 0	0/ 0	6/ 4
EXCRETA/EMESIS				
-MUCOID STOOLS	0/ 0	0/ 0	0/ 0	31/ 17
-SOFT STOOLS	0/ 0	0/ 0	0/ 0	5/ 5
-PEW FECES	0/ 0	0/ 0	0/ 0	9/ 9
-REDDISH COLORED VAGINAL DISCHARGE	4/ 4	7/ 6	21/ 14	33/ 15
BODY				
-SCAB(S) - MOUTH AREA	0/ 0	0/ 0	6/ 2	2/ 1
-SCAB(S) - VENTRAL NECK	0/ 0	3/ 1	0/ 0	0/ 0
-SCAB(S) - MID DORSAL	0/ 0	0/ 0	2/ 1	0/ 0
-SCAB(S) - RIGHT PINNA	11/ 1	0/ 0	0/ 0	0/ 0
-SCAB(S) - RIGHT HIP	7/ 1	0/ 0	0/ 0	0/ 0
-SCAB(S) - LEFT SHOULDER	0/ 0	1/ 1	0/ 0	0/ 0
-SCAB(S) - LEFT FORELIMB	0/ 0	0/ 0	0/ 0	2/ 1
-SWELLING - LEFT HINDLIMB	0/ 0	3/ 1	0/ 0	0/ 0
-SWELLING - RIGHT HINDLIMB	0/ 0	3/ 1	0/ 0	0/ 0
-TAIL DISCOLORATION	0/ 0	0/ 0	0/ 0	13/ 2
-DISCOLORATION - LEFT HINDLIMB	0/ 0	3/ 1	0/ 0	0/ 0
-DISCOLORATION - RIGHT HINDLIMB	0/ 0	3/ 1	0/ 0	0/ 0
-URINE STAIN	0/ 0	1/ 1	0/ 0	114/ 25
-FECAL STAIN	0/ 0	0/ 0	0/ 0	149/ 24

NOTE: DATA REFLECT THE TOTAL OCCURRENCE OF EACH CLINICAL FINDING OVER THE NUMBER OF ANIMALS EXHIBITING THE FINDING.

TABLE 2
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF CLINICAL OBSERVATIONS (OCCURRENCE/ANIMALS AFFECTED)

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

----- F E M A L E -----

	TABLE RANGE:		GESTATION DAYS		3	4
	GROUP:	LEVEL (HG/KG/DAY):	0 - 20	20.0		
BODY					70.0	175.0
-ROUGH COAT	0/ 0		0/ 0		0/ 0	217/ 25
-UNUSUAL APPEARANCE	0/ 0		0/ 0		0/ 0	7/ 6
-OPEN LESION - RIGHT PINNA	2/ 1		0/ 0		0/ 0	0/ 0
-TAIL NECROSIS	0/ 0		0/ 0		0/ 0	3/ 2
HAIRLOSS						
-NOSE AREA	0/ 0		0/ 0		0/ 0	1/ 1
-AROUND RIGHT EYE	0/ 0		0/ 0		0/ 0	4/ 1
-VENTRAL THORACIC	0/ 0		0/ 0		0/ 0	5/ 2
-LEFT FORELIMB	39/ 4		39/ 7		32/ 2	14/ 3
-RIGHT FORELIMB	23/ 3		46/ 7		32/ 2	20/ 2
-LEFT HINDLIMB	12/ 1		0/ 0		0/ 0	5/ 1
-RIGHT HINDLIMB	0/ 0		0/ 0		0/ 0	5/ 1
-LEFT LATERAL ABDOMINAL	16/ 1		0/ 0		0/ 0	2/ 1
-RIGHT LATERAL ABDOMINAL	0/ 0		9/ 1		0/ 0	2/ 1
-ABDOMINAL REGION	1/ 1		0/ 0		0/ 0	17/ 2
-UROGENITAL AREA	0/ 0		0/ 0		0/ 0	21/ 4
EYES						
-LACRIMATION	0/ 0		2/ 1		3/ 2	5/ 5
-DARK MATERIAL AROUND EYE(S)	0/ 0		0/ 0		0/ 0	118/ 23
-OCULAR DISCHARGE - RED	0/ 0		0/ 0		0/ 0	2/ 2
-OCULAR DISCHARGE - CLEAR	0/ 0		0/ 0		0/ 0	1/ 1
-EYE LID: PARTIALLY CLOSED	0/ 0		0/ 0		0/ 0	32/ 14
NOSE/MOUTH						
-DARK MATERIAL AROUND NOSE	1/ 1		4/ 1		1/ 1	62/ 22
-DARK MATERIAL AROUND MOUTH	0/ 0		0/ 0		0/ 0	36/ 18

NOTE: DATA REFLECT THE TOTAL OCCURRENCE OF EACH CLINICAL FINDING OVER THE NUMBER OF ANIMALS EXHIBITING THE FINDING.

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 2
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF CLINICAL OBSERVATIONS (OCCURRENCE/ANIMALS AFFECTED)

PAGE 3

----- F E M A L E -----

POST-DOSE OBSERVATIONS	TABLE RANGE:		GESTATION DAYS 0 - 20		4
	GROUP:	LEVEL (MG/KG/DAY):	1	2	
-SALIVATION		0/ 0	0/ 0	0/ 0	18/ 9
-MUCOID STOOLS		0/ 0	0/ 0	0/ 0	0/ 0
-SOFT STOOLS		0/ 0	0/ 0	0/ 0	1/ 1
-FECAL STAIN		1/ 1	C/ 0	C/ 0	2/ 2
-REDDISH VAGINAL DISCHARGE		0/ 0	0/ 0	0/ 0	1/ 1
			20.0	70.0	175.0

NOTE: DATA REFLECT THE TOTAL OCCURRENCE OF EACH CLINICAL FINDING OVER THE NUMBER OF ANIMALS EXHIBITING THE FINDING.

SLS STUDY NO.: 3044 230
 CLIENT: MORGANTO
 CLIENT NO.: SB-91-433

TABLE 3
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF GESTATION BODY WEIGHT DATA (GRAMS)

GROUP : LEVEL :	1 0.0 MG/KG/DAY		2 20.0 MG/KG/DAY		3 70.0 MG/KG/DAY		4 175.0 MG/KG/DAY	
	MEAN	S.D. N	MEAN	S.D. N	MEAN	S.D. N	MEAN	S.D. N
DAY 0	248	11.5 23	249	8.0 24	252	9.0 24	251	11.9 23
DAY 6	286	13.8 23	287	12.5 24	291	12.5 24	287	14.5 23
DAY 9	298	15.3 23	304	12.3 24	311*	14.6 24	276**	19.6 23
DAY 12	318	15.8 23	322	14.5 24	328	17.6 24	315	14.7 23
DAY 16	352	19.6 23	357	15.2 24	362	19.3 24	341	13.3 23
DAY 20	429	24.7 23	438	19.7 24	439	29.2 24	412	20.3 23
DAY 20 (CORRECTED)	340	18.7 23	343	18.6 24	348	18.5 24	322**	16.1 23

(25)

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05; ** = P<0.01
 NOTE: CORRECTED BODY WEIGHT EQUALS DAY 20 BODY WEIGHT MINUS GRAVID UTERUS WEIGHT.

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 4
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF GESTATION BODY WEIGHT GAIN DATA (GRAMS)

GROUP :	1	2	3	4
LEVEL :	0.0 MG/KG/DAY	20.0 MG/KG/DAY	70.0 MG/KG/DAY	175.0 MG/KG/DAY
DAY 0- 6 MEAN	37	38	39	37
S.D.	7.4	7.3	6.4	7.2
N	23	24	24	23
DAY 6- 9 MEAN	13	17	20	-11**
S.D.	6.5	5.7	5.0	19.6
N	23	24	24	23
DAY 9- 12 MEAN	20	19	18	39**
S.D.	5.1	5.7	7.6	12.9
N	23	24	24	23
DAY 12- 16 MEAN	33	35	34	26*
S.D.	8.7	8.9	11.1	9.4
N	23	24	24	23
DAY 16- 20 MEAN	77	81	77	70
S.D.	10.5	8.4	13.0	12.3
N	23	24	24	23
DAY 6- 16 MEAN	66	70	71	54**
S.D.	8.7	8.7	11.1	13.9
N	23	24	24	23
DAY 0- 20 MEAN	180	189	187	161**
S.D.	20.8	15.5	23.7	15.3
N	23	24	24	23
DAY 0- 20 MEAN (CORRECTED)	92	94	96	72**
S.D.	14.8	14.2	12.6	10.9
N	23	24	24	23

(26)

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05; ** = P<0.01
 NOTE: CORRECTED BODY WEIGHT EQUALS DAY 0-29 BODY WEIGHT GAIN MINUS GRAVID UTERUS WEIGHT.

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 5
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF GESTATION FOOD CONSUMPTION DATA (GRAMS/ANIMAL/DAY)

GROUP : LEVEL :	1 0.0 MG/KG/DAY	2 20.0 MG/KG/DAY	3 70.0 MG/KG/DAY	4 175.0 MG/KG/DAY
DAY 0- 6 MEAN	25	25	26	25
S.D.	2.1	2.5	2.2	2.2
N	23	24	24	23
DAY 6- 9 MEAN	21	21	21	9**
S.D.	3.0	2.0	2.8	3.9
N	23	24	24	23
DAY 9- 12 MEAN	23	23	24	23
S.D.	2.4	1.8	3.3	3.7
N	23	24	24	23
DAY 12- 16 MEAN	25	25	26	21**
S.D.	2.8	2.4	2.9	4.1
N	23	24	24	23
DAY 16- 20 MEAN	30	31	33**	32**
S.D.	2.5	2.8	2.1	2.9
N	23	24	24	23
DAY 6- 16 MEAN	23	23	24	18**
S.D.	2.4	1.7	2.3	3.3
N	23	24	24	23
DAY 0- 20 MEAN	25	25	26*	23**
S.D.	2.2	1.8	2.0	2.0
N	23	24	24	23

(27)

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P < 0.05; ** = P < 0.01

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 6
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF GESTATION FOOD CONSUMPTION DATA (GRAMS/KG/DAY)

GROUP : LEVEL :	1 0.0 MG/KG/DAY	2 20.0 MG/KG/DAY	3 70.0 MG/KG/DAY	4 175.0 MG/KG/DAY
DAY 0- 6 MEAN	94	93	95	94
S.D.	6.2	8.1	6.0	6.7
N	23	24	24	23
DAY 6- 9 MEAN	70	71	70	32**
S.D.	8.0	6.0	7.2	13.7
N	23	24	24	23
DAY 9- 12 MEAN	73	74	74	76
S.D.	5.2	4.7	8.6	11.2
N	23	24	24	23
DAY 12- 16 MEAN	74	74	75	64**
S.D.	5.2	5.9	7.2	12.1
N	23	24	24	23
DAY 16- 20 MEAN	76	79	83**	85**
S.D.	3.9	5.1	3.7	6.4
N	23	24	24	23
DAY 6- 16 MEAN	73	73	73	59**
S.D.	4.9	4.2	4.5	10.0
N	23	24	24	23
DAY 0- 20 MEAN	77	78	79	73**
S.D.	4.2	3.8	3.3	5.3
N	23	24	24	23

(28)

SIGNIFICANTLY DIFFERENT FROM CONTROL: ** - P<0.01

SLS STUDY NO.: 3044 230
 CLIENT: HONSANTO
 CLIENT NO.: SB-91-433

TABLE 7
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF MATERNAL NECROPSY OBSERVATIONS

SCHEDULED EUTHANASIA - GESTATION DAY 20

NUMBER EXAMINED AT SCHEDULED EUTHANASIA	GROUP:			
	1	2	3	4
LEVEL (MG/KG/IMY):	0.0	20.0	70.0	175.0
NO SIGNIFICANT CHANGES OBSERVED	25	25	25	25
NON GRAVID -- AMMONIUM SULFIDE NEGATIVE	17	16	22	15
HAIRLOSS	2	1	1	2
SKIN - SCABBING	4	6	2	7
TAIL - NECROSIS	2	1	0	1
UTERUS - CLEAR YELLOW-GREEN FLUID CONTENTS	0	0	0	2
KIDNEY(S) - DILATED PELVIS	0	1	0	0
ABDOMINAL CAVITY - ADHESION	0	1	0	0
HINDLIMB(S) - SWOLLEN	0	1	0	0
DARK MATERIAL AROUND NOSE	0	1	0	0
SPLEEN - ADHESION	0	1	0	0
SPLEEN - ENLARGED	0	1	0	0
SPLEEN - TAN NODULE(S)	0	1	0	0
LIVER - TANNISH-WHITE AREA(S)	0	1	0	0
ADRENAL(S) - ENLARGED	0	1	0	0

TABLE 8
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF CESAREAN SECTION DATA

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

	GROUP :			
	1 0.0 MG/KG/DAY	2 20.0 MG/KG/DAY	3 70.0 MG/KG/DAY	4 175.0 MG/KG/DAY
FEMALES GRAVID	23	24	24	23
CORPORA LUTEA	TOTAL 402 MEAN 17.5 S.D. 2.7	426 17.8 2.1	427 17.8 2.5	425 18.5 3.4
IMPLANTATION SITES	TOTAL 375 MEAN 16.3 S.D. 1.5	414 17.3 2.2	381 15.9 3.8	384 16.7 2.3
PRE-IMPLANTATION LOSS	TOTAL 27 MEAN 1.2 S.D. 2.1	12 0.5 0.8	46 1.9 2.7	41 1.8 3.4
VIALBE FETUSES	TOTAL 347 MEAN 15.1 S.D. 2.8	396 16.5 1.9	362 15.1 4.0	365 15.9 2.2
DEAD FETUSES	TOTAL 0	0	0	0
LATE RESORPTIONS	TOTAL 0 MEAN 0.0 S.D. 0.0	1 0.0 0.2	1 0.0 0.2	1 0.0 0.2
EARLY RESORPTIONS	TOTAL 28 MEAN 1.2 S.D. 2.1	17 0.7 0.9	18 0.8 1.2	18 0.8 1.2
POST-IMPLANTATION LOSS	TOTAL 28 MEAN 1.2 S.D. 2.1	18 0.8 0.9	19 0.8 1.1	19 0.8 1.3

NONE SIGNIFICANTLY DIFFERENT FROM CONTROL

SLS STUDY NO.: 3044 230
 CLIENT: MINSANTO
 CLIENT NO.: SB-91-433

TABLE 8
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF CESAREAN SECTION DATA

SEX M / F	GROUP : LEVEL :			
	1 0.0 MG/KG/DAY	2 20.0 MG/KG/DAY	3 70.0 MG/KG/DAY	4 175.0 MG/KG/DAY
TOTAL	180 167	193 203	173 189	179 186
MEAN	7.8 7.3	8.0 8.5	7.2 7.9	7.8 8.1
S.D.	2.9 2.4	1.7 2.2	2.5 2.9	2.0 2.5
GRAVID UTERUS WEIGHT (G)	MEAN 88.5	95.2	91.0	89.3
	S.D. 14.6	9.7	22.2	12.5
FETAL WEIGHT (G)	MEAN 3.9	3.8	4.0	3.6**
	S.D. 0.2	0.3	0.3	0.4

SIGNIFICANTLY DIFFERENT FROM CONTROL: ** - $P < 0.01$

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 9
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF FETAL OBSERVATIONS - MALFORMATIONS
 (ABSOLUTE)

PAGE 1

	FETUSES				LITTERS			
	1	2	3	4	1	2	3	4
LEVEL (MG/KG/DAY):	0.0	20.0	70.0	175.0	0.0	20.0	70.0	175.0
NUMBER EXAMINED EXTERNALLY	347	396	362	365	23	24	24	23
MULTIPLE HEAD ANOMALIES	0	0	7	0	0	0	1	0
FILAMENTOUS TAIL WITH ANAL ATRESIA	0	0	1	0	0	0	1	0
NUMBER EXAMINED VISCERALLY	173	197	180	180	23	24	24	23
SITUS INVERSUS	1	0	0	0	1	0	0	0
DIAPHRAGMATIC HERNIA	1	1	0	0	1	1	0	0
NUMBER EXAMINED SKELETALLY	174	199	182	185	23	24	24	23
STERNOSCHISIS	0	0	0	1	0	0	0	1
STERNEBRA(E) MALALIGNED (SEVERE)	0	0	2	0	0	0	2	0
VERTEBRAL ANOMALY WITH OR WITHOUT ASSOCIATED RIB ANOMALY	0	0	1	0	0	0	1	0
SKULL ANOMALY	0	0	0	4	0	0	0	2
VERTEBRAL AGENESIS	0	0	1	0	0	0	1	0
STERNEBRAE FUSED	1	0	0	0	1	0	0	0
TOTAL MALFORMATIONS	0	0	7	0	0	0	1	0
NUMBER WITH EXTERNAL MALFORMATIONS	2	1	0	0	2	1	0	0
NUMBER WITH SOFT TISSUE MALFORMATIONS	1	0	4	5	1	0	4	3
NUMBER WITH SKELETAL MALFORMATIONS	3	1	10	5	3	1	4	3

NONE SIGNIFICANTLY DIFFERENT FROM CONTROL

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SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 9
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF FETAL OBSERVATIONS - MALFORMATIONS
 (PERCENT)

LEVEL (MG/KG/DAY):	FETUSES				LITTERS			
	1	2	3	4	1	2	3	4
NUMBER EXAMINED EXTERNALLY	347	396	362	365	23	24	24	23
MULTIPLE HEAD ANOMALIES	0.0	0.0	1.9	0.0	0.0	0.0	4.2	0.0
FILAMENTOUS TAIL WITH ANAL ATRESIA	0.0	0.0	0.3	0.0	0.0	0.0	4.2	0.0
NUMBER EXAMINED VISCERALLY	173	197	180	180	23	24	24	23
SITUS INVERSUS	0.6	0.0	0.0	0.0	4.3	0.0	0.0	0.0
DIAPHRAGMATIC HERNIA	0.6	0.5	0.0	0.0	4.3	4.2	0.0	0.0
NUMBER EXAMINED SKELETALLY	174	199	182	185	23	24	24	23
STERNOSCHISIS	0.0	0.0	0.0	0.5	0.0	0.0	0.0	4.3
STERNURA(E) MALALIGNED (SEVERE)	0.0	0.0	1.1	0.0	0.0	0.0	8.3	0.0
VERTEBRAL ANOMALY WITH OR WITHOUT ASSOCIATED RIB ANOMALY	0.0	0.0	0.5	0.0	0.0	0.0	4.2	0.0
SKULL ANOMALY	0.0	0.0	0.0	2.2	0.0	0.0	0.0	8.7
VERTEBRAL AGENESIS	0.0	0.0	0.5	0.0	0.0	0.0	4.2	0.0
STERNURAE FUSED	0.6	0.0	0.0	0.0	4.3	0.0	0.0	0.0
TOTAL MALFORMATIONS	0.0	0.0	1.9	0.0	0.0	0.0	4.2	0.0
PERCENT WITH EXTERNAL MALFORMATIONS	1.2	0.5	0.0	0.0	8.7	4.2	0.0	0.0
PERCENT WITH SOFT TISSUE MALFORMATIONS	0.6	0.0	2.2	2.7	4.3	0.0	16.7	13.0
TOTAL PERCENT WITH MALFORMATIONS	0.9	0.3	2.8	1.4	13.0	4.2	16.7	13.0

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

TABLE 10
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF FETAL OBSERVATIONS - VARIATIONS
 (ABSOLUTE)

	FETUSES				LITTERS				
	GROUP:	1	2	3	4	1	2	3	4
LEVEL (MG/KG/DAY):	0.0	20.0	70.0	175.0	0.0	20.0	70.0	175.0	
NUMBER EXAMINED EXTERNALLY	347	396	362	365	23	24	24	23	
NUMBER WITH FINDINGS	0	0	0	0	0	0	0	0	
NUMBER EXAMINED VISCERALLY	173	197	180	180	23	24	24	23	
DISTENDED URETER(S)	4	3	2	4	3	3	2	3	
NUMBER EXAMINED SKELETALLY	174	199	182	185	23	24	24	23	
STERNEBRA(E) MALALIGNED(SLIGHT OR MODERATE)	51	53	45	54	21	22	20	22	
14TH RUDIMENTARY RIB(S)	39	36	43	44	14	15	16	16	
27 PRESACRAL VERTEBRAE	4	2	3	2	3	2	2	2	
STERNEBRA(E) #5 AND/OR #6 UNOSSIFIED	1	9	7	19	1	4	4	8*	
14TH FULL RIB(S)	0	1	0	2	0	1	0	2	
7TH CERVICAL RIB(S)	1	2	2	9	1	2	1	5	
REDUCED OSSIFICATION OF THE 13TH RIB(S)	0	1	2	1	0	1	1	1	
REDUCED OSSIFICATION OF THE SKULL	3	1	1	4	3	1	1	3	
BENT RIB(S)	1	0	1	0	1	0	1	0	
HYOID UNOSSIFIED	2	3	3	4	1	2	3	3	
COSTAL CARTILAGE POSITION VARIATION	0	0	1	3	0	0	1	2	
ACCESSORY SKULL BONE(S)	0	1	0	0	0	1	0	0	

(31)

SIGNIFICANTLY DIFFERENT FROM CONTROL: * = P<0.05

TABLE 10
 TERATOLOGY STUDY IN RATS WITH SANTOVAR A
 SUMMARY OF FETAL OBSERVATIONS - VARIATIONS
 (PERCENT)

SLS STUDY NO.: 3044 230
 CLIENT: MONSANTO
 CLIENT NO.: SB-91-433

	FETUSES				LITTERS			
	1	2	3	4	1	2	3	4
LEVEL (MG/NG/DAY):	0.0	20.0	70.0	175.0	0.0	20.0	70.0	175.0
NUMBER EXAMINED EXTERNALLY	347	396	362	365	23	24	24	23
NUMBER WITH FINDINGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NUMBER EXAMINED VISCERALLY	173	197	180	180	23	24	24	23
DISTENDED URETER(S)	2.3	1.5	1.1	2.2	13.0	12.5	8.3	13.0
NUMBER EXAMINED SKELETALLY	174	199	182	185	23	24	24	23
STERNZERA(E) MALALIGNED(SLIGHT OR MODERATE)	29.3	26.6	24.7	29.2	91.3	91.7	83.3	95.7
14TH RUDIMENTARY RIB(S)	22.4	18.1	23.6	23.8	60.9	62.5	66.7	69.6
27 PRESACRAL VERTERAE	2.3	1.0	1.6	1.1	13.0	8.3	8.3	8.7
STERNZERA(E) #5 AND/OR #6 UNOSSIFIED	0.6	4.5	3.8	10.3	4.3	16.7	16.7	34.8
14TH FULL RIB(S)	0.0	0.5	0.0	1.1	0.0	4.2	0.0	8.7
7TH CERVICAL RIB(S)	0.6	1.0	1.1	4.9	4.3	8.3	4.2	21.7
REDUCED OSSIFICATION OF THE 13TH RIB(S)	0.0	0.5	1.1	0.5	0.0	4.2	4.2	4.3
REDUCED OSSIFICATION OF THE SKULL	1.7	0.5	0.5	2.2	13.0	4.2	4.2	13.0
HEMT RIB(S)	0.6	0.0	0.5	0.0	4.3	0.0	4.2	0.0
HYOID UNOSSIFIED	1.1	1.5	1.6	2.2	4.3	8.3	12.5	13.0
COSTAL CARTILAGE POSITION VARIATION	0.0	0.0	0.5	1.6	0.0	0.0	0.0	8.7
ACCESSORY SKULL BONE(S)	0.0	0.5	0.0	0.0	0.0	4.2	0.0	0.0

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APPENDIX A

Protocol and Protocol Amendments