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Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith lists the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). This report describes a rat developmental toxicity study with Union Carbide® Organofunctional Silane A-187 (CASRN 2530-83-8).

"Developmental Toxicity Evaluation of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats", Bushy Run Research Center, Project Report Report 53-58, December 19, 1990.

This information was previously submitted to the Agency in the following manner:

UCC §8(d) submission of 1/3/91

An additional copy of this study is attached.

A complete summary of this report is attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

A-187

39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

0 0 0 3

(none)

Previous PMN submissions related to this substance are: (none)

This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached report the term "BUSINESS CONFIDENTIAL" is entered on the first page. This precautionary statement was for internal use at the time of issuance of the report. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,

William C. Kuryla, Ph.D.
Assistant Director
Product Safety
(203/794-5230)

WCK/cr
Attachment (3 copies of cover letter, summary, and report)

0 0 0 4

SUMMARY

53-58

Developmental Toxicity Evaluation of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Sponsor: Union Carbide Chemicals and Plastics Company Inc.
Specialty Chemicals Division

* * * * *

ABSTRACT

Timed-pregnant Fischer 344 rats were exposed to the test chemical, Organofunctional Silane A-187 (A-187; CAS No. 2530-83-8), by gavage on gestational days (gd) 6 through 15 at doses of 0.0, 500.0, 1500.0 or 3000.0 mg/kg/day in certified corn oil using 25 plug-positive females per group. The dose volume employed was 5.0 ml/kg based on the weight of each female on gd 6. Clinical observations were taken daily and maternal body weights were measured on gd 0, 6, 12, 15, 18 and 21. Food consumption was measured over three-day intervals throughout gestation, gd 0-21. At scheduled sacrifice on gd 21, the dams were evaluated for body weight, liver weight, gravid uterine weight and status of implantation sites (i.e. resorptions, dead fetuses, live fetuses). Maternal livers were retained in fixative for possible subsequent microscopic examination. Live fetuses were dissected from the uterus, counted, weighed, sexed and examined for external abnormalities. Approximately one-half of the live fetuses in each litter were examined for visceral malformations and variations. These fetuses were then decapitated and the heads fixed in Bouin's solution; serial free hand sections of the heads were examined for soft tissue craniofacial malformations and variations. The remaining (intact) fetuses in each litter were eviscerated, fixed in alcohol, stained with alizarin red S and examined for skeletal malformations and variations.

There were no treatment-related maternal deaths. No dams aborted. One female each at 0.0 and 500.0 mg/kg/day, delivered early, and was removed from study. A total of 17-23 litters were examined in each dose group. There were no statistically significant differences among groups for maternal gestational body weights. Gestational weight gain was significantly reduced at 3000.0 mg/kg/day for gd 6-12 and 6-15 (the treatment period), and food consumption was

significantly reduced at 3000.0 mg/kg/day for gd 9-12. Treatment-related (but not statistically significant) clinical signs, observed only at 3000.0 mg/kg/day, included hypoactivity, audible respiration and unkempt appearance (one to two dams each). At the gd 21 sacrifice there were no effects of treatment on maternal body weight or gestational weight gain (absolute or corrected), on gravid uterine weight or on liver weight (absolute and relative). Gestational parameters, including number of ovarian corpora lutea, total, viable and nonviable implantations per litter, and sex ratio were unaffected by treatment. Fetal body weights per litter (all fetuses, males or females) were equivalent across dose groups.

There was no significant increase in the incidence of malformations (individual, pooled external, visceral, skeletal or total) in any treatment group relative to controls. There were no treatment-related differences among groups for individual external variations, for pooled external, visceral or skeletal variations or for total variations. One skeletal variation, unossified anterior arch of the atlas, exhibited a significantly increased incidence at 3000.0 mg/kg/day, indicating minimal fetotoxicity.

Dosing Fischer 344 rats with Organofunctional Silane A-187 by gavage during organogenesis resulted in evidence of maternal toxicity at 3000.0 mg/kg/day and evidence of developmental delay at 3000.0 mg/kg/day. No embryotoxicity or teratogenicity was observed at any dosage employed, including that which produced maternal toxicity. The "no observable effect level" (NOEL) for maternal toxicity was 1500.0 mg/kg/day, and the NOEL for developmental toxicity was 1500.0 mg/kg/day.

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BUSHY RUN RESEARCH CENTER

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PROJECT REPORT 53-58

TITLE: Developmental Toxicity Evaluation of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

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DATE: December 19, 1990

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Project Report 53-58
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Developmental Toxicity Evaluation of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Sponsor: Union Carbide Chemicals and Plastics Company Inc.
Specialty Chemicals Division

* * * * *

ABSTRACT

Timed-pregnant Fischer 344 rats were exposed to the test chemical, Organofunctional Silane A-187 (A-187; CAS No. 2530-83-8), by gavage on gestational days (gd) 6 through 15 at doses of 0.0, 500.0, 1500.0 or 3000.0 mg/kg/day in certified corn oil using 25 plug-positive females per group. The dose volume employed was 5.0 ml/kg based on the weight of each female on gd 6. Clinical observations were taken daily and maternal body weights were measured on gd 0, 6, 12, 15, 18 and 21. Food consumption was measured over three-day intervals throughout gestation, gd 0-21. At scheduled sacrifice on gd 21, the dams were evaluated for body weight, liver weight, gravid uterine weight and status of implantation sites (i.e. resorptions, dead fetuses, live fetuses). Maternal livers were retained in fixative for possible subsequent microscopic examination. Live fetuses were dissected from the uterus, counted, weighed, sexed and examined for external abnormalities. Approximately one-half of the live fetuses in each litter were examined for visceral malformations and variations. These fetuses were then decapitated and the heads fixed in Bouin's solution; serial free hand sections of the heads were examined for soft tissue craniofacial malformations and variations. The remaining (intact) fetuses in each litter were eviscerated, fixed in alcohol, stained with alizarin red S and examined for skeletal malformations and variations.

There were no treatment-related maternal deaths. No dams aborted. One female each at 0.0 and 500.0 mg/kg/day, delivered early, and was removed from study. A total of 17-23 litters were examined in each dose group. There were no statistically significant differences among groups for maternal gestational body weights. Gestational weight gain was significantly reduced at 3000.0 mg/kg/day for gd 6-12 and 6-15 (the treatment period), and food consumption was

significantly reduced at 3000.0 mg/kg/day for gd 9-12. Treatment-related (but not statistically significant) clinical signs, observed only at 3000.0 mg/kg/day, included hypoactivity, audible respiration and unkempt appearance (one to two dams each). At the gd 21 sacrifice there were no effects of treatment on maternal body weight or gestational weight gain (absolute or corrected), on gravid uterine weight or on liver weight (absolute and relative). Gestational parameters, including number of ovarian corpora lutea, total, viable and nonviable implantations per litter, and sex ratio were unaffected by treatment. Fetal body weights per litter (all fetuses, males or females) were equivalent across dose groups.

There was no significant increase in the incidence of malformations (individual, pooled external, visceral, skeletal or total) in any treatment group relative to controls. There were no treatment-related differences among groups for individual external variations, for pooled external, visceral or skeletal variations or for total variations. One skeletal variation, unossified anterior arch of the atlas, exhibited a significantly increased incidence at 3000.0 mg/kg/day, indicating minimal fetotoxicity.

Dosing Fischer 344 rats with Organofunctional Silane A-187 by gavage during organogenesis resulted in evidence of maternal toxicity at 3000.0 mg/kg/day and evidence of developmental delay at 3000.0 mg/kg/day. No embryotoxicity or teratogenicity was observed at any dosage employed, including that which produced maternal toxicity. The "no observable effect level" (NOEL) for maternal toxicity was 1500.0 mg/kg/day, and the NOEL for developmental toxicity was 1500.0 mg/kg/day.

OBJECTIVES

The present study was designed to evaluate the potential of Union Carbide® Organofunctional Silane A-187 to produce maternal and developmental toxicity (including teratogenicity) when administered by gavage (oral intubation) during organogenesis in Fischer 344 rats.

INTRODUCTION

Union Carbide® Organofunctional Silane A-187 (A-187) has a low order of acute peroral toxicity, having an LD50 of 22.6 ml/kg by gavage in rats (Report 25-52). It is slightly toxic by single sustained contact with skin, having an acute percutaneous LD50 of 3.97 (2.93-5.37) ml/kg by 24-hour occluded contact in rabbits (Report 25-52). Acute inhalation toxicity is low by exposure to vapor generated at ambient temperature, as indicated by the absence of mortalities during an eight hour exposure of six rats to a substantially vapor-saturated atmosphere (21°C) or in a 14-day postexposure observation period (Report 25-52). Undiluted A-187 causes moderate local erythema by unoccluded or occluded application of the liquid to rabbit skin (Allied Corporation 1982a; Report 25-52). Undiluted A-187 instilled into the rabbit

inferior conjunctival sac at a volume of 0.1 ml produced severe and persistent eye injury, as indicated by corneal opacity and pannus formation persisting to the end of a three-week postinstillation observation period (Allied Corporation, 1982b). A 5% aqueous solution of A-187 was nonirritating to the rabbit eye (Allied Corporation, 1982b).

Studies in guinea pigs (Fournier et al., 1977) and controlled clinical trials (TKL Research, 1984) indicate a skin sensitizing potential for A-187.

A short-term repeated skin contact study was conducted by making seven daily applications of 1.0 ml/kg over a 17-day period; a control group received 2.0 ml/kg of distilled water. The A-187 treatment produced no effects with respect to mortality, body weight change, or liver and kidney weight (Special Report 38-50).

In a 28-day study, A-187 was given to groups of male and female Sprague-Dawley rats at 0, 40, 400 or 1000 mg/kg/day. No signs of general or behavioral toxicity were seen over the dosing period. There were no treatment-related mortalities, and no significant differences for the various groups with respect to body weight, organ weight, or food consumption. Also, there were no biologically significant changes in peripheral blood hematology, clinical chemistry, or urinalysis. There was no treatment-related microscopic pathology. Thus, under the conditions of this study, the threshold for systemic toxicity was in excess of 1 ml A-187/kg (Siddiqui et al., 1981).

Detailed studies have been conducted on the acute and short-term repeated exposure toxicity for aerosols of A-187. For the acute studies, rats were exposed for four hours at 0.8, 1.9, or 5.3 g/m^3 of A-187 aerosol having a particle mass median aerodynamic diameter (MMAD) in the range 1.4 to 2.0 µm. There were five males and five females for each exposure concentration. At 5.3 g/m^3, three rats died within two days of exposure, but mortalities did not occur with the 0.8 or 1.9 g/m^3 exposures. Body weight decreases were seen at the intermediate and high dose exposures. Necropsy, carried out at the end of a 14-day postexposure observation period, did not show any gross pathology (Allied Corporation, 1982c). For the repeated exposure studies, groups of 10 male and 10 female rats were exposed daily for nine days to average A-187 aerosol concentrations of 0, 73, 226 or 734 mg/m^3; exposures were for 6 hours/day, and the MMAD averaged 1.7-1.9 µm. Six rats (five males and one female) from the high concentration group died during exposure, but there were no mortalities for the intermediate and low concentration groups. Body weight decreases occurred for the high and intermediate groups. A decreased blood platelet count was reported for the high concentration male rats. There was a statistically significant increase in serum glutamate-pyruvate transaminase activity for the high concentration group, but liver histopathology was not seen microscopically. There was no histological evidence of lung or other tissue injury (Allied Corporation, 1982d).

A number of in vitro studies have shown Silane A-187 to be mutagenic, but only weakly so in comparison with other monofunctional epoxides. Specific tests include positive results in strains TA98 and TA1535 with a Salmonella typhimurium bioassay (Allied Corporation, 1982e; Litton Bionetics, 1976a); a

mouse lymphoma (L5178Y line) producing dose-related effects in the range 0.33-2.6 µm/ml (Litton Bionetics, 1976b); and an increased incidence of sister chromatid exchanges in cultured mammalian cells (Allied Corporation, 1982f). Pretreatment of Silane A-187 with homogenates of liver or lung resulted in reduced mutagenic activity as indicated by an Ames test (Allied Corporation, 1981). There was a clear relationship between concentration of tissue homogenates and decrease in mutagenic activity; the detoxifying activity of the homogenates was inhibited by heating (Allied Corporation, 1981). In vivo studies confirmed the biodetoxification of Silane A-187 with respect to genotoxicity. Thus, A-187 was given by intraperitoneal injection to rabbits at a dose of either 30 or 100 mg/kg for five days per week for two weeks; no increase of sister chromatid exchange frequencies was found in peripheral blood lymphocytes (Allied Corporation, 1982f). In a further in vivo study, the effects of nine daily exposures of six hours each to an aerosol of A-187 (MMAD 1.7-1.9 µm) at concentrations of 0, 73, 226 or 734 mg/m^3 were studied. Blood samples were taken during the exposure period and for up to 12 days after the final exposure. Toxicity was evidenced at the highest concentration by mortality and weight gain decreases. However, there was no increase in the incidence of sister chromatid exchanges in peripheral blood lymphocytes (Allied Corporation, 1982g). The above findings suggest that, in vivo, A-187 is metabolized to non-genotoxic products.

The cutaneous tumorigenic potential of A-187 was investigated by chronic recurrent application to mouse skin. Three groups, each consisting 4[illegible] 18 C3H/HeJ mice, were used. One group received 25% A-187 in acetone, [illegible] acetone alone (solvent control), and the third rece[illegible] in acetone (positive control). Applications of 25µl were made on [illegible] dorsal skin three times weekly. There were no differences in survival [illegible] between acetone-alone and A-187 groups; the respective mean survival times were 502 and 487 days. However, the methylcholanthrene group had a mean survival time of only 204 days. None of the 40 mice receiving A-187 developed tumors of the skin or subcutaneous tissues. In the methylcholanthrene group, two mice developed papillomas and 37 mice developed malignant skin tumors. Thus, under the conditions of the study, A-187 was not oncogenic for mouse skin (Report 45-15).

To extend the information base for assessment of the hazards from exposure to A-187, the developmental toxicity of the material was investigated.

MATERIALS AND METHODS

Test Chemical, Dosage Formulations and Analyses

The test chemical, liquid Union Carbide® Organofunctional Silane A-187 (gamma-Glycidoxy-propyl trimethoxy-silane; Silane, trimethoxy[oxirany-(methoxy)propyl]-; CAS No. 2530-83-8) was received in a five-gallon sealed metal can from Union Carbide Corporation, Sistersville, WV, Lot No. 1119DF082888 on October 5, 1988, and was assigned the Bushy Run Research Center (BRRC) Sample No. 51-431. The purity of the test chemical was >99% according to the Material Safety Data Sheet.

Pre-study test chemical characterization, performed at Union Carbide Chemicals and Plastics Company Inc.'s Technical Skills Center, South Charleston, WV, indicated at test chemical purity of at least 98% as measured by GC/MS and NMR methods (see Appendix 1). Post-study analysis of the test substance initiated on November 19, 1990, can be found in the study notebook for the BRRC Project No. 90-15-51006.

Standard solutions were prepared as follows. A standard stock solution (1.0 mg/ml) was prepared by weighing 1.0 mg of test chemical to a volumetric flask and diluting to volume with toluene. Standards of 100 and 500 ng/µl were prepared by diluting the stock solution with toluene. For each analysis session, a standard curve was generated by injecting 1.0 µl aliquots of each standard solution into the gas chromatograph for analysis. The instrument used was a Hewlett-Packard 5880 Gas Chromatograph with a flame ionization detector. The column was a DB-1 fused Silica Capillary Column, 30 m, 1.0 µm film thickness. The carrier gas was ultra high purity helium and the column flow rate was ~2.0 ml/min. Dosing formulations were prepared by weighing the amount of test chemical into a volumetric flask and diluting to volume with certified corn oil (Mazola®, Best Foods, Inc., CPC International, CAS No. 8001-30-7). The resulting solutions were mixed by repeated inversion. A 1.0 ml aliquot of each dosing solution was appropriately diluted with toluene, and a 1.0 µl sample of each diluted solution was injected into the gas chromatograph for analysis. The volume administered was 5.0 ml/kg based on the body weight of each study female on gestational day (gd) 6. Control group dams received the vehicle (certified corn oil) at a dose volume of 5.0 ml/kg based on the gd 6 body weight.

The dosing solutions as prepared were homogeneous and stable for at least 21 days. Therefore, these dosing formulations were prepared once and analyzed prior to the onset of the dosing period. The doses were 0.0, 500.0, 1500.0 and 3000.0 mg/kg/day (0.0, 100.0, 300.0 and 600.0 mg/ml, respectively). (See Appendix 1 for details of the analytical procedures and results.)

Animals and Animal Husbandry

Virgin male (170) and female (170) Fischer 344 inbred albino rats [CDF® (F344)/Crl/Br] were received from Charles River Breeding Laboratories, Inc., Kingston, NY, on November 28, 1988. Males were approximately 69 days old upon arrival (date of birth September 20, 1988), and weighed approximately 175-200 g; females were approximately 63 days old upon arrival (date of birth September 26, 1988) and weighed approximately 130-150 g. All animals were quarantined for two weeks in animal room 147, during which time representative animals were subjected to fecal sampling, histologic examination of selected organs and to serum viral antibody examination. Quality control results indicated that the animals were suitable for use. Rats were housed in stainless steel wire-mesh cages (22.5 cm x 15.5 cm x 18 cm high for males and females during acclimation and females on study, and 22.5 X 31.0 x 18.0 cm high during mating) with food (Prolab Certified Ground Rodent Chow®, RMH-3200, Batch No. OCT 17 88 W2, Agway, Inc., St. Marys, OH) and water (Municipal Authority of Westmoreland County, Greensburg, PA) available ad libitum. Females and males were housed one-three per cage per sex during quarantine. All animals were assigned a unique number and received a stainless steel "Monel" ear tag (Gey Band and Tag Co., Norristown, PA).

Deotized Animal Cage Board® (Shepherd Specialty Papers, Inc., Kalamazoo, MI) was placed beneath the cages and changed frequently. Animals were kept on a 12-hour photoperiod and room temperatures and humidity were recorded continuously (Cole-Parmer Hygrothermograph Seven-Day Continuous Recorder, Model #8368-00, Cole-Parmer Instrument Company, Chicago, IL). Temperature was maintained at 67-75°F, and relative humidity was maintained at 45-65% throughout the study, except for one (1) hour during which the humidity ranged from 33-45%.

Rats were mated 1:1 (one male:one female) in stainless steel wire-mesh cages (22.5 cm x 31.0 cm x 18.0 cm high) and the paper board beneath the cages was checked twice daily for dropped copulation plugs (Hafez, 1970). Each male was used only once in this study. Successfully mated (plug-positive) females were housed singly in animal room 147 for the duration of the study. The day a copulation plug was found was designated gestational day (gd) 0 (Hafez, 1970). Twenty-five (25) plug-positive females were assigned to each experimental group by a randomization procedure stratified by body weight such that all groups were equivalent in both mean body weight and body weight range on gd 0; mean body weights on gd 0 were 160.97-162.21 g. The mating period for these animals was December 12 through December 17, 1988 (gd 0 was December 13 through December 17, 1988).

Treatment

Timed-pregnant Fischer 344 dams were dosed daily with A-187 in vehicle or vehicle alone (certified corn oil) on gd 6 through 15. All treatments were administered by gavage using a 16 gauge stainless steel dosing tube 3.0 inches long (Perfektum®, Popper and Sons, Inc., New Hyde Park, NY) attached to a 3.0 cc syringe (Becton-Dickinson). A dose volume of 5.0 ml/kg body weight was employed based on the gd 6 body weight of each animal on study. The doses employed were 0.0, 500.0, 1500.0 or 3000.0 mg/kg/day based on results from the dose range-finding study also performed on timed-pregnant Fischer 344 rats (Appendix 6).

All females on study were weighed on gd 0, 6 (prior to onset of dosing), 12, 15 (during the dosing period), 18 and 21. Food consumption was measured at three-day intervals throughout gestation. All females were examined daily for clinical signs of toxicity. The treatment period for all study females was gd 6 through 15, December 19, 1988 through January 1, 1989.

Thoracolaparotomy and Maternal and Fetal Examinations

All surviving study females were sacrificed on gd 21 by carbon dioxide asphyxiation. The sacrifice period was January 3 through January 7, 1989. The maternal body cavities were opened by midline thoracolaparotomy. The gravid uterus, ovaries (including corpora lutea), cervix, vagina and abdominal and thoracic cavities were examined grossly. Ovarian corpora lutea of pregnancy were counted. Maternal liver and uterine weights were determined. Maternal livers were fixed in buffered neutral 10% formalin for possible subsequent histopathologic examination. The uterus was externally examined for signs of hemorrhage, removed from the abdominal cavity and dissected longitudinally to expose the contents. All live and dead fetuses and early and late resorption sites were noted and recorded. Uteri from females that appeared nongravid were placed in a 10% ammonium sulfide solution for detection of early resorptions (Salewski, 1964).

All live fetuses were weighed and sexed. All fetuses were examined for external malformations including cleft palate, and variations. One-half of the fetuses (even-numbered fetuses from litters with an even number of live fetuses, odd-numbered fetuses from litters with an odd number of live fetuses) in each litter were examined for thoracic and abdominal visceral abnormalities by modification of methods described by Staples (1974). These fetuses were decapitated and their heads were fixed in Bouin's solution for examination of craniofacial structures by sectioning methods modified from Wilson (1965; 1973). The remaining (intact) fetuses in each litter were eviscerated, fixed in ethanol, and then processed for skeletal staining with alizarin red S (Crary, 1962; Peltzer and Schardein, 1966), and examined for skeletal malformations and variations. The decapitated fetuses were also processed for staining but were not examined.

Statistical Analyses

The unit of comparison was the pregnant female or the litter (Weil, 1970). Results of the quantitative continuous variables (e.g., maternal body weights, organ weights, etc.) were intercompared for the three A-187-exposed groups and the vehicle control group by use of Levene's test for equal variances (Levene, 1960), analysis of variance (ANOVA), and t-tests with Bonferroni probabilities for pairwise comparisons. When Levene's test indicated homogeneous variances and the ANOVA was significant, the pooled t-test was used. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances (Brown and Forsythe, 1974) followed, when necessary, by the separate variance t-test.

Nonparametric data obtained following laparohysterectomy were statistically treated using the Kruskal-Wallis test (Sokal and Rohlf, 1969) followed by the Mann-Whitney U test (Sokal and Rohlf, 1969) when appropriate. Incidence data were compared using Fisher's Exact Test (Sokal and Rohlf, 1969). For all statistical tests, the fiducial limit of 0.05 (two-tailed) was used as the criterion for significance.

Personnel

The evaluation of A-187 for developmental toxicity in Fischer 344 rats was conducted at Bushy Run Research Center (BRRC), Export, PA under contract to the Specialty Chemicals Division, Union Carbide Corporation, Sistersville, WV, under the direction of Dr. E. Ballantyne, Director of Corporate Applied Toxicology, Union Carbide Corporation, and Dr. W. F. Gorham, Director of Product Safety and Liability, Specialty Chemicals Division, Union Carbide Corporation. The BRRC personnel indicated below contributed to the completion of this study.

Dr. E. W. Lyl served as Study Director during the in-life phase of the study and during the phase of fetal evaluations until June 9, 1989. Dr. T. L. Harper-Bradley served as Study Director from June 9, 1989 until completion of the study. Developmental toxicology personnel included R. R. Altman and M. A. Copeman, T. R. Brownfield, B. L. Butler, D. L. Fait, L. C. Fisher, L. J. Fosnight, M. S. Kubena and D. J. Tarasi. (R. R. Altman and M. A. Copeman served as study leaders for both the definitive and dose range-finding studies.) Analytical personnel included Dr. J. P. Van Miller and M. A. Vrbanic. Animal care personnel included G. W. Klingensmith, Jr., L. E. Lipko and R. J. Klim. Quality Assurance personnel included L. J. Calisti, J. R. Bernard and [illegible] L. Coleman.

The final report was prepared by Drs. T. L. Neeper-Bradley and R. W. Tyl with assistance from L. C. Fisher on data compilation and statistical analyses. The individual scientist reports were prepared and signed by the author(s).

The protocol and three (3) amendments detailing the design and conduct of the study are presented in Appendix 5.

Storage of Records

All original data sheets for the present study are stored in the BRRC Archives along with all biological samples collected during the course of the study which remain the responsibility of BRRC. Work sheets and computer printouts which were generated in the statistical analysis of data are stored in the BRRC Archives. Copies of this report will be filed with the BRRC Archives as well as with The Specialty Chemicals Division, Union Carbide Corporation, Bound Brook, NJ.

Compliance

All records, data and reports will be maintained in storage for ten (10) years or for as long as the quality of the preparation affords evaluation, whichever is less. This study was performed according to Environmental Protection Agency (EPA) Good Laboratory Practices (EPA, 1983), and EPA TSCA Testing Guidelines (1985; 1987).

RESULTS

Analysis of dosing formulations prior to the dosing period indicated that all formulations were within 104.5-105.7% of the target concentrations (Table 1). The dosing solutions were homogeneous and stable for at least 21 days (see Appendix 1 for details).

The distribution and fate of all plug-positive rats on study are presented in Table 2. No females aborted. One female each at 0.0 and 500.0 mg/kg/day delivered early (on gd 21), was euthanized, and removed from study. Their data were eliminated from the results. Pregnancy rate was approximately equivalent for all dose groups except for a slight, nonsignificant reduction at 3000.0 mg/kg/day. With the exception of one litter each at 500.0 and 3000.0 (but not at 1500.0) mg/kg/day, all litters had one or more live fetuses at scheduled sacrifice. A total of 17 to 23 litters were examined in each group.

Periodic maternal body weights (Table 3) exhibited no significant differences across groups. Gestational weight gain was reduced at 3000.0 mg/kg/day for days 6 to 12 and days 6 to 15 (the entire treatment period).

Clinical observations of the dams are summarized in Table 4. There were no statistically increased clinical signs of maternal toxicity. However, biologically significant treatment-associated clinical signs were observed at 3000.0 mg/kg/day and included hypoactivity (in one female) and audible respiration (in two females) during treatment.

Food consumption, expressed as grams/dam/day, was significantly reduced on day 9 to 12 of gestation at 3000.0 mg/kg/day. At mid and low dose levels, food consumption was unaffected by treatment (Table 5). Individual maternal in-life data are presented in Appendix 2.

There were no treatment-related necropsy findings of the dams at scheduled sacrifice on gd 21 (Table 6). There were no treatment-related differences in maternal terminal body weight, corrected terminal body weight (body weight at sacrifice minus gravid uterine weight), corrected body weight change (gestational weight gain minus gravid uterine weight), in gravid uterine weight or in liver weight (absolute or relative to corrected body weight) (Table 7).

Gestational parameters are presented in Table 8. There was no effect of treatment on the number of ovarian corpora lutea, total, viable or nonviable (early and late resorptions and dead fetuses) implantations per litter or on sex ratio (percent males). Percent preimplantation loss was equivalent across groups. Individual maternal necropsy and laparotomy data are presented in Appendix 3.

Fetal body weights (all fetuses, male or female) per litter were equivalent across dose groups.

The results of fetal external, visceral and skeletal evaluations are summarized in Table 9 for malformations and Table 10 for variations. There were no significant differences in the incidence of individual malformations, of malformations by category (external, visceral including craniofacial or skeletal), or of total malformations among all groups (Table 9).

There were no significant differences among groups in the incidences of individual fetal external or visceral variations. A total of 57 different types of fetal skeletal variations were observed. Of these, only one finding, unossified anterior arch of the atlas, exhibited an increased incidence at 3000.0 mg/kg/day. There were no treatment-related increases in the incidence of variations by category (external, visceral including craniofacial, or skeletal) or of total variations (Table 10).

DISCUSSION

Union Carbide® Organofunctional Silane A-187, administered by gavage during organogenesis in Fischer 344 rats, produced indications of maternal toxicity, including clinical signs of toxicity and reductions in gestational body weight gain and food consumption at 3000.0 mg/kg/day.

The reduced ossification in the anterior arches of the atlas of the fetal axial skeleton at 3000.0 mg/kg/day was observed in the absence of any other indication of fetotoxicity. However, as suggested by Aliverti (1979), reduced ossification need not occur in conjunction with reduction in fetal body weights. If reduced ossification alone is viewed as indicative of developmental toxicity, then the A/D ratio (the ratio of the adult lowest observable effect level to the developmental lowest observable effect level, 3000.0/3000.0) is 1.0, indicating no preferential susceptibility of the conceptuses to the test chemical under the conditions of this study.

CONCLUSIONS

Administration of Union Carbide® Organofunctional Silane A-187 by gavage to timed-pregnant Fischer 344 rats during organogenesis at 0.0, 500.0, 1500.0 or 3000.0 mg/kg/day resulted in maternal toxicity at 3000.0 mg/kg/day (reduced gestational body weight change and decreased food consumption) and slight fetotoxicity (reduced skeletal ossification) at 3000.0 mg/kg/day. There was no treatment-related increase in the incidence of malformation at any dosage employed. The "no observable effect level" (NOEL) for maternal toxicity as well as for developmental toxicity was 1500.0 mg/kg/day.

Reviewed and Approved by:

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Table 1

Analyses of Dosing Formulations

Target Concentrations mg/kg/day	mg/ml[a]	Analytical Concentrations[b] mg/ml	% of Target
3000.0	600.0	626.8	104.5
1500.0	300.0	315.3	105.1
500.0	100.0	105.7	105.7
0.0	0.0	<MDL[c]	-

a The dosing solutions were formulated with certified corn oil based on a dosing volume of 5.0 ml/kg.

b The formulations were homogeneous and stable for at least 21 days at room temperature, so they were made once and analyzed prior to use.

c Less than the minimum detection limit of approximately 0.01 mg/ml.

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TABLE 2
DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF DISTRIBUTION AND FATE[a]

GROUP: MG/KG/DAY	0.0	500.0	1500.0	3000.0
FEMALES ON STUDY	25	25	25	25
FEMALES THAT DIED	0 0.0	0 0.0	0 0.0	0 0.0
PREGNANT	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES THAT ABORTED	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES THAT DELIVERED EARLY[b]	1 4.0	1 4.0	0 0.0	0 0.0
FEMALES REMOVED FROM STUDY	0 0.0	0 0.0	0 0.0	0 0.0
FEMALES EXAMINED AT LAPAROTOMY	24 96.0	24 96.0	25 100.0	25 100.0
NONPREGNANT	3 12.5	1 4.2	2 8.0	7 28.0
PREGNANT	21 87.5	23 95.8	23 92.0	18 72.0
FEMALES WITH NON-VIABLE IMPLANTS ONLY	0 0.0	1 4.3	0 0.0	1 5.6
FEMALES WITH VIABLE FETUSES	21 100.0	22 95.7	23 100.0	17 94.4
FEMALES THAT WERE PREGNANT	22 88.0	24 96.0	23 92.0	18 72.0

[a] For all parameters, the data are presented as the number of dams on top and the percentage beneath.
[b] Females that delivered early were automatically removed from study.

Table 3

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS
SUMMARY OF GESTATIONAL BODY WEIGHT AND WEIGHT CHANGE (GRAMS)

FEMALES

GROUP: MG/KG/DAY	0.0	500.0	1500.0	3000.0
GESTATIONAL BODY WEIGHTS (g)				
DAY 0				
MEAN	161.69	160.97	162.21	161.59
S.D.	9.098	9.218	8.532	6.795
N	21	23	23	18
DAY 6				
MEAN	172.63	171.46	173.61	173.32
S.D.	8.500	9.753	8.926	8.808
N	21	23	23	18
DAY 12				
MEAN	183.84	181.65	183.67	179.02
S.D.	10.994	11.246	9.305	13.941
N	21	23	23	18
DAY 15				
MEAN	192.20	187.97	189.70	182.96
S.D.	11.847	11.705	10.207	16.211
N	21	23	23	18
DAY 18				
MEAN	212.08	206.09	210.41	201.40
S.D.	16.523	18.542	11.057	20.762
N	21	23	23	18
DAY 21				
MEAN	234.69	224.58	235.09	221.81
S.D.	23.475	23.192	15.644	27.776
N	21	23	23	18
GESTATIONAL BODY WEIGHT CHANGES (g)				
DAY 0 TO 6 (PRETREATMENT)				
MEAN	10.94	10.50	11.40	11.73
S.D.	3.224	2.857	3.327	3.259
N	21	23	23	18
DAY 6 TO 12				
MEAN	11.21	10.19	10.06	5.69*a
S.D.	4.255	4.477	3.534	7.978
N	21	23	23	18
DAY 12 TO 15				
MEAN	8.36	6.31	6.03	3.94
S.D.	3.047	5.929	6.712	8.156
N	21	23	23	18
DAY 15 TO 18				
MEAN	19.88	18.12	20.71	18.45
S.D.	8.158	11.306	8.518	10.684
N	21	23	23	18
DAY 18 TO 21				
MEAN	22.61	18.49	24.68	20.41
S.D.	9.294	8.444	9.914	10.466
N	21	23	23	18
DAY 6 TO 15 (TREATMENT)				
MEAN	19.57	16.50	16.09	9.63**
S.D.	5.801	7.073	6.422	11.986
N	21	23	23	18
DAY 15 TO 21 (POST-TREATMENT)				
MEAN	42.49	36.61	45.39	38.85
S.D.	14.107	16.194	12.334	17.127
N	21	23	23	18
DAY 0 TO 21 (GESTATION)				
MEAN	73.00	63.61	72.88	60.22
S.D.	19.029	20.663	14.832	21.998
N	21	23	23	18

* Significantly different from control group ($p < .05$)
** Significantly different from control group ($p < .01$)
[a] Significant using Brown-Forsythe ANOVA and separate variance t-test only.

TABLE 4

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

CATEGORY	FINDING (LOCATION)	GESTATIONAL DAYS	MG/KG/DAY 0.0	500.0	1500.0	3000.0
NORMAL						
	NO SIGNIFICANT CLINICAL OBSERVATIONS					
		0- 5	20	23	23	18
		6- 15	21	23	23	18
		16- 21	20	23	23	17
DEAD						
	SCHEDULED SACRIFICE					
		16- 21	21	23	23	18
BEHAVIOR/CNS						
	HYPOACTIVE					
		6- 15	0	0	0	1
BODY						
	UNKEMPT					
		16- 21	0	1	0	1
CARDIO-PULMONARY						
	AUDIBLE RESPIRATION					
		6- 15	0	0	0	2
EYES/EARS/NOSE						
	REDDENED EYES (EYE-LEFT)					
		16- 21	0	1	0	0
	LACRIMATION (EYE-BOTH)					
		6- 15	0	0	0	1
	PERIOCULAR ENCRUSTATION (EYE-BOTH, EYE-LEFT, EYE-RIGHT)					
		0- 5	1	2	0	1
		6- 15	2	0	0	1
		16- 21	2	1	0	1
	PERINASAL ENCRUSTATION					
		6- 15	0	0	0	1
ORAL/DENTAL						
	PERIORAL WETNESS					
		6- 15	0	0	0	1
OTHER						
	MISSING EAR TAG					
		0- 5	7	3	4	1
		6- 15	3	0	1	2

None significantly different from control group

Table 5
DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS
SUMMARY OF GESTATIONAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

FEMALES

GROUP: MG/KG/DAY	0.0	500.0	1500.0	3000.0
DAY 0 TO 3				
MEAN	10.85	10.18	10.75	10.41
S.D.	1.321	1.634	1.559	3.066
N	21	23	22	18
DAY 3 TO 6				
MEAN	12.45	12.05	11.57	11.68
S.D.	1.859	1.142	2.723	2.675
N	21	22	23	18
DAY 6 TO 9				
MEAN	11.70	11.01	11.49	11.66
S.D.	1.647	2.048	1.080	1.725
N	21	22	21	14
DAY 9 TO 12				
MEAN	12.60	11.89	12.00	10.23*a
S.D.	1.539	1.294	0.975	3.028
N	20	21	21	16
DAY 12 TO 15				
MEAN	12.79	12.37	12.56	11.21
S.D.	1.640	1.214	1.657	3.270
N	19	20	21	16
DAY 15 TO 18				
MEAN	14.89	15.05	15.02	15.84
S.D.	1.561	2.203	1.440	2.181
N	19	22	22	15
DAY 18 TO 21				
MEAN	16.14	15.70	16.06	16.45
S.D.	1.124	1.368	1.110	1.607
N	21	23	22	17
DAY 0 TO 6 (PRETREATMENT)				
MEAN	11.65	11.20	11.36	11.05
S.D.	0.920	1.177	1.727	2.788
N	21	22	22	18
DAY 6 TO 15 (TREATMENT)				
MEAN	12.49	11.92	12.01	11.54
S.D.	1.035	1.097	0.849	1.620
N	19	20	21	14
DAY 15 TO 21 (POST-TREATMENT)				
MEAN	15.52	15.39	15.62	16.03
S.D.	1.247	1.617	1.072	1.482
N	19	22	21	15

* Significantly different from control group ($p < .05$)
a Significant using Brown-Forsythe ANOVA and separate variance t-test only.
Data not included for animals with excessive amounts of excrement in feeder.

TABLE 8

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ALL PREGNANT FEMALES SACRIFICED AT SCHEDULED LAPAROTOMY

GROUP: MG/KG/DAY	0.0	500.0	1500.0	2000.0
NUMBER OF ANIMALS IN DOSE GROUP	25	25	25	25
NUMBER OF ANIMALS SACRIFICED	21	23	23	18
LIVER				
ANOMALY	0	0	1	0
UTERUS				
NO IMPLANTS IN ONE UTERINE HORN	3	5	4	4
CYST	1	0	0	0
PLACENTAS				
APPARENT TUBE ATTACHED TO HILUS	0	1	0	0

None significantly different from control group

Table 7
DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS
SUMMARY OF MATERNAL ORGAN WEIGHTS (GRAMS)

FEMALES

GROUP: MG/KG/DAY	0.0	500.0	1500.0	3000.0
INITIAL BODY WEIGHT (g)				
MEAN	161.69	160.97	162.21	161.59
S.D.	9.098	9.218	8.532	8.795
N	21	23	23	18
BODY WEIGHT AT SACRIFICE (g)				
MEAN	234.69	224.58	235.09	221.81
S.D.	23.475	23.192	15.644	27.776
N	21	23	23	18
GRAVID UTERINE WEIGHT (g)				
MEAN	46.029	36.480	45.555	36.139
S.D.	21.4101	22.0533	15.0262	21.6653
N	21	23	23	18
CORRECTED BODY WEIGHT (g)[a]				
MEAN	188.66	188.10	189.53	185.67
S.D.	9.706	11.438	10.892	13.898
N	21	23	23	18
CORRECTED WEIGHT CHANGE (g)[b]				
MEAN	26.97	27.13	27.32	24.08
S.D.	6.448	8.245	7.502	9.295
N	21	23	23	18
LIVER WEIGHT (g)				
MEAN	8.657	8.420	8.786	8.414
S.D.	0.8745	0.9358	0.8024	1.1586
N	21	23	23	18
RELATIVE LIVER WEIGHT (%)[c]				
MEAN	4.588	4.475	4.633	4.532
S.D.	0.4039	0.4024	0.2867	0.5313
N	21	23	23	18

None significantly different from control group
a Corrected body weight = body weight at sacrifice minus gravid uterine weight.
b Corrected weight change = corrected body weight minus initial body weight.
c Value is a percentage of corrected body weight.

Table 8
DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS
SUMMARY OF GESTATIONAL PARAMETERS

FEMALES

GROUP: MG/KG/DAY	0	500.0	1500.0	3000.0
CORPORA LUTEA				
MEAN	11.4	11.3	11.4	10.5
S.D.	2.53	1.58	1.41	2.64
N	21	23	23	18
TOTAL IMPLANTS				
MEAN	8.0	8.3	8.0	7.1
S.D.	4.21	4.03	2.93	4.00
N	21	23	23	18
PERCENT PREIMPLANTATION LOSS[a]				
MEAN	34.3	40.2	30.4	36.9
S.D.	29.03	31.08	24.30	28.81
N	21	23	23	18
VIABLE IMPLANTS				
MEAN	7.8	8.0	7.7	6.1
S.D.	4.01	4.06	2.82	4.11
N	21	23	23	18
NON-VIABLE IMPLANTS				
MEAN	0.2	0.3	0.3	1.0
S.D.	0.40	0.56	0.63	2.81
N	21	23	23	18
EARLY RESORPTIONS				
MEAN	0.1	0.3	0.3	0.9
S.D.	0.38	0.56	0.62	2.81
N	21	23	23	18
LATE RESORPTIONS				
MEAN	0.0	0.0	0.0	0.1
S.D.	0.00	0.00	0.21	0.24
N	21	23	23	18
DEAD FETUSES				
MEAN	0.0	0.0	0.0	0.1
S.D.	0.22	0.00	0.00	0.24
N	21	23	23	18
PERCENT LIVE FETUSES				
MEAN	98.5	92.3	96.6	87.9
S.D.	3.23	21.58	6.89	25.58
N	21	23	23	18
SEX RATIO (% MALE FETUSES)				
MEAN	38.3	42.6	46.8	45.4
S.D.	20.05	21.54	19.44	25.27
N	21	22[b]	23	17[b]
FETAL BODY WEIGHTS PER LITTER (GRAMS)				
ALL FETUSES				
MEAN	4.384	4.432	4.359	4.362
S.D.	0.2850	0.2850	0.2167	0.3098
N	21	22	23	17
MALE FETUSES				
MEAN	4.459	4.543	4.480	4.345
S.D.	0.1936	0.2653	0.2234	0.1936
N	18[c]	19[c]	22[c]	14[c]
FEMALE FETUSES				
MEAN	4.277	4.299	4.245	4.230
S.D.	0.3075	0.3333	0.2407	0.4539
N	21	22	23	17

None significantly different from control group

[a] Percent preimplantation loss=[(corpora lutea - total implants)/corpora lutea] X 100.
[b] The N is reduced due to the litters that consist of nonviable implants only.
[c] The N is reduced due to the litters that consist of female fetuses only.

TABLE 9

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF MALFORMATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED EXTERNALLY[b]	164	139	176	110	21	22	23	17
FETUS EDEMATOUS	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
ANOPHTHALMIA - BILATERAL	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
CLEFT PALATE	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
ANOTIA - BILATERAL	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
ADACTYLY	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
NO EXTERNAL GENITALIA	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
LIMBS ROTATED DORSALLY	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
MICROMELIA	0 0.0	1 0.7	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0

None significantly different fr control (0.0 MG/KG/DAY)
See footnotes on last page of ile.

TABLE 9

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF MALFORMATIONS IN FETUSES AND LITTERS®

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED VISCERALLY[c]	89	75	93	59	21	22	23	17
CLEFT PALATE	0 0.0	1 1.3	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
EYE MISSING	1 1.1	0 0.0	0 0.0	0 0.0	1 4.8	0 0.0	0 0.0	0 0.0
LATERAL VENTRICLE DILATED - TISSUE DEPRESSED	1 1.1	1 1.3	0 0.0	0 0.0	1 4.8	1 4.5	0 0.0	0 0.0
HYDROURETER - UNILATERAL	0 0.0	1 1.3	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
ABDOMINAL SKIN MISSING	0 0.0	1 1.3	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 9

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF MALFORMATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED SKELETALLY[d]	75	64	83	51	18	20	23	14
NO FINDINGS								

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 9

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF MALFORMATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
TOTAL MALFORMATIONS								
NUMBER WITH EXTERNAL MALFORMATIONS	0	1	0	0	0	1	0	0
PERCENT WITH EXTERNAL MALFORMATIONS	0.0	0.7	0.0	0.0	0.0	4.5	0.0	0.0
NUMBER WITH SOFT TISSUE MALFORMATIONS	2	2	0	0	2	2	0	0
PERCENT WITH SOFT TISSUE MALFORMATIONS	2.2	2.7	0.0	0.0	9.5	9.1	0.0	0.0
NUMBER WITH SKELETAL MALFORMATIONS	0	0	0	0	0	0	0	0
PERCENT WITH SKELETAL MALFORMATIONS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
TOTAL NUMBER WITH MALFORMATIONS	2	2	0	0	2	2	0	0
TOTAL PERCENT WITH MALFORMATIONS	1.2	1.4	0.0	0.0	9.5	9.1	0.0	0.0

None significantly different from control (0.0 MG/KG/DAY)

[a] For all findings, the number (of fetuses affected or litters with one or more affected fetuses) is presented on top and the percentage of the total (fetuses or litters) examined is presented beneath. A single fetus may be represented more than once in listing individual defects. Only live fetuses were examined.

[b] All fetuses were examined externally.

[c] Approximately 50% of each litter were examined viscerally (Staples, 1974), and for soft tissue craniofacial defects (Wilson, 1965; van Julsinghe and Bennett, 1977).

[d] Approximately 50% of each litter were examined for skeletal defects after staining with Alizarin Red S.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED EXTERNALLY[b]	164	139	176	110	21	22	23	17
ECCHYMOSIS - TRUNK	8	8	14	10	7	8	9	7
	4.9	5.8	8.0	9.1	33.3	36.4	39.1	41.2
ECCHYMOSIS - HEAD	1	1	1	1	1	1	1	1
	0.6	0.7	0.6	0.9	4.8	4.5	4.3	5.9

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED VISCERALLY[c]	89	75	93	59	21	22	23	17
DARK BROWN MATERIAL IN NASAL PASSAGES	1 1.1	0 0.0	0 0.0	2 3.4	1 4.8	0 0.0	0 0.0	2 11.8
DARK BROWN MATERIAL IN NASOPHARYNX	1 1.1	0 0.0	0 0.0	2 3.4	1 4.8	0 0.0	0 0.0	2 11.8
DARK BROWN MATERIAL WITHIN BRAIN SECTIONS	1 1.1	0 0.0	0 0.0	0 0.0	1 4.8	0 0.0	0 0.0	0 0.0
BROWN DISCOLORATION WITHIN BRAIN SECTIONS	1 1.1	1 1.3	1 1.1	0 0.0	1 4.8	1 4.5	1 4.3	0 0.0
LATERAL VENTRICLE DILATED - NO DEPRESSION	0 0.0	1 1.3	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0
PARTIAL FETAL ATELECTASIS	29 32.6	24 32.0	27 29.0	21 35.6	13 61.9	11 50.0	15 65.2	11 64.7
FETAL ATELECTASIS	13 14.6	12 16.0	11 11.8	13 22.0	10 47.6	9 40.9	8 34.8	9 52.9
NODULE - LIVER	1 1.1	0 0.0	0 0.0	0 0.0	1 4.8	0 0.0	0 0.0	0 0.0
DILATED RENAL PELVIS - UNILATERAL	1 1.1	3 4.0	1 1.1	0 0.0	1 4.8	3 13.6	1 4.3	0 0.0
DILATED RENAL PELVIS - BILATERAL	0 0.0	0 0.0	0 0.0	1 1.7	0 0.0	0 0.0	0 0.0	1 5.9
DILATED URETERS - BILATERAL	0 0.0	1 1.3	0 0.0	0 0.0	0 0.0	1 4.5	0 0.0	0 0.0

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED SKELETALLY[d]	75	64	83	51	18	20	23	14
CERVICAL CENTRA #1,#2,#3 AND/OR #4 POORLY OSSIFIED	30 40.0	26 40.6	37 44.6	13 25.5	15 83.3	14 70.0	17 73.9	9 64.3
CERVICAL CENTRA #1,#2,#3 AND/OR #4 UNOSSIFIED	75 100.0	64 100.0	83 100.0	51 100.0	18 100.0	20 100.0	23 100.0	14 100.0
CERVICAL CENTRA #1,#2,#3 AND/OR #4 BILOBED	1 1.3	0 0.0	1 1.2	0 0.0	1 5.6	0 0.0	1 4.3	0 0.0
CERVICAL CENTRUM #5 POORLY OSSIFIED	31 41.3	17 26.6	33 39.8	23 45.1	15 83.3	13 65.0	16 69.6	11 78.6
CERVICAL CENTRUM #5 UNOSSIFIED	11 14.7	14 21.9	7 8.4	11 21.6	9 50.0	9 45.0	5 21.7	7 50.0
CERVICAL CENTRUM #6 POORLY OSSIFIED	23 30.7	14 21.9	24 28.9	17 33.3	12 66.7	13 65.0	16 69.6	7 50.0
CERVICAL CENTRUM #6 UNOSSIFIED	7 9.3	7 10.9	4 4.8	2 3.9	6 33.3	6 30.0	3 13.0	2 14.3
CERVICAL CENTRUM #7 POORLY OSSIFIED	15 20.0	5 7.8	7 8.4	4 7.8	10 55.6	5 25.0	6 26.1	4 28.6
CERVICAL CENTRUM #7 UNOSSIFIED	0 0.0	1 1.6	0 0.0	0 0.0	0 0.0	1 5.0	0 0.0	0 0.0
CERVICAL CENTRUM #7 BILOBED	1 1.3	0 0.0	1 1.2	0 0.0	1 5.6	0 0.0	1 4.3	0 0.0
ANTERIOR ARCH OF THE ATLAS POORLY OSSIFIED	65 86.7	52 81.2	67 80.7	26 51.0	18 100.0	20 100.0	21 91.3	12 85.7
ANTERIOR ARCH OF THE ATLAS UNOSSIFIED	2 2.7	2 3.1	4 4.8	20 33.2	2 11.1	2 10.0	4 17.4	10** 71.4

**= significantly different from control (0.0 MG/KG/DAY) at .01 level using two-tailed Fisher's exact test.
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED SKELETALLY[d]	75	64	83	51	18	20	23	14
ANTERIOR ARCH OF THE ATLAS BILOBED	1 1.3	0 0.0	0 0.0	1 2.0	1 5.6	0 0.0	0 0.0	1 7.1
ANTERIOR ARCH OF THE ATLAS SPLIT	2 2.7	2 3.1	3 3.6	3 5.9	1 5.6	2 10.0	3 13.0	3 21.4
CERVICAL CENTRUM #1 SPLIT	3 4.0	4 6.2	3 3.6	1 2.0	1 5.6	4 20.0	2 8.7	1 7.1
BONE ISLAND ON CERVICAL ARCHES #7	1 1.3	0 0.0	0 0.0	0 0.0	1 5.6	0 0.0	0 0.0	0 0.0
THORACIC CENTRUM #12 POORLY OSSIFIED	7 9.3	7 10.9	4 4.8	2 3.9	5 27.8	6 30.0	4 17.4	1 7.1
THORACIC CENTRUM #12 BILOBED	7 9.3	5 7.8	6 7.2	8 15.7	7 38.9	4 20.0	6 26.1	6 42.9
THORACIC CENTRUM #11 POORLY OSSIFIED	6 8.0	5 7.8	9 10.8	4 7.8	6 33.3	4 20.0	8 34.8	2 14.3
THORACIC CENTRUM #11 BILOBED	7 9.3	7 10.9	11 13.3	6 11.8	7 38.9	6 30.0	10 43.5	5 35.7
THORACIC CENTRUM #10 POORLY OSSIFIED	1 1.3	0 0.0	7 8.4	1 2.0	1 5.6	0 0.	6 26.1	1 7.1
THORACIC CENTRUM #10 BILOBED	8 10.7	2 3.1	3 3.6	6 11.8	7 38.9	2 10.0	3 13.0	5 35.7
THORACIC CENTRUM #6 BILOBED	1 1.3	0 0.0	0 0.0	0 0.0	1 5.6	0 0.0	0 0.0	0 0.0
THORACIC CENTRUM #5 POORLY OSSIFIED	0 0.0	0 0.0	2 2.4	0 0.0	0 0.0	0 0.0	2 8.7	0 0.0

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED SKELETALLY[d]	75	64	83	51	18	20	23	14
THORACIC CENTRUM #13 POORLY OSSIFIED	0 0.0	1 1.6	1 1.2	2 3.9	0 0.0	1 5.0	1 4.3	2 14.3
THORACIC CENTRUM #13 BILOBED	0 0.0	0 0.0	1 1.2	1 2.0	0 0.0	0 0.0	1 4.3	1 7.1
THORACIC CENTRUM #3 BILOBED	1 1.3	1 1.6	1 1.2	0 0.0	1 5.6	1 5.0	1 4.3	0 0.0
THORACIC CENTRUM #5 SPLIT	0 0.0	1 1.6	0 0.0	0 0.0	0 0.0	1 5.0	0 0.0	0 0.0
THORACIC CENTRUM #1 BILOBED	4 5.3	1 1.6	3 3.6	0 0.0	3 16.7	1 5.0	2 8.7	0 0.0
THORACIC CENTRUM #1 POORLY OSSIFIED	1 1.3	4 6.2	1 1.2	4 7.8	1 5.6	4 20.0	1 4.3	4 28.6
THORACIC CENTRUM #2 BILOBED	0 0.0	0 0.0	0 0.0	1 2.0	0 0.0	0 0.0	0 0.0	1 7.1
THORACIC CENTRUM #5 BILOBED	1 1.3	1 1.6	0 0.0	0 0.0	1 5.6	1 5.0	0 0.0	0 0.0
THORACIC CENTRUM #9 BILOBED	4 5.3	1 1.6	3 3.6	2 3.9	4 22.2	1 5.0	3 13.0	1 7.1
THORACIC CENTRUM #11 SPLIT	0 0.0	1 1.6	1 1.2	0 0.0	0 0.0	1 5.0	1 4.3	0 0.0
THORACIC CENTRUM #3 POORLY OSSIFIED	0 0.0	0 0.0	0 0.0	1 2.0	0 0.0	0 0.0	0 0.0	1 7.1
THORACIC CENTRUM #7 BILOBED	0 0.0	1 1.6	0 0.0	0 0.0	0 0.0	1 5.0	0 0.0	0 0.0

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED SKELETALLY[d]	75	64	82	51	18	20	23	14
REDUCED NUMBER OF CAUDAL SEGMENTS (5 OR LESS)	0 0.0	1 1.6	0 0.0	0 0.0	0 0.0	1 5.0	0 0.0	0 0.0
SOME PROXIMAL PHALANGES (FORELIMB) POORLY OSSIFIED	14 18.7	6 9.4	13 15.7	7 13.7	8 44.4	5 25.0	8 34.8	5 35.7
SOME PROXIMAL PHALANGES (FORELIMB) UNOSSIFIED	10 13.3	10 15.6	7 8.4	16 31.4	7 38.9	7 35.0	6 26.1	6 42.9
SOME PROXIMAL PHALANGES (HINDLIMB) POORLY OSSIFIED	32 42.7	22 34.4	28 33.7	14 27.5	17 94.4	12* 60.0	15 65.2	10 71.4
MAJORITY PROXIMAL PHALANGES (HINDLIMB) POORLY OSSIFIED	6 8.0	11 17.2	11 13.3	1 2.0	4 22.2	9 45.0	9 39.1	1 7.1
SOME PROXIMAL PHALANGES (HINDLIMB) UNOSSIFIED	28 37.3	26 40.6	41 49.4	8 15.7	11 61.1	16 80.0	20 87.0	6 42.9
MAJORITY PROXIMAL PHALANGES (HINDLIMB) UNOSSIFIED	21 28.0	16 25.0	15 18.1	9 17.6	11 61.1	10 50.0	10 43.5	7 50.0
ALL PROXIMAL PHALANGES (HINDLIMB) UNOSSIFIED	23 30.7	15 23.4	24 28.9	32 62.7	9 50.0	8 40.0	13 56.5	12 85.7
STERNEBRA #1 POORLY OSSIFIED	1 1.3	1 1.6	1 1.2	0 0.0	1 5.6	1 5.0	1 4.3	0 0.0
STERNEBRA #2 POORLY OSSIFIED	5 6.7	3 4.7	2 2.4	3 5.9	5 27.8	3 15.0	1 4.3	3 21.4
STERNEBRA #3 POORLY OSSIFIED	4 5.3	3 4.7	4 4.8	2 3.9	3 16.7	3 15.0	4 17.4	2 14.3
STERNEBRA #4 POORLY OSSIFIED	17 22.7	14 21.9	15 18.1	17 33.3	11 61.1	9 45.0	11 47.8	10 71.4

*= significantly different from control (0.0 MG/KG/DAY) at .05 level using two-tailed Fisher's exact test.
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
NUMBER EXAMINED SKELETALLY[d]	75	64	83	51	18	20	23	14
STERNEBRA #5 POORLY OSSIFIED	32 42.7	26 40.6	40 48.2	23 45.1	16 88.9	13 65.0	19 82.6	13 92.9
STERNEBRA #6 POORLY OSSIFIED	0 0.0	2 3.1	0 0.0	1 2.0	0 0.0	2 10.0	0 0.0	1 7.1
STERNEBRA #4 BILOBED	1 1.3	0 0.0	9 10.8	3 5.9	1 5.6	0 0.0	8 34.8	2 14.3
STERNEBRA #5 BILOBED	18 24.0	12 18.7	22 26.5	11 21.6	11 61.1	10 50.0	14 60.9	7 50.0
STERNEBRA #5 UNOSSIFIED	8 10.7	3 4.7	6 7.2	8 15.7	7 38.9	3 15.0	5 21.7	8 57.1
STERNEBRA #5 SPLIT	4 5.3	4 6.2	5 6.0	2 3.9	4 22.2	4 20.0	5 21.7	2 14.3
STERNEBRA #3 BILOBED	1 1.3	0 0.0	1 1.2	0 0.0	1 5.6	0 0.0	1 4.3	0 0.0
STERNEBRA # 3 SPLIT	0 0.0	0 0.0	1 1.2	0 0.0	0 0.0	0 0.0	1 4.3	0 0.0
STERNEBRA #4 SPLIT	1 1.3	0 0.0	1 1.2	0 0.0	1 5.6	0 0.0	1 4.3	0 0.0

None significantly different from control (0.0 MG/KG/DAY)
See footnotes on last page of table.

TABLE 10

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

SUMMARY OF VARIATIONS IN FETUSES AND LITTERS[a]

DOSE GROUP: MG/KG/DAY	FETUSES 0	500	1500	3000	LITTERS 0	500	1500	3000
TOTAL VARIATIONS								
NUMBER WITH EXTERNAL VARIATIONS	9	9	15	11	8	9	9	7
PERCENT WITH EXTERNAL VARIATIONS	5.5	6.5	8.5	10.0	38.1	40.9	39.1	41.2
NUMBER WITH SOFT TISSUE VARIATIONS	44	39	40	35	15	16	18	13
PERCENT WITH SOFT TISSUE VARIATIONS	49.4	52.0	43.0	59.3	71.4	72.7	78.3	76.5
NUMBER WITH SKELETAL VARIATIONS	75	64	83	51	18	20	23	14
PERCENT WITH SKELETAL VARIATIONS	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
TOTAL NUMBER WITH VARIATIONS	123	107	127	88	18	22	23	14
TOTAL PERCENT WITH VARIATIONS	75.0	77.0	72.2	80.0	85.7	100.0	100.0	82.4

None significantly different from control (0.0 MG/KG/DAY)

[a] For all findings, the number (of fetuses affected or litters with one or more affected fetuses) is presented on top and the percentage of the total (fetuses or litters) examined is presented beneath. A single fetus may be represented more than once in listing individual defects. Only live fetuses were examined.

[b] All fetuses were examined externally.

[c] Approximately 50% of each litter were examined viscerally (Staples, 1974), and for soft tissue craniofacial defects (Wilson, 1965; van Julsingha and Bennett, 1977).

[d] Approximately 50% of each litter were examined for skeletal defects after staining with Alizarin Red S.

UNION CARBIDE

BUSHY RUN RESEARCH CENTER

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GOOD LABORATORY PRACTICES COMPLIANCE

The portions of the study conducted at the Bushy Run Research Center were conducted in full compliance with the Good Laboratory Practices (GLP) Standards promulgated by the U. S. Environmental Protection Agency Toxic Substances Control [Federal Register 48(230), 53922-53944, 1983].

Prepared by:

T.L. Neeper-Bradley 9.28.90
T. L. Neeper-Bradley, Ph.D. Date
Study Director

PATH/esk/1685P-2
09-19-90

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Quality Assurance Unit Study Inspection Summary

Test Substance: Union Carbide® Organofunctional Silane A-187

Study: Developmental Toxicity Evaluation, Administered by Gavage to Fischer 344 Rats

Study Director: T. L. Neeper-Bradley, Ph.D.

The Quality Assurance Unit of BRRC conducted the inspections listed below and reported the results to the study director and to management on the dates indicated. It is the practice of this Quality Assurance Unit to report the results of each inspection to both the study director and management.

Inspection Date	Inspection Type	Date QAU Report Issued To Study Director	Date QAU Report Issued To Management
10-24-88	Protocol, Probe Study	10-25-88	10-27-88
10-27-88	Event-Animal Receipt, Probe Study	10-27-88	12-14-88
11-2-88	Protocol, Full Study	11-2-88	11-7-88
11-8-88	Event-Mating, Probe Study	11-8-88	12-14-88
11-15-88	Event-Dosing, Probe Study	11-16-88	12-14-88
11-30-88	Event-Sacrifice, Probe Study	11-30-88	12-14-88
12-1-88	Event-Animal Receipt, Full Study	12-2-88	12-14-88
12-12-88	Protocol Amendment #1, Probe and Full Studies	12-13-88	12-15-88
12-20-88	Event-Dosing, Full Study	12-20-88	1-24-89
1-5-89	Event-Sacrifice, Full Study	1-5-89	1-24-89
1-6-89	Event-Fetal Visceral Examination, Full Study	1-23-89	1-24-89
1-7-89	Event-Fetal External Examination, Full Study	1-23-89	1-24-89

Inspection Date	Inspection Type	Date QAU Report Issued To Study Director	Date QAU Report Issued To Management
4-13 to 5-16-89	Analytical Data and Report, Probe and Full Studies	5-16-89	11-30-90
5-4 to 5-17-89	Raw Data and Report, Probe Study	5-19-89	11-30-90
5-4 to 6-13-89	Raw Data and Report, Full Study	6-15-89	11-30-90
7-13-89	Protocol Amendment #2, Probe and Full Studies	7-19-89	7-24-89
4-12-90	Protocol Amendment #3, Probe and Full Studies	4-13-90	4-19-90
11-29-90	Archives	11-30-90	11-30-90

Linda J. Calisti 12/18/90
Linda J. Calisti, Manager Date
Good Laboratory Practices/Quality Assurance

APPENDIX 1

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Analytical Chemistry Report

(23 pages)

APPENDIX 1

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Analytical Chemistry Report

SUMMARY

The concentration of Organofunctional Silane A-187 (A-187) in corn oil was determined using gas chromatography. Chemical analyses for the developmental toxicity dose-range finding and developmental toxicity studies included stability, homogeneity, and concentration verification of the dosing solutions. The stability study showed that A-187 remained stable in corn oil at concentrations of 8, 400, and 600 mg/ml for at least 21 days. The homogeneity study results indicated that the distribution of A-187 in corn oil was uniform. Concentration verification analyses on formulations used for actual dosing for the dose range-finding study showed analytical values ranging from 98.8 to 102.4 percent of nominal. Concentration verification analyses on formulations used for actual dosing for the developmental toxicity study showed analytical values ranging from 104.5 to 105.7 percent of nominal.

INTRODUCTION

A developmental toxicity dose-range finding study of A-187 administered by gavage to Fischer 344 rats was conducted at the Bushy Run Research Center (BRRC). The concentrations of A-187 designated for this study were 0, 8, 80, 200, and 400 mg/ml (0, 40, 400, 1000, and 2000 mg/kg/day). A stability and homogeneity study of the 8 and 400 mg/ml dosing formulations was initiated prior to the onset of actual dosing. In addition, actual dosing solutions were prepared once before the study and analyzed prior to use for A-187 concentration.

Following the dose-range finding study, the developmental toxicity evaluation of A-187 in Fischer 344 rats was conducted. The concentrations of A-187 designated for use in this study were 0, 100, 300, and 600 mg/ml (0, 500, 1500, and 3000 mg/kg/day). Validation of the stability and homogeneity of a 600 mg/ml dosing solution was initiated prior to actual dosing. Solutions prepared for actual dosing were prepared once before the study and analyzed prior to use for A-187 concentration.

CHEMICAL

A 5 gallon container of A-187 was received from Union Carbide Corporation, Sistersville, WV on October 5, 1988. The sample bore the Lot Number 1119DF082888 and was assigned BRRC Sample Number 51-431. An analysis of the test material was performed at the Union Carbide Good Laboratory Practice Skill Center (South Charleston, WV). The results confirmed that the test material was at least 98% pure. The report is included as Attachment 1 to this appendix.

EQUIPMENT

A Hewlett-Packard 5880 Gas Chromatograph (GC) equipped with a flame-ionization detector, automatic sampler, and Level 1v integrator was used for all analyses. The GC operating parameters are listed in Table 1.

METHODS

The procedure for the determination of A-187 in corn oil was a method developed at BRRC and is discussed briefly below.

Dosing Solution Preparation

The following table summarizes the dosage levels used in the studies:

Dose-Range Finding Study		Developmental Toxicity Study	
Target Dose (mg/kg/day)	Nominal Concentration[a] (mg/ml)	Target Dose (mg/kg/day)	Nominal Concentration[a] (mg/ml)
2000.0	400.0	3000.0	600.0
1000.0	200.0	1500.0	300.0
400.0	80.0	500.0	100.0
40.0	8.0	0.0	0.0
0.0	0.0		

[a]Nominal concentration was based on a dose volume of 5 ml/kg animal weight.

Dosing solutions were prepared by adding the appropriate amount of A-187 to a volumetric flask and diluting to volume with corn oil. Each solution was mixed manually by repeated inversions.

Analysis of Dosing Solutions

A standard stock solution of A-187 (1 mg/ml) was prepared as needed by weighing 0.1 g of A-187 into a 100 ml volumetric flask and diluting to volume with toluene (Burdick & Jackson, Muskegon, MI). Standards (100 and 500 ng/µl) were prepared by diluting the stock solution with toluene. A standard curve ranging from 100 to 1000 ng/µl was generated for each analysis session.

An aliquot of each dosing solution was appropriately diluted with toluene. One microliter of each diluted dosing solution was injected onto the GC.

The measured concentration of each sample was calculated from the equation for the standard curve developed by linear regression.

RESULTS

Stability Study

Table 2 contains a summary of results from the stability study conducted on the 8, 400, and 600 mg/ml dosing solutions of A-187 in corn oil. The 8 and 400 mg/ml dosing solutions were analyzed for concentration of A-187 on 0, 7, 14, 17, and 21 days. The 600 mg/ml dosing solution was analyzed for concentration of A-187 on 0, 7, 14, and 18 days. The measured concentrations of the 8, 400, and 600 mg/ml dosing solutions ranged from 92.0 to 103.6, 94.6 to 109.6, and 94.9 to 104.6 percent of nominal, respectively. These results indicated that A-187 in corn oil remained stable at the specified concentrations for at least 21 days when stored at room temperature.

Homogeneity Study

Homogeneity of each dosing solution (8, 400, and 600 mg/ml) was evaluated to ensure that A-187 was uniformly distributed throughout the formulation by the proposed mixing procedure. One sample was analyzed from three regions of each solution (top, middle, and bottom). The results of the homogeneity study are presented in Table 3. The mean concentrations (± SD) of A-187 in the 8, 400, and 600 mg/ml solutions were 103.6 (± 1.7), 105.9 (± 1.7), and 104.6 (± 1.2) percent of nominal, respectively.

Concentration Verification

Table 4 contains a summary of the results for the dose-range finding study concentration verification analyses of A-187 in corn oil. Dosing solutions were prepared once and analyzed prior to dosing. The measured concentrations ranged from 98.8 to 102.4 percent of nominal. A-187 was not detected in the control dosing solution.

Table 5 contains a summary of the results for the developmental toxicity study concentration verification analyses of A-187 in corn oil. Dosing solutions were prepared once and analyzed prior to dosing. The measured concentrations ranged from 104.5 to 105.7 percent of nominal. A-187 was not detected in the control dosing solution.

Prepared and Reviewed by:

M. A. Vrbanic 11-29-90

M. A. Vrbanic, B.A. Date
Analytical Chemist

Table 1

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Gas Chromatographic Operating Parameters

Instrument:	Hewlett-Packard 5880 Gas Chromatograph (GC)
Column:	DB-1 30 m x 0.3 mm i.d. fused silica capillary, 1.0 um film thickness, (J & W Scientific)
Detector:	Flame Ionization (FID) Hydrogen flow ~30 ml/min. Air flow ~400 ml/min. Helium auxiliary ~30 ml/min.
Carrier:	Helium, ~2.0 ml/min
Split flow:	~30 ml/min
Injector temperature:	250°C
Detector temperature:	300°C
Oven Temperature:	190°C, isothermal
Run Time:	6 minutes
Injection volume:	1 ul
Limit of Detection:	~0.01 mg/ml

Table 2

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Results of the Stability Study[a]

Nominal Concentration = 8.0 mg/ml

Date of Analysis	Stability Day	Measured Concentration (mg/ml)	% of Nominal
10-28-88	0[b]	8.29	103.6
11-04-88	7	7.56	94.5
11-11-88	14	7.36	92.0
11-14-88	17	8.28	103.5
11-18-88	21	8.21	102.6

Nominal Concentration = 400.0 mg/ml

Date of Analysis	Stability Day	Measured Concentration (mg/ml)	% of Nominal
10-28-88	0[b]	423.7	105.9
11-04-88	7	402.0	100.5
11-11-88	14	378.3	94.6
11-14-88	17	438.2	109.6
11-18-88	21	435.0	108.8

[a]The measured concentration and % of nominal are reported as means of duplicate analyses.
[b]The measured concentration and % of nominal are reported as means of triplicate analyses for the homogeneity study.

Table 2 (continued)

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Results of the Stability Study[a]

Nominal Concentration = 600.0 mg/ml

Date of Analysis	Stability Day	Measured Concentration (mg/ml)	% of Nominal
12-05-88	0[b]	627.3	104.6
12-12-88	7	617.2	102.8
12-19-88	14	620.4	103.4
12-23-88	18	569.3	94.9

[a]The measured concentration and % of nominal are reported as means of duplicate analyses.
[b]The measured concentration and % of nominal are reported as means of triplicate analyses for the homogeneity study.

Table 3

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Results of the Homogeneity Study

Nominal Concentration = 8.0 mg/ml

Area of Sampling	Measured Concentration (mg/ml)	% of Nominal
Top	8.21	102.6
Middle	8.44	105.5
Bottom	8.21	102.6
Mean	8.29	103.6
Standard Deviation	0.13	1.7

Nominal Concentration = 400.0 mg/ml

Area of Sampling	Measured Concentration (mg/ml)	% of Nominal
Top	421.2	105.3
Middle	418.6	104.6
Bottom	431.4	107.8
Mean	423.7	105.9
Standard Deviation	6.8	1.7

Nominal Concentration = 600.0 mg/ml

Area of Sampling	Measured Concentration (mg/ml)	% of Nominal
Top	627.3	104.6
Middle	620.4	103.4
Bottom	634.1	105.7
Mean	627.3	104.6
Standard Deviation	6.8	1.2

Table 4

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-137 Administered by Gavage to Fischer 344 Rats

Results of Concentration Verifications for the Dose Range-Finding Study[a]

Nominal Concentration (mg/ml)	Measured Concentration (mg/ml)	% of Nominal
0.0	<MDL[b]	--
8.0	8.20	102.4
80.0	80.7	100.9
200.0	197.4	98.8
400.0	397.9	99.5

[a]The measured concentration and % of nominal are reported as means of duplicate analyses.
[b]Less than the minimum detection limit (approximately 0.01 mg/ml).

Table 5

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Results of Concentration Verifications for the Developmental Toxicity Study[a]

Nominal Concentration (mg/ml)	Measured Concentration (mg/ml)	% of Nominal
0.0	<MDL[b]	--
100.0	105.7	105.7
300.0	315.3	105.1
600.0	626.8	104.5

[a]The measured concentration and % of nominal are reported as means of duplicate analyses.
[b]Less than the minimum detection limit (approximately 0.01 mg/ml).

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ATTACHMENT 1

BUSINESS CONFIDENTIAL PROJECT REPORT

γ-GLYCIDOXYPROPYLTRIMETHOXYSILANE (UCC ORGANOFUNCTIONAL SILANE A-187)

GLP ANALYSIS - FINAL REPORT

AUTHORS: S. L. Wellons (2)
A. M. Harrison (4)
P. C. Price (2)

SUPERVISORS: L. D'Esposito
T. L. Dawson (3)

DATE: May 11, 1990

STUDY #: 88-SLW-53

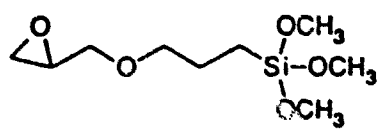
FILE NO: 37712

SUMMARY Two samples of UCC Organofunctional silane A-187 (A-187) for toxicity testing at Bushy Run Research Center were analyzed by Good Laboratory Practice standards (GLP) to meet EPA requirements. Gas chromatography-mass spectrometry (GC/MS) and nuclear magnetic resonance spectroscopy (NMR) techniques were independently used to confirm the samples' identity. Sample purities, measured by GC analyses, are at least 98%. All raw data, documentation, records, protocols, sample and final reports are being retained.

INTRODUCTION Dr. William F. Gorham, this study's sponsor, requested that the Bushy Run Research Center (BRRC) test A-187 in several toxicity studies. Such studies are required to be conducted in compliance with the GLP standards established by the EPA. The applicable regulations are "TSCA, 40 CFR, Part 792" and "FIFRA, 40 CFR, Part 160." The TSCA (Toxic Substances Control Act) and FIFRA (Federal Insecticide, Fungicide and Rodenticide Act) GLP standards are essentially equivalent. A part of these standards require that the toxicology study be conducted with materials whose identity and purity have been verified analytically.

Two 100 gram samples of A-187 (88-SLW-60; BRRC# 51-431; Sistersville lot# 1119DF082888 03341E and 88-SLW-78; BRRC# 52-515B; Sistersville lot# 1117OH061289) were submitted from BRRC by Ms. Marlyn A. Vrbanic and by Dr. Irvin M. Pritts, respectively, for analytical characterization. A GLP protocol describing the analytical characterization of the samples was prepared (Appendix 1). The protocol called for structural identification by NMR and GC/MS and the GC measurement of any impurities at the concentration of 0.1 weight percent or greater identified by GC/MS.

The Chemical Abstracts Service Registry number (CAS #) of A-187 is 2530-83-8. Its CAS name in silane, trimethoxy (3-(oxiranylmethoxy)propyl)-. Its chemical name is γ-Glycidoxypropyltrimethoxysilane.



γ-Glycidoxypropyltrimethoxysilane (A-187)

KEY WORDS: γ-GLYCIDOXYPROPYLTRIMETHOXYSILANE. GLP. GOOD LABORATORY PRACTICE. BRRC. A-187.

RESEARCH AND DEVELOPMENT
UNION CARBIDE CHEMICALS AND PLASTICS COMPANY INC.
SOUTH CHARLESTON, WEST VIRGINIA

ATTACHMENT 1 (Continued)

BUSINESS CONFIDENTIAL

DISCUSSION The data from the analyses are summarized below.

NMR Analyses Proton NMR data were collected in the UCC NMR Skill Center using a General Electric GN-300NB spectrometer. The acquisition parameters are indicated in the figures; for the ^{1}H NMR spectra, the pulses used correspond to <3° flip angles; the ^{13}C flip angles were 30°; the $^{13}C\{^{1}H\}$ (proton decoupled ^{13}C) spectra used Waltz 16 modulation for ^{1}H decoupling. The spectra were not acquired under quantitative conditions; the acquisition conditions were established to determine the identity of the major component and to look for any substantial impurities. Each compound was dissolved in deuterochloroform for analysis; tetramethylsilane (TMS) was added to each sample to provide an internal chemical shift reference. The ^{13}C spectra were referenced to TMS by using the solvent triplet as a secondary reference (77 ppm). The TMS and deuterochloroform were not analyzed, but used as received.

The ^{1}H NMR spectra obtained from the samples 88-SLW-60 and -78 are shown in Figures 1-2. The two spectra are essentially identical. The observed chemical shifts and relative intensities are appropriate for A-187, with the strong methoxy hydrogen singlet at 3.6 ppm, the central methylene between the other two methylenes at 1.70 ppm, the methylene bonded to silicon at 0.67 ppm, the non-equivalent hydrogens of the methylene group in the ring at 2.59 and 2.77 ppm, the methine hydrogen in the ring at 3.13 ppm, and the other two methylenes adjacent to the ether-type oxygen between 3.3 and 3.8 ppm; these spectra are complicated by the chiral center in the molecule making all the methylene pairs diastereotopic, leading to complex splitting patterns. The observed spectra are consistent with the samples being A-187.

The $^{13}C\{^{1}H\}$ spectra for the same samples are shown in Figures 3-4. No unusual or unexpected resonances are seen. The methoxy carbons appear at 49.9 ppm; the two methylenes bound to the ether oxygen are at 71.0 and 72.9 ppm; the methine carbon in the ring is at 50.3 ppm; the ring methylene carbon at 43.6 ppm; the central methylene between the other two methylenes is at 22.4 ppm; and the methylene bound to silicon is at 4.8 ppm and exhibits small ^{29}Si satellites as expected. These assignments are consistent with spectra of similar compounds which are collected by Sadtler Research Laboratories in their "Standard Spectra." The NMR spectra are totally consistent with the samples being A-187 which contains no major organic impurities.

GC/MS Analysis Electron ionization (EI) and isobutane chemical ionization (CI) mass spectral data were collected in the UCC MS Skill Center using a Finnigan TSQ-70 mass spectrometer interfaced to a Hewlett-Packard 5890 gas chromatograph. The samples were analyzed as received by injecting 0.05 µL aliquots onto DB-1 capillary columns held at 30°C for 4 minutes, and then programmed to 250°C at 8 degrees/minute. Figures 5-6 show the EI total ion current chromatogram for "88-SLW-60" and "88-SLW-78" (scanned from m/z 10 to m/z 510 EI mode, and m/z 60-560 in the CI mode). The chromatograms are annotated with information based on EI and CI spectra. EI and CI spectra of the major component were consistent with the structure of A-187. The main peak (possibly greater than 0.1 %) eluting in front of the matrix peak is an isomer of the desired compound. No other components were observed co-eluting with the major component.

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CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC Skill centers indicate that the samples submitted for analysis are A-187. These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purities, measured by GC analyses, are at least 98%.

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BUSINESS CONFIDENTIAL

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NOTEBOOK REFERENCE: 88-SLW-53 and related pages

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GLP Compliance This study was conducted so as to fully comply with the following GLP standards: TSCA 40 CFR Part 792
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Stephen L. Wellons 5/8/90
Stephen L. Wellons, Ph. D., Study Director date

Arnold M. Harrison 5/8/90
Arnold M. Harrison, Ph. D., NMR Skill Center date

Philip C. Price 5/8/90
Philip C. Price, Ph. D., MS Skill Center date

SLW/AMH/PCP
Date Study initiated: September 20, 1989
Manuscript date (Date Study completed): April 25, 1990
Attachments: 1 Table
6 Figures
Sample Protocol
QAU statement

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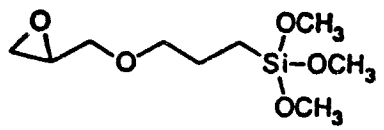

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GC Analyses A Hewlett-Packard 5700 gas chromatograph equipped with a thermal conductivity detector was used to analyze the samples. Aliquots (1 µL) were injected manually onto a 12' x 1/8" od. stainless steel column containing 20% OV-101 on 60/80 mesh Chromosorb W-HP. The oven temperature started at 150°C and then was programmed to 320° at 8°/minute and held for 4 minutes. The raw data are given in Table 1.

CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC Skill centers indicate that the samples submitted for analysis are A-187. These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purities, measured by GC analyses, are at least 98%.

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Stephen L. Wellons 5/8/90
Stephen L. Wellons, Ph. D., Study Director — date

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ATTACHMENT 1 (Continued)

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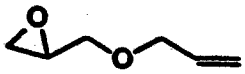
Table 1 — Gas Chromatographic Analyses of 88-SLW-60 and -78 (A-187)

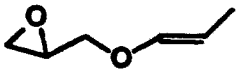
Component name	Retention time, min.	88-SLW-60 1st	88-SLW-60 2nd	88-SLW-78 1st	88-SLW-78 2nd
Methanol	1.0	.148	.143	.136	.131
Toluene	2.3	.028	.033	nd	nd
AGE	3.0	nd	nd	.075	.081
AGE isomers	3.3	nd	nd	.179	.188
Beta-products	10.2	.759	.766	.847	.848
A-187	11.7	98.762	98.725	98.350	98.327
all other impurities		.303	.333	.413	.425

Explanation of acronyms and component names

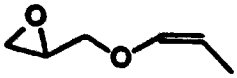
AGE - 114 mw
(allyl glycidyl ether)



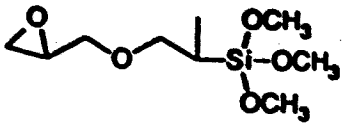
AGE isomer
(trans-propenyl glycidyl ether) - 114 mw



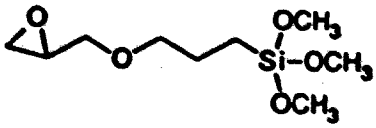
AGE isomer
(cis-propenyl glycidyl ether) - 114 mw



Beta-products - 236 mw
(2 pairs of diasteroisomers)



A-187 - 236 mw
γ-Glycidoxypropyltrimethoxysilane



ATTACHMENT 1 (Continued)

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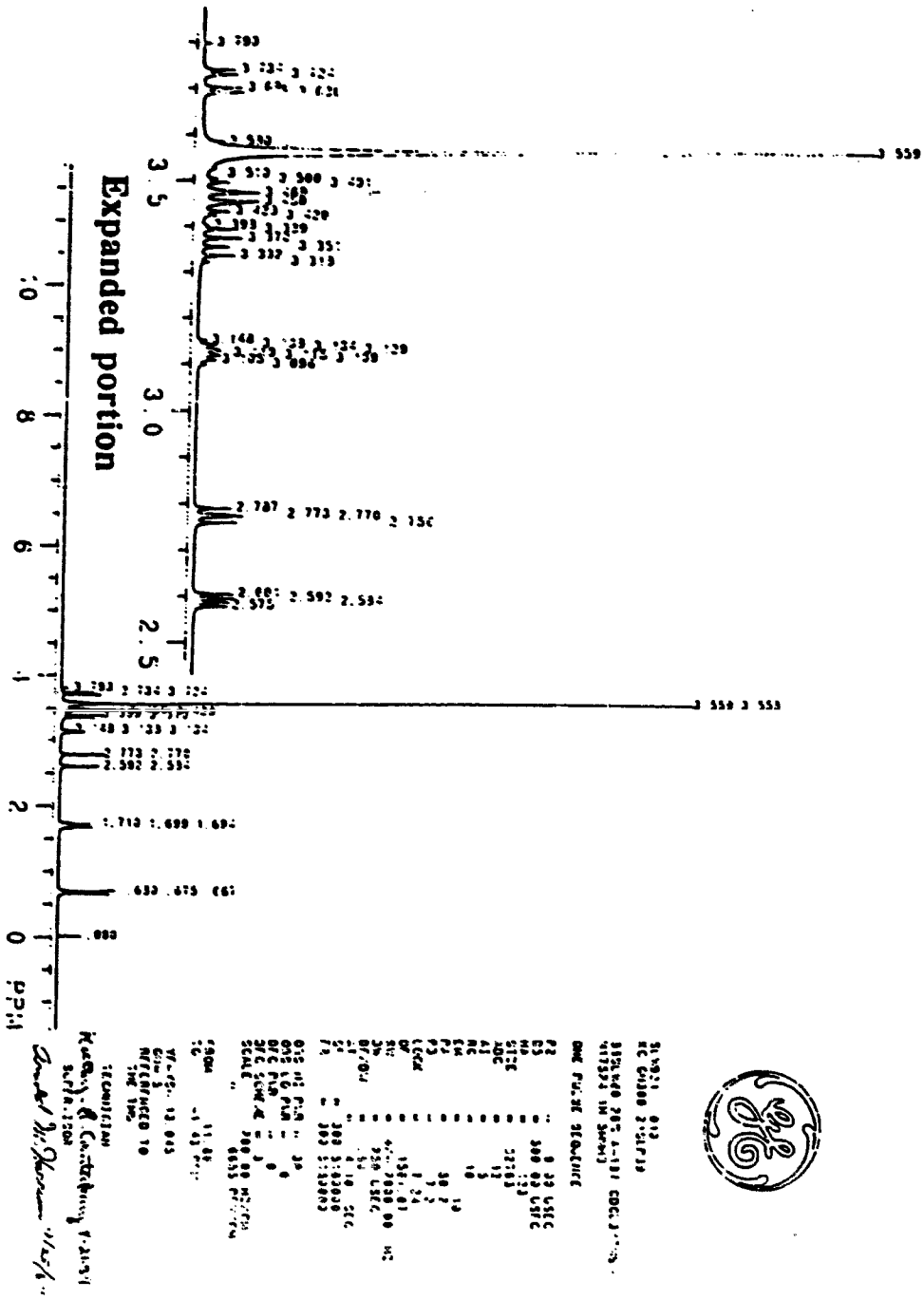
Figure 1 — ^{1}H NMR Spectrum of 88-SLW-60 (A-187)



ATTACHMENT 1 (Continued)

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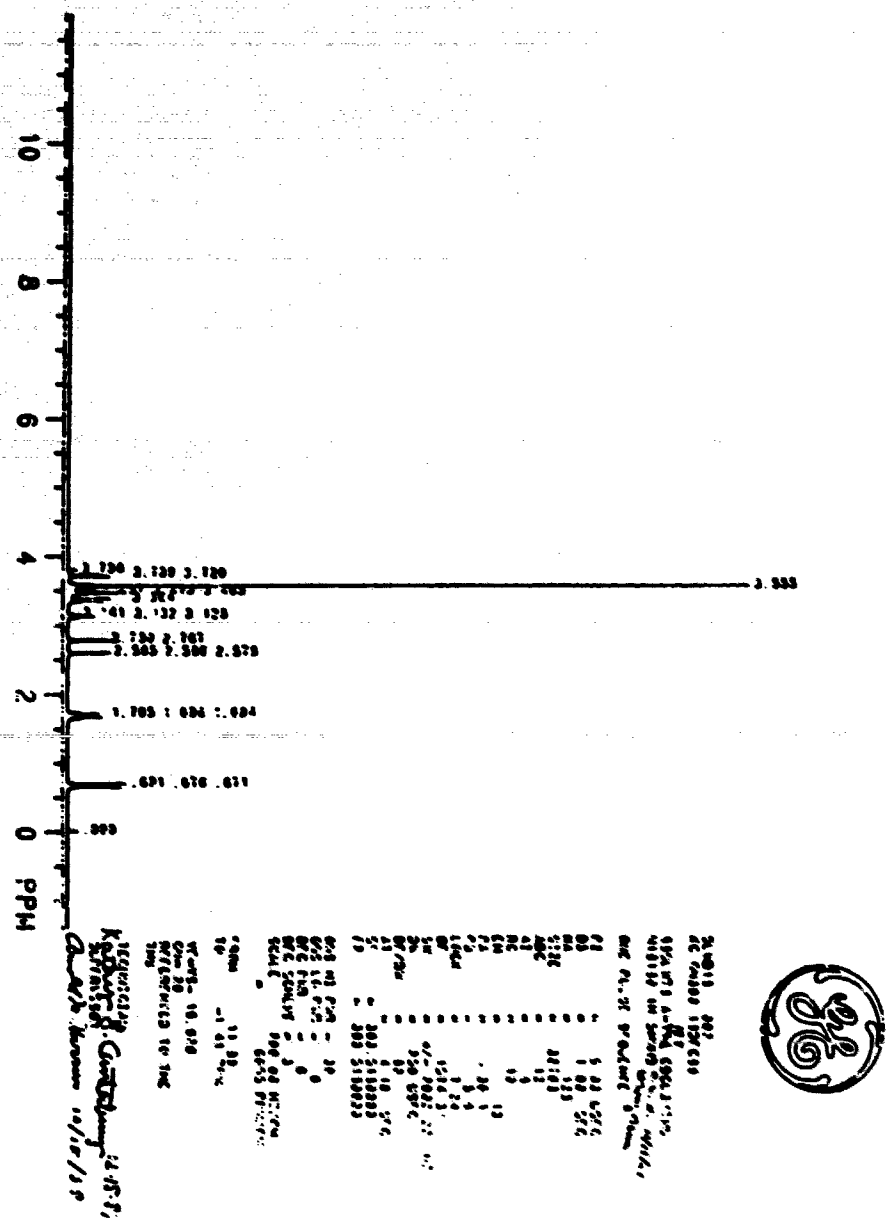
Figure 2 — ^1H NMR Spectrum of 88-SLW-78 (A-187)



ATTACHMENT 1 (Continued)

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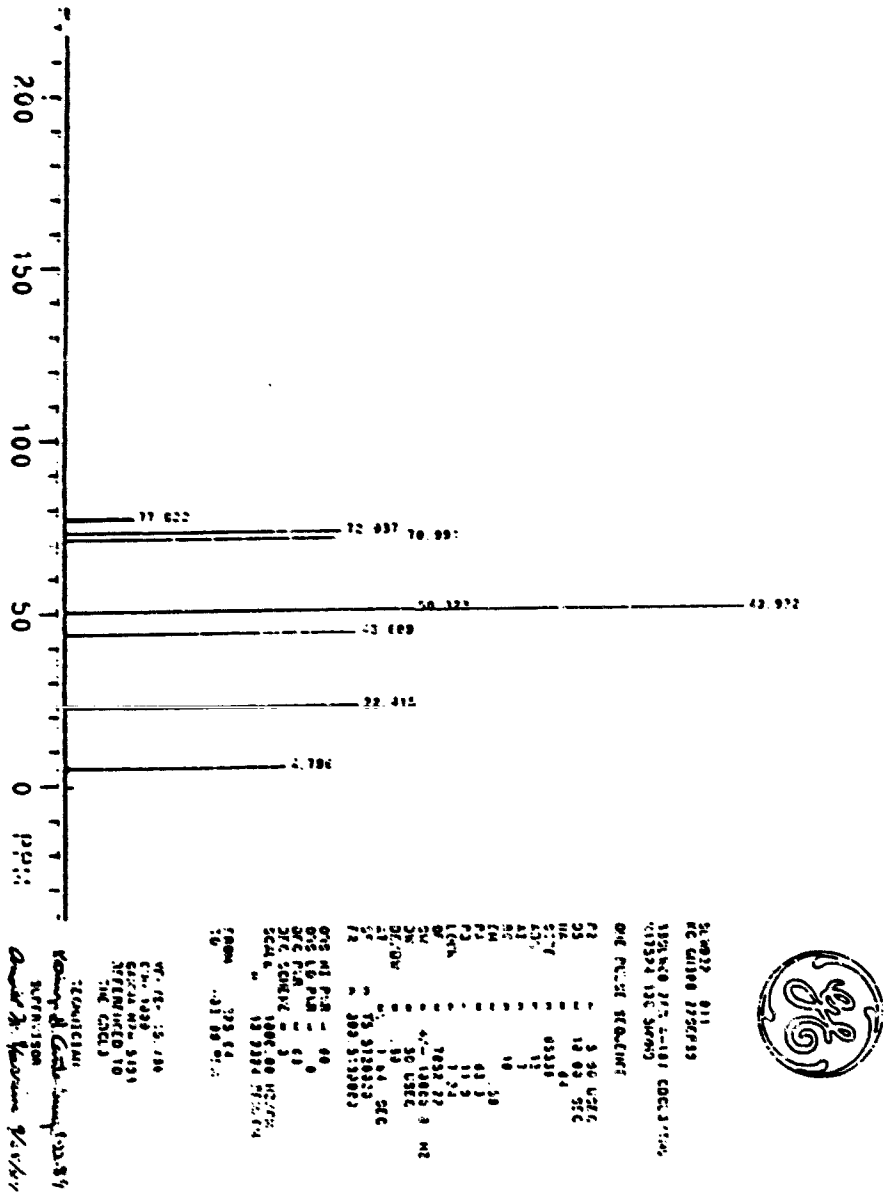
Figure 3 — ^{13}C NMR Spectrum of 88-SLW-60 (A-187)



ATTACHMENT 1 (Continued)

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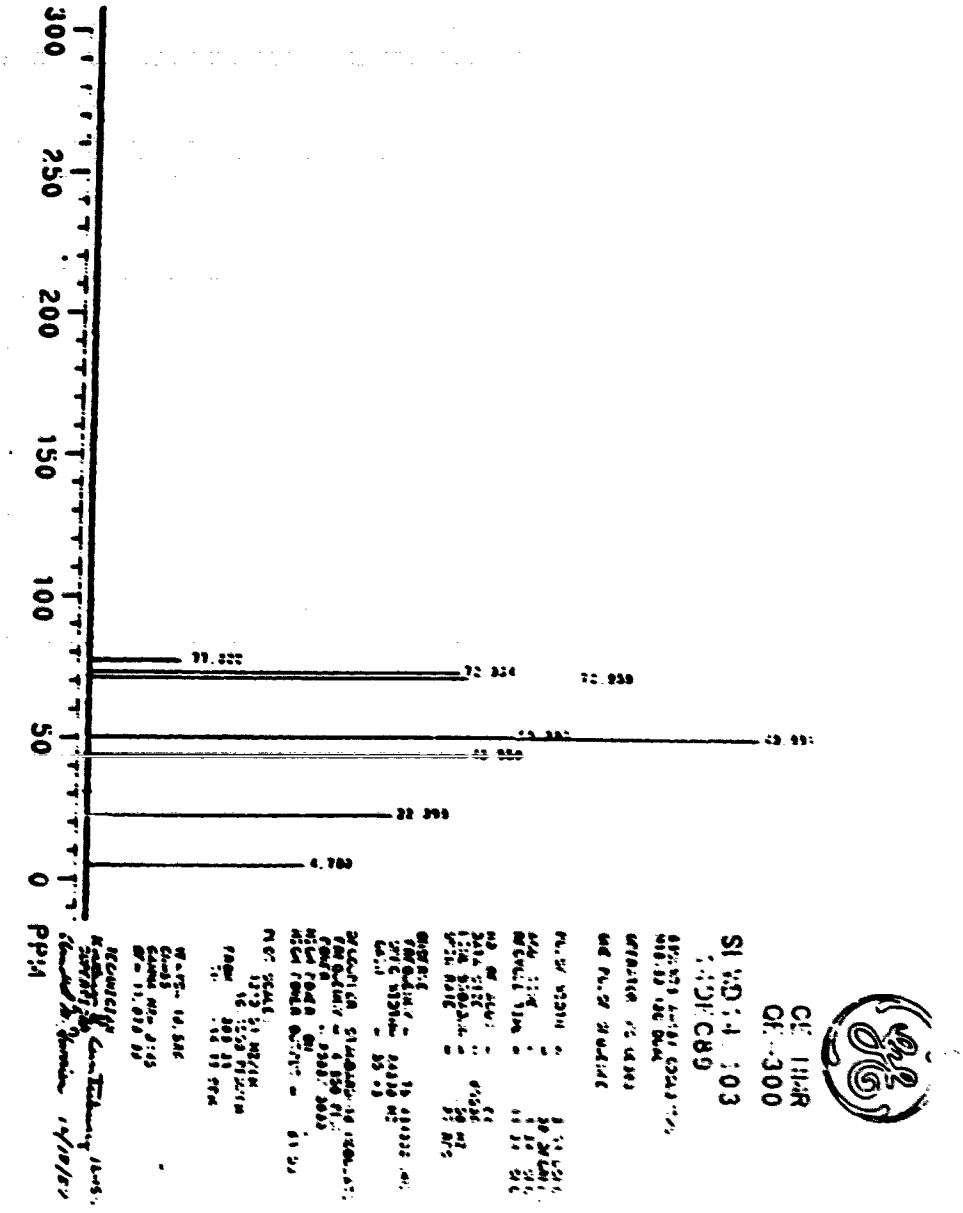
Figure 4 — ^{13}C NMR Spectrum of 88-SLW-78 (A-187)



ATTACHMENT 1 (Continued)

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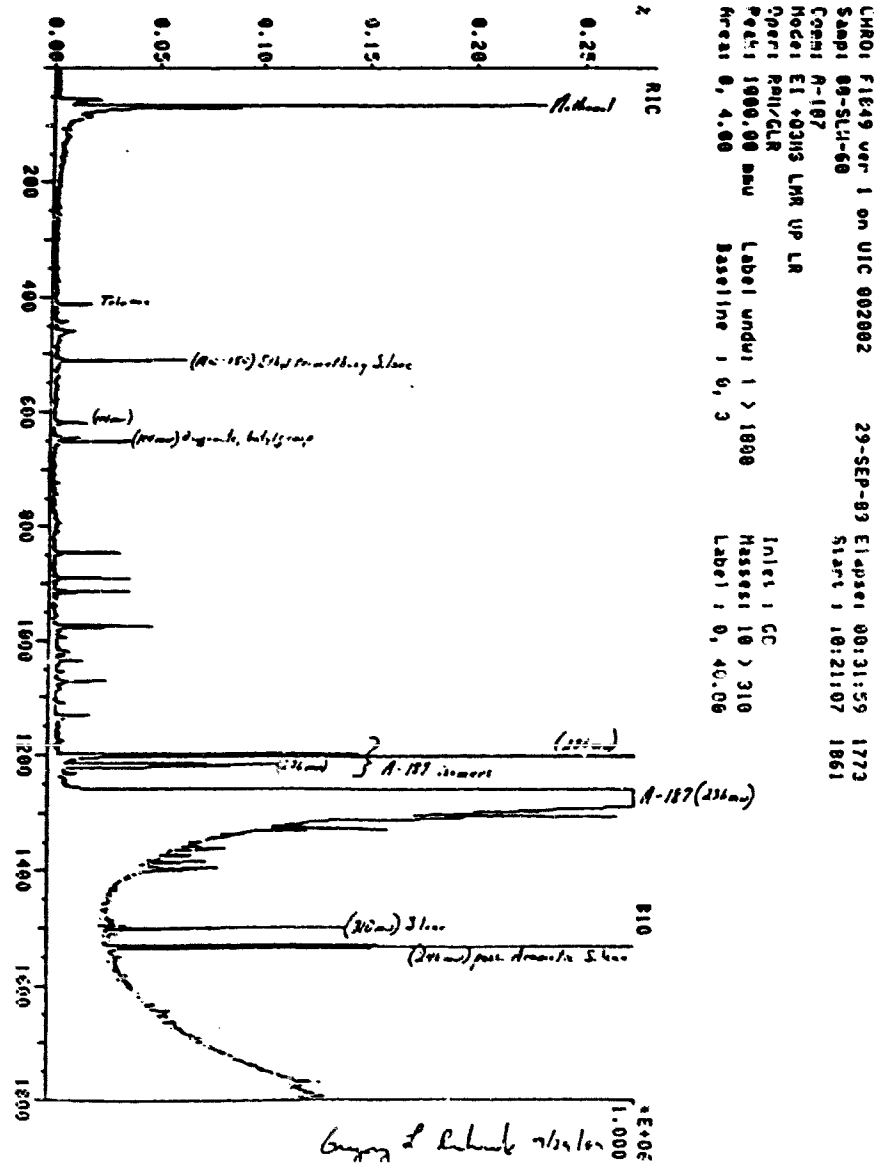
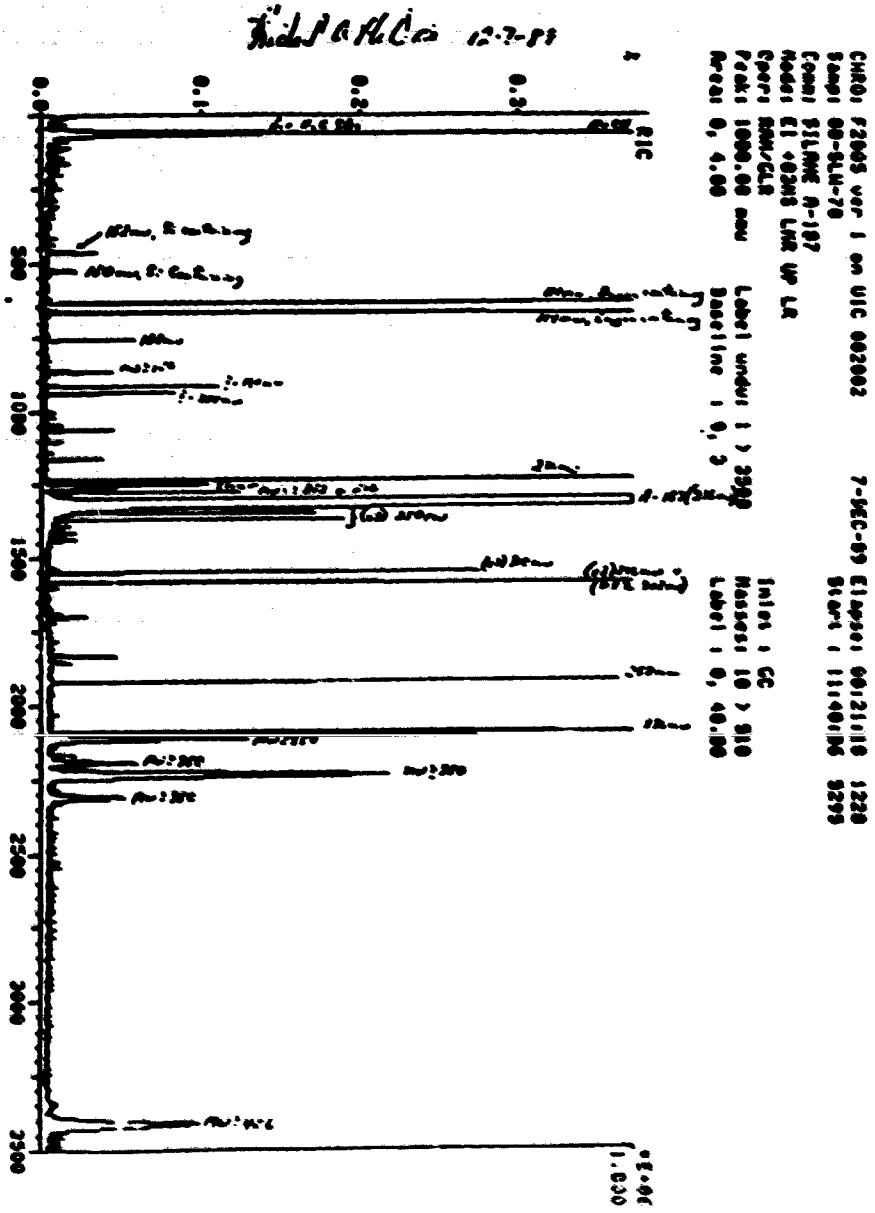
Figure 5 — Capillary GC/MS RIC of 88-SLW-60 (A-187)



ATTACHMENT 1 (Continued)

BUSINESS CONFIDENTIAL

Figure 6 — Capillary GC/MS RIC of 88-SLW-78 (A-187)



ATTACHMENT 1 (Continued)

BUSINESS CONFIDENTIAL

APPENDIX 1 88-SLW-53 Protocol

UNION CARBIDE

PROTOCOL

UNION CARBIDE CORP
Technical Center
P. O. Box 8361, South Charleston, WV 25303

GOOD LABORATORY PRACTICE STUDY

title UCC ORGANOFUNCTIONAL SILANE A-187

purpose ANALYTICAL CHARACTERIZATION OF SAMPLE(S) FOR TOXICOLOGY STUDIES AT BUSHY RUN RESEARCH CENTER

study number 88-SLW-53

sponsor SPECIALITY CHEMICALS DIVISION
UNION CARBIDE CORPORATION
39 Old Ridgebury Road,
Danbury, Conn. 06817-0001

testing facility UCC Technical Center,
So. Chas., WV 25303 (Location 511)

Proposed Starting Date: September 21, 1989
Proposed Completion Date: February 1, 1990
Estimated Date of Final Report: March 1, 1990

Reviewed and Approved by:

Union Carbide Corporation:

Stephen L. Wellons 12/10/89
Stephen L. Wellons, Ph. D. date
Good Laboratory Practices/Study Director

James L. Hansen 12/11/89
James L. Hansen, Ph. D. date
Good Laboratory Practices/Quality Assurance

Sponsor

12/15/89
William F. Gorham, Ph. D. date
Product Safety Director
Speciality Chemicals Division

Basis for the Study/Good Laboratory Practice Compliance

This study will be performed in compliance with the following standards:

Good Laboratory Practice Regulations TSCA, 40CFR, Part 792 and
FIFRA, 40CFR, Part 160.

The UCC Technical Center assures compliance of generally accepted good laboratory practices.

Page 1 of 2

ATTACHMENT 1 (Continued)

BUSINESS CONFIDENTIAL

APPENDIX 1 88-SLW-53 Protocol continued

PROTOCOL/study no.: 88-SLW-53 page 2 Sunday, December 10, 1989

Alteration of Design

Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Study Director or Sponsor.

In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification.

If the Study Director makes a change, the Sponsor shall be notified of the change as soon as possible, and written verification of the change will be the responsibility of the Study Director. All protocol changes will be signed by the Study Director and the Sponsor or representative.

Test Substance No. 1 (88-SLW-60 and -78)

Product Name	UCC Organofunctional Silane A-187
Chemical Name	gamma-Glycidoxypropyltrimethoxysilane
Source	BRRC # 51-431; Lot # 1119DF082888 03341E - UCC, Sistersville, WV BRRC # 51-515B; Lot # 1117OH061289 - UCC, Sistersville, WV
CAS Registry No.	2530-83-8
Description	clear lightly-colored liquid; ester odor.
Purity	98%, minimum
Health/Safety	toxic; stable. MSDS available on request.
Storage Conditions	room temperature conditions

Study Design

The test substance will be characterized by:

- verification of identity by proton- and carbon-NMR
- verification of identity by capillary GC/MS. An attempt will be made to identify all impurities at 0.1 wt% or greater concentration
- Measurement by GC of impurities identified and present at 0.1 wt% or greater concentrations.

Records

All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. Prior to discarding any of the above data or samples, the Sponsor will be contacted and given the option of obtaining it or arranging for continued storage. All data and samples will remain the sole property of the Sponsor and can be removed from Location 511 at the Sponsor's discretion.

Report

A final report will be submitted to the Sponsor within one month after the completion of the analysis. This report will be a comprehensive report which will include all information necessary to provide a complete and accurate description and evaluation of the analysis. A draft of the final report may be submitted to the BRRC for review. The final report will be audited by the Quality Assurance Unit and will contain a signed quality assurance statement.

ATTACHMENT 1 (Continued)

UCC BUSINESS CONFIDENTIAL

QAU STATEMENT

Quality Assurance Unit Study Inspection Summary

Test Substance: γ-GLYCIDOXYPROPYLTRIMETHOXYSILANE
(UCC ORGANOFUNCTIONAL SILANE A-187)

Study No.: 88-SLW-53

Study Director: Stephen L. Wellons, Ph.D.

The Quality Assurance Unit of the Union Carbide Technical Center conducted the inspections listed below and reported the results to the study director and management on the date indicated. It is the practice of this Quality Assurance Unit to report the results to both the study director and management.

Inspection Date	Inspection Type	Date QAU Report Issued To Study Director	Date QAU Report Issued To Management
Dec. 11, 1989	Protocol Compliance Review	Dec. 11, 1989	Dec. 11, 1989
Mar. 9, 1990	Laboratory Compliance Review	Apr. 11, 1990	Apr. 11, 1990
May 10, 1990	Final Report Compliance Review	May 10, 1990	May 10, 1990

Denise L Johnson 5/10/00
Denise L. Johnson, QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

APPENDIX 2

Developmental Toxicity Dose-Range Finding Study and Developmental Toxicity Evaluation Study of Union Carbide® Organofunctional Silane A-187 Administered by Gavage to Fischer 344 Rats

Individual In-Life Maternal Data

Clinical Observation Abbreviations:

EYB = Both Eyes, EYL = Left Eye, EYR = Right Eye

(14 pages)

TABLE 1

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
GROUP: 0.0 MG/KG/DAY

	PREGNANCY STATUS	DAY 0	6	12	15	18	21
29382	P	146.10	160.07	164.56	172.66	183.17	199.30
29381	P	151.32	166.16	174.60	187.80	208.12	242.58
29389	P	153.37	171.35	185.78	197.12	215.86	246.64
29285	NP	154.97	161.59	163.99	163.44	161.83	167.72
29300	P	158.83	168.21	172.83	180.56	185.19	196.97
29275	NP	160.97	169.[illegible]7	167.64	171.88	176.81	179.01
29327	P	161.46	176.28	182.04	187.97	194.07	210.05
29355	P	164.82	177.20	187.50	194.32	205.03	223.57
29301	P	167.16	170.97	179.60	190.37	205.68	230.45
29358	P	170.44	181.98	192.12	203.91	219.05	253.48
29351	P	177.76	187.00	202.11	211.13	234.96	268.74
29288	P	165.31	176.04	190.34	202.87	227.57	266.48
29368	P	157.27	169.43	182.06	192.01	203.76	228.20
29371	RFS	150.79	156.72	169.68	175.94	193.90	165.77
29372	P	157.07	166.21	182.57	193.15	220.55	247.53
29293	P	165.08	171.84	185.50	197.80	221.48	247.34
29299	P	168.15	177.82	195.18	201.75	228.32	257.85
29279	NP	177.58	185.79	185.86	180.45	187.03	186.02
29359	P	173.38	184.02	194.15	199.03	222.89	239.34
29331	P	162.60	173.23	187.19	189.79	221.75	245.71
29276	P	156.15	163.43	177.40	183.11	217.03	234.85
29260	P	140.07	150.82	153.44	156.85	172.62	175.39
29297	P	163.71	173.20	169.71	198.73	227.35	250.21
29386	P	163.72	178.92	190.81	197.78	222.02	236.92
29298	P	171.78	181.13	191.17	197.59	217.30	226.91
MEAN		161.69	172.63	183.84	192.20	212.08	234.69
S.D.		9.098	8.500	10.994	11.847	16.523	23.475
N		21	21	21	21	21	21

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 1

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
GROUP: 500.0 MG/KG/DAY

	PREGNANCY STATUS	DAY 0	6	12	15	18	21
29319	P	148.35	165.29	179.13	192.28	211.49	246.03
29255	P	149.79	158.66	165.72	177.25	192.45	219.59
29336	P	154.50	162.69	173.03	178.92	184.34	199.40
29417	P	145.55	152.68	160.32	165.42	180.43	184.83
29315	P	159.16	171.98	181.06	190.05	199.98	219.55
29390	P	159.85	173.89	182.46	193.67	204.69	227.16
29398	P	161.70	173.99	185.19	198.07	212.86	246.69
29313	P	165.30	175.72	180.64	186.53	193.93	210.61
29265	P	167.06	174.98	183.57	189.97	196.89	214.85
29273	P	170.28	177.99	178.16	177.83	177.10	182.58
29309	P	178.66	191.86	196.38	207.23	217.17	236.96
29350	NP	171.29	185.60	183.32	184.41	183.93	188.65
29345	P	156.38	164.29	169.16	175.21	182.52	195.18
29378	P	151.29	163.60	171.09	178.98	184.66	199.30
29341	P	156.86	164.34	181.02	188.96	212.29	233.01
29303	RFS	158.30	170.03	183.93	195.83	231.12	180.09
29318	P	169.29	176.20	187.77	177.37	212.67	239.75
29323	P	170.20	181.04	198.04	188.41	229.45	262.57
29388	P	178.79	189.09	206.02	213.92	244.04	262.21
29410	P	157.11	167.47	175.07	183.08	205.81	215.19
29322	P	150.51	159.51	171.37	177.51	203.46	218.98
29264	P	157.83	170.60	183.12	192.57	223.71	245.79
29333	P	160.11	172.58	186.33	193.62	214.18	224.92
29329	P	162.55	169.32	180.26	187.14	211.87	221.48
29262	P	171.17	185.82	201.15	209.28	244.00	258.69
MEAN		160.97	171.46	181.65	187.97	206.09	224.58
S.D.		9.218	9.753	11.246	11.705	18.542	23.192
N		23	23	23	23	23	23

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 1

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
GROUP: 1500.0 MG/KG/DAY

	PREGNANCY STATUS	DAY 0	6	12	15	18	21
29284	P	147.74	162.41	174.79	185.85	205.12	238.59
29257	P	148.81	162.27	170.38	177.80	185.49	204.57
29278	P	152.81	161.38	169.64	181.83	199.24	231.08
29311	P	155.61	163.28	171.20	183.07	199.31	229.35
29296	P	157.43	167.56	178.16	178.01	195.93	219.38
29308	P	160.15	175.18	191.34	204.86	227.86	270.85
29344	NP	162.99	175.01	172.83	173.70	169.39	178.54
29268	P	163.04	180.92	189.41	200.60	214.05	248.45
29305	P	165.81	168.64	182.25	197.56	213.13	257.48
29259	P	173.91	184.74	190.42	198.85	206.27	232.54
29366	P	181.44	193.89	200.19	208.03	215.77	239.26
29383	P	170.62	186.13	197.43	207.49	220.98	246.30
29295	P	153.92	167.32	176.76	185.00	205.91	236.28
29349	P	153.27	166.51	171.82	181.16	198.60	224.78
29409	P	162.91	175.12	189.70	182.60	222.21	248.36
29277	P	164.58	172.51	187.78	179.30	213.11	241.94
29280	P	166.52	175.68	189.63	179.70	214.31	238.47
29354	NP	174.16	177.82	176.19	165.90	176.11	175.99
29384	P	170.88	181.86	192.76	197.95	226.66	248.01
29314	P	158.69	168.78	173.33	178.98	197.22	204.17
29402	P	157.06	166.88	180.09	184.58	210.62	232.72
29302	P	161.00	170.68	177.08	182.23	205.95	213.67
29352	P	162.96	174.63	187.90	193.46	218.58	233.84
29414	P	167.41	183.30	193.49	198.48	220.06	226.40
29327	P	174.29	183.38	188.95	195.75	223.09	240.54
MEAN		162.21	173.61	183.67	189.70	210.41	235.09
S.D.		8.532	8.926	9.305	10.207	11.057	15.644
N		23	23	23	23	23	23

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 1

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL GESTATIONAL BODY WEIGHT (GRAMS)
GROUP:3000.0 MG/KG/DAY

	PREGNANCY STATUS	DAY 0	6	12	15	18	21
29403	NP	147.55	162.74	158.19	163.06	156.69	170.12
29373	P	150.16	164.57	161.24	170.49	183.42	205.77
29256	P	152.13	168.42	166.46	177.54	180.89	195.04
29347	P	155.48	164.79	166.18	172.89	176.95	190.00
29324	NP	156.51	170.28	163.63	165.26	159.70	171.70
29377	P	161.20	173.70	177.53	191.38	208.51	248.04
29312	P	131.60	167.36	177.67	186.42	197.00	229.88
29326	P	164.43	179.41	181.19	190.69	201.69	229.60
29338	P	167.75	182.43	191.33	198.22	203.72	223.15
29320	NP	170.73	182.56	177.17	181.32	177.00	187.75
29365	NP	173.10	179.53	175.45	173.50	177.32	179.87
29335	P	166.98	183.73	182.00	191.39	205.61	228.52
29416	NP	158.19	174.16	169.47	164.79	164.42	171.62
29356	P	150.36	162.64	146.12	128.00	148.58	155.26
29361	NP	156.92	155.73	157.18	143.80	156.61	157.74
29267	NP	163.80	165.56	162.85	151.30	162.79	165.03
29286	P	168.72	182.00	195.39	185.10	220.04	254.54
29370	P	181.27	188.83	202.71	196.20	232.84	267.78
29316	P	177.18	188.74	200.03	201.50	226.33	243.17
29346	P	161.45	173.24	183.37	190.86	220.26	243.95
29369	P	150.65	159.62	170.42	174.38	194.21	207.67
29325	P	155.67	164.49	175.32	180.62	189.84	195.79
29406	P	157.94	173.43	181.40	189.74	225.47	247.83
29401	P	161.38	170.93	184.58	184.63	204.46	211.05
29391	P	164.22	173.46	179.34	183.15	205.43	215.52
MEAN		161.59	173.32	179.02	182.96	201.40	221.81
S.D.		8.795	8.808	13.941	16.211	20.762	27.776
N		18	18	18	18	18	18

P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY, NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 2

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
0.0 MG/KG/DAY					
	29382	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29381	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29389	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	4	MISSING EAR TAG
	29285	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29300	NORMAL	12	6- 15	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	16	4- 21	PERIOCULAR ENCRUSTATION (EYB 14, EYR 2)
		OTHER	1	4	MISSING EAR TAG
	29275	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	4	MISSING EAR TAG
	29327	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	4	MISSING EAR TAG
	29355	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29301	NORMAL	27	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	11	MISSING EAR TAG
	29358	NORMAL	27	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	11	MISSING EAR TAG
	29351	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	3	MISSING EAR TAG
	29288	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29368	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29371	NORMAL	27	4- 20	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	EUTHANIZED - DELIVERED EARLY
		EYES/EARS/NOSE	3	2- 21	PERIOCULAR ENCRUSTATION (EYL 3)
		OTHER	1	2	MISSING EAR TAG
	29372	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	2	MISSING EAR TAG
	29293	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE

TABLE 2

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
0.0 MG/KG/DAY					
	29299	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	2	MISSING EAR TAG
	29279	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	2	MISSING EAR TAG
	29359	NORMAL	30	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	8	MISSING EAR TAG
	29331	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29276	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29260	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	1	MISSING EAR TAG
	29297	NORMAL	25	0- 17	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	7	10- 21	PERIOCULAR ENCRUSTATION (EYL 7)
	29386	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29298	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
500.0 MG/KG/DAY					
	29319	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29255	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29336	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29417	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	0	MISSING EAR TAG
	29315	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29390	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29398	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29313	NORMAL	27	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	18	PERIOCULAR ENCRUSTATION (EYR 1)
	29265	NORMAL	25	4- 18	NO SIGNIFICANT CLINICAL OBSERVATIONS

TABLE 2

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
500.0 MG/KG/DAY					
	29265	DEAD	1	21	SCHEDULED SACRIFICE
		BODY	2	19- 20	UNKEMPT
	29273	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29309	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29350	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29345	NORMAL	28	3- 19	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	20- 21	REDDENED EYES (EYL 2)
			1	4	PERIOCULAR ENCRUSTATION (EYL 1)
		OTHER	1	4	MISSING EAR TAG
	29376	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29341	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29303	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	EUTHANIZED - DELIVERED EARLY
	29318	NORMAL	29	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	3	PERIOCULAR ENCRUSTATION (EYL 1)
	29323	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	2	MISSING EAR TAG
	29388	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29410	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29322	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29264	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29333	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29329	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29262	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
1500.0 MG/KG/DAY					
	29284	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29257	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS

TABLE 2

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
1500.0 MG/KG/DAY					
	29257	DEAD	1	21	SCHEDULED SACRIFICE
	29278	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29311	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29296	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29308	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	4	MISSING EAR TAG
	29344	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29268	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29305	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29259	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29366	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29383	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29295	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29349	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29409	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	2	MISSING EAR TAG
	29277	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29280	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29354	NORMAL	29	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	3	PERIOCULAR ENCRUSTATION (EYR 1)
	29384	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29314	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	1	MISSING EAR TAG
	29402	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE

TABLE 2

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
1500.0 MG/KG/DAY					
	29302	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29352	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		OTHER	1	21	SCHEDULED SACRIFICE
	29414	NORMAL	1	0	MISSING EAR TAG
		DEAD	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
	29337	NORMAL	1	21	SCHEDULED SACRIFICE
		DEAD	31	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		OTHER	1	21	SCHEDULED SACRIFICE
3000.0 MG/KG/DAY			1	6	MISSING EAR TAG
	29403	NORMAL	27	4- 20	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	21	PERIOCULAR ENCRUSTATION (EYL 1)
	29373	NORMAL	27	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	13	MISSING EAR TAG
	29256	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29347	NORMAL	27	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	13	MISSING EAR TAG
	29324	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29377	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29312	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29326	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29338	NORMAL	28	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29320	NORMAL	27	4- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	10	MISSING EAR TAG
	29365	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29335	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29416	NORMAL	29	3- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29356	NORMAL	27	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE

TABLE 2

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INCIDENCE OF CLINICAL OBSERVATIONS BY GESTATION DAY
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	GESTATIONAL DAYS	FINDING
3000.0 MG/KG/DAY					
	29356	BEHAVIOR/CNS	2	9- 10	HYPOACTIVE
		CARDIO-PULMONARY	2	10- 11	AUDIBLE RESPIRATION
		EYES/EARS/NOSE	1	10	PERINASAL ENCRUSTATION
			1	9	LACRIMATION (EYB 1)
	29361	NORMAL	29	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	10	PERIOCULAR ENCRUSTATION (EYL 1)
	29267	NORMAL	30	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29286	NORMAL	28	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		BODY	2	17- 18	UNKEMPT
	29370	NORMAL	29	2- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	3	PERIOCULAR ENCRUSTATION (EYB 1)
	29316	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29346	NORMAL	20	1- 15	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	11	6- 21	PERIOCULAR ENCRUSTATION (EYR 11)
	29369	NORMAL	31	1- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29328	NORMAL	31	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		ORAL/DENTAL	1	15	PERIORAL WETNESS
	29406	NORMAL	31	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		CARDIO-PULMONARY	1	10	AUDIBLE RESPIRATION
	29401	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
	29391	NORMAL	32	0- 21	NO SIGNIFICANT CLINICAL OBSERVATIONS
		DEAD	1	21	SCHEDULED SACRIFICE
		OTHER	1	0	MISSING EAR T/G

TABLE 3

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
GROUP: 0.0 MG/KG/DAY

ANIMAL	PS	DAY 0- 3	3- 6	6- 9	9-12	12-15	15-18	18-21	0- 6	6-15	15-21
29382	P	11.40	12.64	10.60	11.04	13.77	13.09	15.92	12.02	11.80	14.51
29381	P	12.24	13.90	11.84	11.77	13.95	12.66	16.41	13.07	12.52	14.54
29389	P	10.59	12.13	9.89	11.11	15.34	r/e	16.67	11.38	12.11	a
29285	NP	9.84	10.86	10.63	10.60	11.88	9.35	12.05	10.25	10.84	10.70
29300	P	6.17	17.82	11.25	10.55	r/e	11.89	13.67	12.00	a	12.78
29275	NP	11.26	12.53	11.07	10.88	11.43	10.85	14.05	11.89	11.13	12.45
29327	P	9.62	9.86	6.64	r/e	r/e	r/e	15.56	9.74	a	a
29355	P	10.87	14.30	11.76	13.58	13.30	13.11	15.26	12.58	12.88	14.19
29301	P	9.77	11.44	10.51	11.90	13.67	14.06	16.10	10.61	12.03	15.08
29358	P	10.92	12.77	11.58	12.49	13.45	14.49	17.14	11.85	12.51	15.81
29351	P	11.04	14.05	11.76	14.91	14.06	16.94	17.63	12.54	13.58	17.29
29288	P	11.37	10.68	11.06	13.86	12.94	16.77	18.27	11.03	12.82	17.52
29368	P	10.45	11.96	11.50	13.71	13.76	14.74	16.45	11.20	13.01	15.59
29371	RFS	9.75	11.47	11.56	13.72	11.66	14.57	12.27	10.61	12.32	13.42
29372	P	12.46	12.85	12.59	14.51	13.43	15.90	16.77	12.66	13.51	16.33
29293	P	11.05	12.18	11.69	12.83	13.56	15.59	16.15	11.62	12.69	15.87
29299	P	11.87	13.59	13.68	14.77	12.72	15.78	16.88	12.73	13.72	16.33
29279	NP	9.13	11.77	12.79	12.87	9.97	11.38	13.44	10.45	11.87	12.41
29359	P	11.87	11.76	12.72	11.78	10.25	14.25	14.95	11.82	11.58	14.60
29331	P	12.06	11.73	12.43	12.48	9.81	14.79	15.95	11.89	11.58	15.37
29276	P	11.32	9.11	12.84	12.13	11.44	16.31	14.64	10.21	12.13	15.47
29260	P	10.31	10.90	10.90	8.79	8.88	13.34	14.35	10.60	9.52	13.84
29297	P	11.30	12.57	13.80	13.30	13.25	16.25	16.39	11.94	13.45	16.32
29386	P	11.05	14.13	14.77	13.82	13.65	17.17	17.51	12.59	14.08	17.34
29298	P	10.08	11.07	11.81	12.63	11.74	15.73	16.35	10.57	12.06	16.04
MEAN		10.85	12.45	11.70	12.60	12.79	14.89	16.14	11.65	12.49	15.52
S.D.		1.321	1.859	1.647	1.539	1.640	1.561	1.124	0.920	1.035	1.247
N		21	21	21	20	19	19	21	21	19	19

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
GROUP: 500.0 MG/KG/DAY

ANIMAL	PS	DAY 0- 3	3- 6	6- 9	9-12	12-15	15-18	18-21	0- 6	6-15	15-21
29319	P	11.88	14.01	12.20	12.81	12.56	14.99	16.37	12.95	12.52	15.68
29255	P	10.23	11.80	9.69	11.56	11.55	14.52	14.22	11.01	10.93	14.37
29336	P	9.67	10.34	9.97	10.98	11.21	13.40	14.94	10.00	10.72	14.17
29417	P	9.82	10.23	10.86	10.91	11.58	14.16	13.47	10.02	11.12	13.82
29315	P	7.39	11.36	11.83	13.33	13.44	14.93	17.19	9.37	12.86	16.06
29390	P	11.26	12.69	11.93	11.81	13.53	14.09	16.65	11.98	12.42	15.37
29398	P	10.39	13.05	11.41	13.24	13.06	14.10	17.14	11.72	12.57	15.82
29313	P	11.80	13.13	10.18	9.84	11.61	12.73	14.67	12.47	10.54	13.70
29265	P	10.38	11.69	8.82	10.91	11.42	12.44	15.43	11.03	10.38	13.94
29273	P	9.79	12.01	10.95	10.25	9.65	10.45	13.17	10.90	10.28	11.81
29309	P	9.86	12.38	9.44	10.35	r/e	21.53	17.95	11.12	a	19.74
29350	NP	11.91	11.55	11.31	11.92	10.03	11.11	13.11	11.73	11.09	12.11
29345	P	10.34	11.06	10.53	12.22	12.43	14.06	15.97	10.70	11.73	15.02
29376	P	11.49	12.39	10.62	13.13	13.30	14.18	16.21	11.94	12.35	15.20
29341	P	10.64	12.14	12.10	13.52	14.13	16.08	17.01	11.38	13.25	16.54
29303	RFS	10.91	12.79	12.29	13.46	12.29	16.92	14.72	11.85	12.68	15.82
29318	P	6.08	9.62	4.03	r/e	r/e	r/e	15.05	7.85	a	a
29323	P	12.54	12.32	12.89	12.28	10.76	16.04	16.95	12.43	11.98	16.50
29388	P	9.85	12.92	14.30	12.96	13.79	17.80	17.57	11.39	13.68	17.68
29410	P	6.32	r/e	r/e	r/e	r/e	16.10	16.41	a	a	16.26
29322	P	10.81	10.64	11.18	9.53	11.31	14.16	13.71	10.73	10.87	13.93
29264	P	11.56	13.53	12.23	12.57	12.43	16.44	15.68	12.55	12.41	16.06
29333	P	11.24	13.05	13.45	13.43	14.29	16.13	16.29	12.14	13.72	16.21
29329	P	9.79	11.74	11.12	10.90	12.70	15.64	14.19	10.77	11.57	14.92
29262	P	10.89	12.96	12.47	13.19	12.58	17.12	14.92	11.92	12.74	16.02
MEAN		10.18	12.05	11.01	11.89	12.37	15.05	15.70	11.20	11.92	15.39
S.D.		1.634	1.142	2.048	1.294	1.214	2.203	1.368	1.177	1.097	1.617
N		23	22	22	21	20	22	23	22	20	22

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
GROUP: 1500.0 MG/KG/DAY

ANIMAL	PS	DAY 0- 3	3- 6	6- 9	9-12	12-15	15-18	18-21	0- 6	6-15	15-21
29284	P	11.42	11.68	11.03	12.81	13.66	14.61	16.06	11.55	12.50	15.34
29257	P	10.48	11.95	10.93	11.53	11.79	13.32	15.37	11.21	11.41	14.34
29278	P	9.28	11.24	9.61	10.85	11.49	13.16	14.90	10.26	10.65	14.03
29311	P	8.49	11.46	9.95	11.85	12.75	17.93	16.95	9.98	11.52	17.44
29296	P	10.30	11.40	11.26	11.76	8.83	11.51	15.45	10.85	10.62	13.48
29308	P	11.64	13.50	12.86	13.56	15.17	16.74	18.16	12.57	13.87	17.45
29344	NP	10.37	12.55	11.79	10.18	11.68	10.05	12.55	11.46	11.21	11.30
29268	P	11.99	13.92	12.45	11.75	14.73	15.36	17.14	12.95	12.98	16.25
29305	P	5.26	3.53	r/e	r/e	r/e	r/e	14.38	4.40	a	a
29259	P	11.31	12.61	10.27	10.48	13.63	14.26	15.14	11.96	11.46	14.70
29366	P	11.06	12.81	11.95	10.48	14.45	15.74	16.88	11.94	12.29	16.31
29383	P	12.08	13.19	10.81	12.87	14.86	15.59	17.30	12.63	12.85	16.45
29295	P	10.96	12.12	10.68	12.12	12.73	13.72	15.44	11.54	11.84	14.58
29349	P	12.21	11.65	11.06	11.39	13.97	15.35	16.24	11.93	12.14	15.80
29409	P	11.33	12.63	11.90	13.30	11.06	16.04	16.72	11.98	12.09	16.38
29277	P	9.64	11.73	11.65	12.85	10.64	13.66	17.15	10.69	11.71	15.40
29280	P	10.66	12.05	11.42	12.33	12.06	15.46	17.96	11.36	11.94	16.71
29354	NP	10.72	10.67	9.90	10.61	8.62	10.10	13.03	10.70	9.71	11.57
29384	P	11.00	13.30	11.32	12.71	10.75	16.54	16.42	12.15	11.59	16.48
29314	P	11.88	11.71	10.58	11.21	12.31	15.63	15.09	11.79	11.37	15.36
29402	P	12.09	12.74	11.09	11.79	10.79	15.16	14.53	12.41	11.53	14.85
29302	P	r/e	2.97	r/e	r/e	r/e	13.60	r/e	a	a	a
29352	P	10.78	12.82	13.27	13.36	12.77	15.96	16.00	11.80	13.14	15.98
29414	P	12.06	12.82	13.91	12.57	13.57	15.03	14.64	12.44	13.35	14.83
29337	P	10.60	12.30	12.32	10.39	11.71	16.12	15.48	11.45	11.47	15.80
MEAN		10.75	11.57	11.49	12.00	12.56	15.02	16.06	11.36	12.01	15.62
S.D.		1.559	2.723	1.080	0.975	1.657	1.440	1.110	1.727	0.849	1.072
N		22	23	21	21	21	22	22	22	21	21

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

TABLE 3

DEVELOPMENTAL TOXICITY STUDY OF UNION CARBIDE® ORGANOFUNCTIONAL SILANE A-187
ADMINISTERED BY GAVAGE TO FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMED DURING GESTATION (GRAMS/ANIMAL/DAY)
GROUP:3000.0 MG/KG/DAY

ANIMAL	PS	DAY 0- 3	3- 6	6- 9	9-12	12-15	15-18	18-21	0- 6	6-15	15-21
29403	NP	11.54	13.31	10.87	8.98	8.06	11.35	13.26	12.43	9.30	12.30
29373	P	11.68	11.77	r/e	7.21	10.72	14.93	15.63	11.73	a	15.28
29256	P	10.51	12.40	9.16	10.41	12.83	22.00	15.91	11.45	10.80	18.96
29347	P	9.22	11.56	9.70	9.88	10.13	14.37	15.71	10.40	9.90	15.04
29324	NP	11.94	13.25	10.64	8.46	8.37	9.86	12.61	12.64	9.16	11.23
29377	P	9.90	12.23	9.97	11.80	12.35	17.04	17.06	11.07	11.37	17.05
29312	P	4.90	4.62	r/e	r/e	r/e	r/e	16.27	4.76	a	a
29326	P	13.09	13.86	10.98	12.35	12.50	14.82	16.39	13.48	11.94	15.61
29338	P	12.42	14.33	12.77	13.53	15.51	16.36	19.88	13.38	13.94	18.12
29320	NP	10.84	12.53	9.90	10.90	10.73	11.17	13.20	11.68	10.51	12.19
29365	NP	10.70	11.51	10.70	11.32	12.76	13.74	12.46	11.11	11.60	13.10
29335	P	12.95	13.19	10.96	8.65	12.91	14.75	16.05	13.07	10.84	15.40
29416	NP	12.64	13.12	10.96	11.68	11.15	11.82	14.40	12.88	11.26	13.11
29356	P	11.69	13.01	9.06	4.83	7.46	11.76	14.08	12.35	7.12	12.92
29361	NP	8.39	9.42	6.98	8.11	7.56	10.22	11.98	8.91	7.55	11.10
29267	NP	9.85	10.33	7.59	7.82	9.83	11.94	11.93	10.09	8.41	11.94
29286	P	11.26	11.17	12.15	13.24	10.62	15.94	17.37	11.21	12.00	16.66
29370	P	7.15	12.59	r/e	2.80	0.77	r/e	20.19	9.87	a	a
29316	P	12.49	13.07	12.73	12.78	11.60	16.27	16.73	12.78	12.40	16.50
29346	P	12.06	12.73	12.32	11.44	11.95	15.66	16.45	12.41	11.90	16.06
29360	P	11.24	11.77	11.85	10.34	12.05	15.98	15.85	11.51	11.42	15.92
29325	P	11.12	12.18	13.41	11.97	12.80	14.35	14.01	11.65	12.72	14.18
29406	P	11.62	12.15	13.86	10.38	13.28	17.43	16.46	11.88	12.51	16.95
29401	P	12.67	12.60	14.31	12.11	11.83	15.94	15.68	12.78	12.75	15.81
29391	P	1.42	4.67	r/e	r/e	r/e	r/e	r/e	3.05	a	a
MEAN		10.41	11.68	11.66	10.23	11.21	15.84	16.45	11.05	11.54	16.03
S.D.		3.066	2.675	1.725	3.028	3.270	2.181	1.607	2.788	1.620	1.482
N		16	18	14	16	16	15	17	18	14	15

PS=PREGNANCY STATUS, P=PREGNANT, NP=NOT PREGNANT, RFS=REMOVED FROM STUDY
NP AND RFS WEIGHT(S) NOT INCLUDED IN CALCULATION OF MEAN

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