Ref. 5

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CHEMICAL MANUFACTURERS ASSOCIATION

FYI-AX-1285-0468 INITIAL SEQUENCE A

GERALDINE V. COX, Ph.D.
Vice President
Technical Director

December 11, 1985

12/23/85
TOB/CSB

The Honorable Lee M. Thomas
Administrator
U.S. Environmental Protection Agency
1200 West Tower
401 M Street, SW
Washington, DC 20460

Dear Mr. Thomas:

In accordance with the Chemical Manufacturers Association's policy of making publicly available all final reports developed in research projects that it administers, the following report is enclosed:

"Hydroquinone: A Developmental Toxicity Study in Rats"

To preserve the investigators' prerogative to publish these data in a suitable scientific journal, we request that you attempt to confine distribution of these reports to your agency only.

Sincerely yours,

Geraldine V. Cox

Enclosure

188528F
TX-85-50

Hydroquinone: A Developmental Toxicity Study in Rats*

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Health and Environment Laboratories
Eastman Kodak Company
Rochester, N.Y. 14650

September 25, 1985

*Sponsored by the Hydroquinone/Quinone Program Panel under the auspices of the Chemical Manufacturers Association, CMA Contract HYQ-2.0-Kodak.

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Hydroquinone: A Development Toxicity Study in Rats

Summary

The objective of this study was to determine the developmental toxicity potential of hydroquinone in the rat. Pregnant Crl: COBS®CD®(SD)BR rats were given 0, 30, 100 or 300 mg/kg of hydroquinone by gavage on the 6th through the 15th days of gestation and fetuses were examined near term.

Maternal toxicity was seen as a slight but statistically significant reduction in body weight gain and feed consumption during the treatment period in the dams given 300 mg/kg hydroquinone.

A few spontaneous malformations were seen, but no compound-related teratogenic effects were found. Minor soft tissue and skeletal changes, variations commonly found in developmental toxicity studies, did not occur at a significantly higher incidence in the treated groups than in the control group. Reproductive indices of the hydroquinone dams were comparable to the controls. A reduction in mean fetal body weight seen at the high dose level (300 mg/kg) correlated with the reduced body weight seen in the dams at this dose level.

In conclusion, doses as high as 300 mg/kg hydroquinone did not produce teratogenic effects, other embryotoxicity, or fetotoxicity in the rat.

Hydroquinone: Developmental Toxicity Study in Rats

The following key personnel were involved in the conduct of this study. Others are identified by signatures on the raw data sheets:

Walter J. Krasavage, M.S.	Teratologist-Study Director
Lisa G. Bernard, A.A.S.	Study Technician
John W. Mosher, B.S.	Study Technician
Milan S. Vlaovic, D.V.M., Ph.D.	Pathologist
Richard A. Schumacher, M.S.	Analytical Chemist
M. Susan James, A.A.S.	Quality Assurance Coordinator
E. V. Jeszenka, V.M.D., M.S.	Laboratory Animal Care
Robert Emmons, B.S.	Animal Clinical Chemistry

The animals for this study were received on January 23, 1985. Breeding to obtain 120 inseminated females was done on February 19 through February 22, 1985 and the treatment period was February 25 through March 9, 1985. The in-life phase of the study was completed on March 14, 1985. The study was conducted in the Toxicological Sciences Section, Health and Environment Laboratories (HAEL), Building 320, Eastman Kodak Company, Rochester, NY 14650 under contract for the Hydroquinone/Quinone Program Panel of the Chemical Manufacturers Association, Washington, D.C. All raw data relating to the study are in the archives of the HAEL. The data presented in this report summarize these data and accurately reflects the results of this study. Individual data pertinent to the summary tables presented in this report are included in the appendices.

Walter J. Krasavage
Study Director

9-27-85
Date

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TX-85-50

Hydroquinone: A Developmental Toxicity Study in Rats

Introduction

The Interagency Testing Committee (ITC) recommended hydroquinone for testing under the Toxic Substances Control Act (TSCA). Subsequent to discussions between the Office of Toxic Substances (OTS) and the Hydroquinone Program Panel of the Chemical Manufacturers Association, the Health and Environment Laboratories (HAEL), Eastman Kodak Company was retained by the Panel to develop a protocol (see Appendix 1) to determine the potential developmental toxicity of hydroquinone. A probe study was conducted by HAEL in order to select appropriate dose levels for the study reported here. A report of the results of this probe study, including recommended dose levels for the main study, was submitted by HAEL to OTS prior to initiating the main developmental toxicity study. The Health and Environment Review Division (HERD) of the OTS agreed with the suggested dose levels in a letter dated January 8, 1985, (Appendix I).

OFFICE OF TOXIC SUBSTANCES

The objective of the study presented here was to determine the maternal and embryo/fetotoxicity of hydroquinone in rats.

Materials and Methods

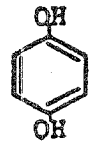
Test Compound

Hydroquinone (CAS# 123-31-9) was obtained from Eastman Kodak Company (Kodak Laboratory Chemicals, #356) in sufficient quantity so that the same batch (A13) was used for both the probe study and the study reported here. The test compound was further identified by an Eastman Kodak Accession number, 900356, and a Health and Environment Laboratories number, 83-0155. Prior to beginning the study and at the end of the in-life phase of the study, samples of the compound were analyzed for purity by the Kodak Park Industrial Laboratory using gas chromatography and high pressure liquid chromatography. The purity of the hydroquinone used in this study was 99+% both before and at the conclusion of the in-life portion of the study (Appendix II).

Hydroquinone was administered to the test animals by gavage as a 5% solution in distilled water. Fresh solutions were made daily and analyses to verify the concentration of hydroquinone were done three times a week (Appendix II).

Following are some pertinent physical-chemical properties of hydroquinone:

Structural Formula:



Molecular Formula: $C_6H_6O_2$

Molecular Weight: 110.1

Melting Point: 174°C

Vapor Pressure: 1 mmHg at 132°C

Form: white crystalline solid

Solubility: very soluble in water, acetone and ethanol

Test Animals

A stock of 158 seven week old male rats and 209 six week old female rats (COBS®CD®(SD)BR) were received from the Charles River Breeding Laboratories, Lakeview, NJ on January 23, 1985 and were uniquely identified with metal ear tags. Immediately upon receipt, several animals of each sex were selected using a random numbers table for a quality control screen. Blood was collected for hematologic and clinical chemistry determinations and a serologic screen for virus antibodies was done. Animals were killed, examined grossly and sections of lungs, trachea, liver, kidneys, salivary glands and nasal passages were collected for histologic examination. Hematology and clinical chemistries were within normal ranges for rats of this age and no viral antibody titers were present. However, during the first week of the acclimation period (February 1, 1985) both the male and female animals exhibited clinical signs of sialodacryoadenitis virus (SDA) infection. Therefore, the acclimation period was extended an additional two weeks in order to let the infection run its course. During this time the majority of the animals had swollen salivary glands and watery eyes. Follow-up serologic determinations (February 11 and 18, 1985) showed increased SDA titers in randomly selected animals, but at this time only a few of the animals exhibited clinical signs of SDA. On February 15, 1985, no females and only a few males exhibited signs of SDA. On February 19, 1985 all animals appeared clinically normal, therefore, breeding was begun to obtain the inseminated females needed to begin the study. No

signs of SDA were noted during the remainder of the study. The extension of the acclimation period allowed the SDA infection to run its course and it is our conclusion that the SDA infection did not compromise the results of this study.

The males and females were mated 1:1 over a 4-day period to obtain 120 inseminated females. Copulation was detected by the presence of a vaginal plug and the day on which a plug was found was considered day 0 of gestation. As the females became inseminated, they were assigned to the treatment and control groups on the basis of day 0 body weight using a computer-generated randomization program. The females were housed randomly on the racks in individual stainless steel suspended wire bottom cages in a laminar airflow room. Purina Rodent Laboratory Chow 5002 and tap water, delivered by an automatic watering system, were available ad libitum. Room temperature was 68°-76°F except on one occasion when it dropped to 64°F and on another rose to 78°F. Each of these excursions lasted about 15 minutes. Relative humidity was 45-50% throughout the study. A photocycle of 12 hours light/dark was maintained.

Experimental Design

ARE DAYS 6-15 SENSITIVE DAYS FOR FETUS.

Hydroquinone (5% in distilled water) was administered to groups of 30 plug positive females daily by gavage on gestation days 6 through 15. Dose levels were 30, 100 or 300 mg/kg and were calculated using the female's body weight on day 0 of gestation. A negative control group of 30 animals received a volume of distilled water daily on gestation days 6-15 equivalent to the largest volume given a treated animal. Individual

maternal body weights were recorded on gestation days 0, 6, 9, 12, 16 and 19 and individual feed consumption was measured from days 0-6, 6-9, 9-12, 12-16 and 16-19 of gestation. All animals were observed for clinical signs of toxicity twice daily (a.m. and p.m.) on nontreatment days and three times daily (a.m., post-dose and p.m.) on treatment days. Clinical observations were "cageside" observations except for those times when it was necessary to handle the animals (e.g. record body weights, dose). At these times all dams were examined more closely for signs of toxicity. On weekends during the non-treatment period, cageside observations for morbidity and mortality were made.

On the 20th day of gestation, the females were anesthetized by CO_2 inhalation and the abdominal viscera were exposed by a midline incision through the ventral body wall. All females were fasted overnight prior to cesarian section. Following exsanguination by severing the inferior vena cava, the dams were weighed and the gravid uteri were removed and weighed. The ovaries were removed, identified as left or right, and the corpora lutea of pregnancy were counted. The uterine horns were opened and the implantation sites were counted and categorized as viable fetus, dead fetus, early resorption or late resorption. A resorption was classified as "early" when no placenta or conceptus was distinguishable, and as "late" when a placenta containing an embryo in the process of being resorbed (partially to fully formed) was present. The viable fetuses were removed from the placenta, blotted dry on absorbent paper, sexed, examined for gross external abnormalities, and weighed individually. Approximately one half of the fetuses from each litter

were fixed in Bouin's solution and examined for internal soft tissue anomalies using Wilson's free-hand razor blade technique.[1] The other half of the fetuses were fixed in 95% ethanol, macerated in a 2% potassium hydroxide solution, stained with Alizarin Red S, and examined for skeletal defects.[2] The thoracic and abdominal viscera of the dams were examined in situ for gross abnormalities at the time of cesarean section. The liver and kidneys were weighed for organ/body weight comparisons and only sections of these organs were collected for histologic examination. The uteri of apparently nonpregnant females were stained with 10% sodium sulfide and examined for implantations.[3]

Statistical Analyses

Treated groups were compared to the control group at a level of significance of $p \leq 0.05$. Continuous data were analyzed using a one-way analysis of variance with significant "F" values further analyzed using Duncan's Multiple Range test. Discrete data were analyzed similarly following a Freeman-Tukey transformation. Incidence data were compared using Chi square contingency tables (2x4) and, when significant, each test group was compared to the control group using Fisher's Exact Test (two-tailed). Both the proportion of fetuses affected and the proportion of litters involved were analyzed.

Good Laboratory Practices

This study was conducted according to Good Laboratory Practices as promulgated by the Food and Drug Administration 21CFR, Part 58,

December 22, 1978 and the Environmental Protection Agency 40CFR, Part 792, November 29, 1983. Quality assurance inspections were conducted periodically by the Quality Assurance Section of HAEL, Eastman Kodak Company. Information regarding these inspections are included in this report (page 14).

Results

Test Solution Analyses

Test solutions of 5% hydroquinone in distilled water were prepared daily. Analyses of the solutions prepared on the first two days of dosing indicated that the concentration of the test compound was on target and therefore only those solutions prepared on Mondays, Wednesdays and Fridays were analyzed thereafter. The solutions were analyzed immediately after preparation prior to dosing. On the days when all females were dosed, the solutions were also analyzed after the dosing period which took approximately 45-60 minutes. A summary of the analytical results is presented in Table 1. The mean concentrations of hydroquinone in the test solutions used in this study were within ±6% of the target concentration and the analyses done following the dosing period indicated that the solutions were stable during the time they were administered.

Maternal Observations

Body Weight Response and Feed Consumption

Though not statistically significant, the mean maternal body weight of the high-dose dams (300 mg/kg) was slightly reduced from the third treatment day (day 9 of gestation, Table 2) to the end of the study. This weight depression was caused by a significant decrease in the mean body weight gain of these dams during the first three days of treatment (days 6-9 of gestation, Table 3). Subsequent weight gain of the high dose animals was comparable to the controls but the body weight of these dams never reached the control level. The corrected body weight (day 20 body weight minus gravid uterine weight) of this group was also slightly less than that of the controls. Feed intake of the 300 mg/kg dams was slightly but significantly less than the controls during the treatment period (Table 4).

Clinical Signs, Gross and Histopathology

The only treatment related clinical sign noted was the appearance of brown colored urine during the treatment period on dropping trays of all hydroquinone-treated dams. This discoloration was probably due to the oxidation of free hydroquinone which may have been present in the urine.

One dam died immediately following the 6th dose of 100 mg/kg hydroquinone (day 11 of gestation). Gross pathologic changes included dark brown discoloration around the nose. The lungs were reddish colored and did not collapse when the thoracic cavity was opened. These changes

are indicative of the presence of the compound in the lungs. Histologic examination revealed congestion of the lungs, inflammatory infiltrates in the bronchioles and alveolar wall hyperplasia. It was concluded that this dam died due to an intubation error. No compound related gross pathology was seen in any of the treated groups.

Histologic examinations of the livers and kidneys of all high-dose (300 mg/kg) and control dams were normal. These tissues were not examined in the intermediate and low dose animals.

Terminal Body Weights and Organ Weights

Mean absolute liver and kidney weights of the hydroquinone treated dams were comparable to those of the control animals (Table 5). The relative liver and kidney weights of all hydroquinone treated dams were slightly greater than the control weights. Although some of these increases were statistically significant, the fact that the magnitude of the increase was so small, the lack of a dose response and no evidence of histopathologic changes suggest that these changes are not toxicologically significant. When the relative liver and kidney weights were calculated using the corrected body weights (terminal body weight minus gravid uterus), and analyzed statistically, none of the treated groups were different ($p \leq 0.05$) compared to controls (table not included).

Observations at the Time of Cesarian Sections

Reproductive Indices

Pregnancy rate, number of litters with resorptions and the mean corpora lutea, implantation sites, viable fetuses, and resorptions per dam; the pre- and post- implantation losses, mean gravid uterine weights, and the fetal sex ratios did not differ among the hydroquinone and control groups (Table 6). The combined (males and females) mean fetal body weight was significantly ($p \leq 0.05$) reduced in the 300 mg/kg group compared to the controls. When the fetal weight of the males and females were analyzed separately, the female weight was statistically less than the controls and the male fetal body weight, though slightly less than the control weight, was not statistically different.

Fetal Examinations

External, internal soft tissue and skeletal examinations of the fetuses revealed no treatment-related malformations in any of the hydroquinone groups or in the control group (Table 7). Major malformations, which occurred spontaneously, included micrognathia and incomplete closure of the palatine bone in one control fetus, a diaphragmatic hernia in one fetus from a 300 mg/kg hydroquinone litter and a mispositioned right subclavian artery (appeared to arise directly off the aortic arch) in one fetus from a 30 mg/kg litter.

Externally, minor alterations consisted of small hematomas seen on one fetus each in the control, 30 and 100 mg/kg groups and in three fetuses in the 300 mg/kg group.

Minor internal soft tissue alterations included dilated renal pelvis (due to shortened renal papillae), hydronephrosis (absent renal papillae), and hydroureter. These changes were seen more frequently in the treated groups than the controls. However they did not appear to be dose-related and when analyzed individually and as total soft tissue alterations, the incidence of fetuses with an alteration and the percentage of litters with at least one fetus with an alteration were not statistically different from the controls.

Skeletal alterations included partial/nonossification of some intramembranous bones of the skull and particularly the hyoid bone, vertebral variations such as partial/nonossification of the first and second thoracic centra and bilobed or split thoracic centra particularly the 10th, 11th and 12th. The 3rd and 4th sacral arches were partially ossified in many of the fetuses in all groups including the control group. A few fetuses had rib variations. These variations are commonly seen in 20-day old rat fetuses in developmental toxicity studies[4] and except for two cases, they did not occur at a significantly higher incidence in the treated groups compared to the control group. Partially ossified 1st and 2nd thoracic centra were seen less frequently in the 100 mg/kg fetuses than the controls and the incidence of total vertebral variations was greater in the 300 mg/kg group than in the control group. However, there was no dose response in either of these cases, and since statistical analyses of individual vertebral variations, as well as analysis of all skeletal alterations combined, indicated no significant

increase in skeletal alterations between the hydroquinone-treated and the control groups, these findings are not considered toxicologically significant.

Discussion

Hydroquinone exhibited a low order of maternal toxicity resulting in a slight reduction in body weight gain and feed intake in those dams given 300 mg/kg hydroquinone. There were no clinical signs of toxicity and absolute and relative liver and kidney weights were comparable to the control weights. Gross and histologic appearance of the livers and the kidneys were normal.

A few spontaneous malformations were found, but no compound-related major malformations were seen. Thus, doses as high as 300 mg/kg of hydroquinone given during the sensitive period of gestation were not teratogenic in the rat. Renal and skeletal alterations, variations commonly found in developmental toxicity studies,[4/5] did not occur at a significantly higher incidence in the treated groups when compared to the controls. During late gestation in the rat, the rapid growth of renal parenchyma in relation to a slower increase in the length of the renal papillae may result in kidneys with a large pelvis. This is a transitory condition and if not accompanied by gross renal malformation, these kidneys appear normal at weaning.[5]

Reproductive indices of the dams treated with hydroquinone were comparable to the controls. The reduction in the fetal body weight seen in the 300 mg/kg fetuses was statistically significant only for the

female fetuses and correlated with the depressed body weight seen in the dams at this dose level.

Conclusions

Ten consecutive oral doses of 300 mg/kg of hydroquinone given to pregnant rats during the most sensitive period of organogenesis did not produce teratogenic effects,other embryotoxicity, or fetotoxicity. This dose level (300 mg/kg) produced maternal toxicity which was manifested as a slight reduction in body weight gain and feed intake. Thus, 300 mg/kg was a no-observed effect level (NOEL) for developmental toxicity and is probably very close to the NOEL for maternal toxicity.

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Approved by:

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Study Director

10-31-85
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Gary V. Katz, Ph.D.
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11-1-85
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References

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3. Kopf, R., Lorenz, D. and Salewski, E. Procedure for staining implantation sites of fresh rat uteri. Nauny-Schmiedebergs Arch. Exp. Path. Pharmacol. 247:121-135, 1964.

4. Wilson, J.G., Environment and Birth Defects, Chapter 9, pp. 181-188, Academic Press, Inc., New York, N.Y., 1973.

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Q.A. INSPECTION STATEMENT
(CFR 58.35(B)(7))

STUDY: 83-0155-3 STUDY DIRECTOR: KRASAVAGE,W.J.
ACCESSION NUMBER: 900356

'UDY TYPE: TERATOLOGY

M. Lee James
(AUDITOR, QUALITY ASSURANCE UNIT)

9/23/85
DATE

THIS STUDY WAS INSPECTED BY 1 OR MORE PERSONS OF THE QUALITY ASSURANCE UNIT OF THE HAEL, EASTMAN KODAK COMPANY, ROCHESTER, N.Y. AND WRITTEN STATUS REPORTS WERE SUBMITTED ON THE FOLLOWING DATES:

INSPECTION DATES	PHASE(S) INSPECTED	STATUS REPORT DATES
01/30/85	PROTOCOL SUBMISSION	
02/20/85	VAGINAL SMEARS AND/OR CHECK FOR PLUGS TEST SYSTEM RANDOMIZATION TEST SYSTEM WEIGHTS FEEDER WEIGHTS	02/20/85
03/04/85	TEST ARTICLE CARRIER MIXTURE DOSING OF TEST SYSTEMS CONTROL ARTICLE DOSING OF TEST SYSTEM TEST ARTICLE CARRIER MIXTURE PREPARATION RECORDS REVIEW SAMPLE/SPECIMEN SENT FOR ANALYSIS TEST SYSTEM WEIGHTS FEEDER WEIGHTS CLINICAL SIGNS A.M. CLINICAL SIGNS POSTDOSE	03/04/85
03/13/85	TEST SYSTEM WEIGHTS BLEEDING GROSS PATHOLOGY CAESAREAN SECTIONS COUNT IMPLANTATION SITES COUNT CORPORA LUTEA	03/14/85
03/15/85	PROTOCOL AMENDMENT GRAVID UTERUS TO BE REMOVED AND WEIGHED BEFORE OPENING	
05/02/85	SOFT TISSUE SECTIONING OF FETUSES SOFT TISSUE EXAMINATION OF FETUSES	05/02/85

Q.A. INSPECTION STATEMENT
(CFR 58.35(B)(7))

STUDY: 83-0155-3 STUDY DIRECTOR: KRASAVAGE,W.J.
ACCESSION NUMBER: 900356

06/06/85	SOFT TISSUE EXAMINATION OF FETUSES SOFT TISSUE SECTIONING OF FETUSES SKELETAL EXAMINATION OF FETUSES DATA RECORDING	06/06/85
07/22/85	STATUS OF FINAL REPORT PAPER BEING WRITTEN	
08/23/85	PROTOCOL AMENDMENT ADD JUSTIFICATION FOR SELECTION OF TEST SYSTEM ADD NO CONTAMINANTS THAT MAY COMPROMISE STUDY ADD CHOICE OF ROUTE OF ADMINISTRATION ADD START WILL BE WHEN BREEDING STARTS ADD FINAL REPORT WILL BE ISSUED WITHIN 9 MONTHS OF START	
09/11/85	FINAL REPORT REVIEW	
09/12/85	FINAL REPORT REVIEW	
09/13/85	FINAL REPORT REVIEW	
09/16/85	FINAL REPORT REVIEW	
09/17/85	FINAL REPORT REVIEW	
09/18/85	FINAL REPORT REVIEW	
09/19/85	FINAL REPORT REVIEW	09/19/85

Table 1

Hydroquinone - Developmental Toxicity Study in Rats

Summary of Test Solution Analyses[a]

Date of Treatment	-% Hydroquinone- Prior to Dosing	After Dosing[b]
2-25-85	5.0 ± 0.4[c]	-[d]
2-26-85	5.0 ± 0.2	-
3-01-85	5.1 ± 0.3	4.7 ± 0.1
3-04-85	5.0 ± 0.04	5.0 ± 0.1
3-06-85	4.8 ± 0.2	4.9 ± 0.1
3-08-85	5.0 ± 0.1	-

[a]Test solutions were prepared daily during the 13 day treatment period. The target concentration was 5% hydroquinone in distilled H_2O.

[b]Time interval between pre- and post-analyses was approximately 45-60 minutes.

[c]Mean ± 1 S.D. of 4 replicates except 3-4-85 pre-dose was 3 replicates.

[d]Analyses were only performed on days when all females were treated.

Table 2

Hydroquinone -- Developmental Toxicity Study in Rats

Maternal Body Weight (g)

Dose Group (mg/kg)	0	30	100	300
Mortality/Pregnant Female	0/24	0/29	1/28[a]	0/26
Gestation Days:				
0	215 ± 11[b]	215 ± 16	215 ± 14	216 ± 13
6	249 ± 14	250 ± 19	251 ± 17	249 ± 13
9	262 ± 16	263 ± 20	261 ± 18	255 ± 15
12	278 ± 19	279 ± 22	277 ± 21	268 ± 14
16	305 ± 24	307 ± 26	301 ± 24	293 ± 17
19	341 ± 23	342 ± 31	334 ± 27	330 ± 20
Corrected Body Weight(g)[c]	240 ± 20	243 ± 20	240 ± 20	231 ± 14

[a]One dam died immediately following dosing on the 11th day of gestation due to an intubation error.

[b]Mean ± 1 standard deviation.

[c]Body weight (fasted) on day 20 of gestation minus the gravid uterine weight.

Table 3

Hydroquinone - Developmental Toxicity Study in Rats

Maternal Body Weight Change (g/dam)

Dose Group (mg/kg)	0	30	100	300
Mortality/Pregnant Female	0/24	0/29	1/28[a]	0/26
Gestation Days:				
0 - 6	35 ± 7[b]	35 ± 7	36 ± 6	33 ± 6
6 - 9	12 ± 4	13 ± 7	11 ± 3	6 ± 6[c]
9 - 12	15 ± 9	16 ± 7	15 ± 5	14 ± 6
12 - 16	27 ± 9	28 ± 8	24 ± 7	25 ± 7
16 - 19	36 ± 8	35 ± 9	33 ± 9	37 ± 8
6 - 16	55 ± 16	57 ± 11	50 ± 9	44 ± 11[c]

[a]One dam died immediately following dosing on the 11th day of gestation due to an intubation error.

[b]Mean ± 1 standard deviation.

[c]Statistically different from controls (Anova and Duncan's Multiple Range Test, $p \leq 0.05$).

Table 4

Hydroquinone - Developmental Toxicity Study in Rats

Maternal Feed Consumption (g/rat/day)

Dose Group (mg/kg)	0	30	100	300
Mortality/Pregnant Female	0/24	0/29	1/28[a]	0/26
Gestation Days:				
0 - 6	21.2±2.7[b]	22.3±3.5	22.1±2.4	22.0±2.0
6 - 9	22.4±4.5	23.4±3.0	22.2±2.3	19.6±2.1[c]
9 - 12	26.1±5.1	26.0±2.5	25.1±2.6	23.2±2.4[c]
12 - 16	25.4±5.2	26.4±2.5	25.5±2.9	24.2±2.4
16 - 19	28.7±2.5	29.3±3.1	28.5±2.6	29.1±2.1
6 - 16	24.6±3.3	25.3±2.3	24.4±2.5	22.6±1.9[c]

[a]One dam died immediately following dosing on the 11th day of gestation due to an intubation error.

[b]Mean ± 1 standard deviation.

[c]Statistically different from controls, (Anova and Duncan's Multiple Range Test, $p \leq 0.05$).

Table 5

Hydroquinone - Developmental Toxicity Study in Rats

Mean Terminal Body and Organ Weights

Dose Group (mg/kg)	0	30	100	300
Mortality/Pregnant Female	0/24	0/29	1/28[a]	0/26
Terminal Body Weight (g)[b]	305 ± 22[c]	305 ± 29	296 ± 25	291 ± 20
Liver Weight (g)	10.60±1.08	10.91±1.06	10.51±1.01	10.56±0.87
% Body Weight	3.47±0.19	3.59±0.20[d]	3.56±0.21	3.62±0.17[d]
Kidney Weight (g)	1.89±0.16	1.96±0.19	1.91±0.21	1.92±0.16
% Body Weight	0.62±0.04	0.65±0.06	0.65±0.06	0.66±0.05[d]

[a]One dam died immediately following dosing on the 11th day of gestation due to an intubation error.

[b]Dams were fasted overnight prior to cesarian sections.

[c]Mean ± 1 standard deviation.

[d]Statistically different from controls, (Anova and Duncan's Multiple Range Test, $p \leq 0.05$).

Table 6

Hydroquinone - Developmental Toxicity Study in Rats

Summary of Observations at Time of Cesarean Sections

Dose Group (mg/kg)	0	30	100	300
Number of Females Inseminated	30	30	30	30
Number of Females Pregnant	24(80)[a]	29(97)	28(93)[b]	26(87)
Number of Litters Completely Resorbed	0	0	0	0
Number Litters with Resorptions	14(58)	16(55)	15(54)	13(50)
Corpora Lutea Per Dam	15 ± 2[c]	14 ± 2	14 ± 3	14 ± 3
Implantations Per Dam	14 ± 2	14 ± 3	12 ± 4	13 ± 3
Viable Fetuses Per Litter	13 ± 3	12 ± 4	11 ± 4	12 ± 3
Resorptions Per litter	1.2 ± 1.4	1.6 ± 2.3	1.1 ± 1.2	1.1 ± 1.8
Dead Fetuses Per Litter	0	0	0	0
Gravid Uterine Weight (g)	65.5±10.8	61.7±17.1	55.3±16.6	59.9±15.0
Pre-Implantation Loss (%)[d]	7.8 ± 9.4	7.7 ±12.1	16.2±24.2	6.7 ± 8.9
Post-Implantation Loss (%)[e]	8.7 ±12.3	13.0±19.6	7.9 ± 8.6	9.1 ±16.1
Sex Ratio (M:F)	48:52	49:51	46:54	47:53
Fetal Body Weight M & F (g)[f]	3.18±0.24	3.26±0.27	3.19±0.23	3.01±0.29*
Male	3.26±0.26	3.32±0.32	3.24±0.27	3.09±0.33
Female	3.13±0.25	3.21±0.25	3.13±0.23	2.95±0.27*

[a]Numbers in parentheses are percentages. None of the uteri stained with sodium sulfide had implantations.

[b]One dam died immediately following dosing on the 11th day of gestation due to an intubation error.

[c]Mean ± 1 standard deviation.

[d]Calculated for each dam $\frac{(\text{Number of Corpora Lutea} - \text{Number of Implantations})\times 100}{\text{Number of Corpora Lutea}}$

[e]Calculated for each dam $\frac{(\text{Number of Corpora Lutea} - \text{Number of Viable Implantations})\times 100}{\text{Number of Implantations}}$

[f]Mean of the litter means ± 1 standard deviation).

*Statistically different from controls (Anova and Duncan's Multiple Range Test, $p \leq 0.05$).

Table 6

Table 7

Hydroquinone Developmental Toxicity Study in Rats

Summary of External, Internal Soft Tissue and Skeletal Examinations of Fetuses[a]

Dose mg/kg	-Fetuses- 0		30		100		300		-Litters- 0		30		100		300	
	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Total Examined:																
External	100	312	100	349	100	295	100	321	100	24	100	29	100	27	100	26
Soft tissue	50	156	50	175	49	146	50	160	100	24	100	29	100	27	100	26
Skeletal	50	156	50	174	51	149	50	161	100	24	100	29	100	27	100	26
External Alterations:																
Hematoma	*	1	*	1	*	1	9	3	4	1	3	1	4	1	12	3
Soft Tissue Alterations:																
Dilated renal pelvis	1	2	4	7	5	7	4	6	4	1	17	5	22	6	12	3
Hydronephrosis	1	1	2	3	3	5	2	3	4	1	7	2	15	4	4	1
Hydroureter			2	3	1	1	1	2			7	2	4	1	4	1
Hispositioned Subclavian Artery[b]			1	1							3	1				
Diaphragmatic Hernia[b]							1	1							4	1
Total Soft Tissue Alterations:	2	3	6	11	8	12	6	10	8	2	21	6	33	9	15	4
Skeletal Alterations:																
Skull																
Micrognathia[b]	1	1							4	1						
Enlarged Fontanelles					1	1							4	1		
Partial Ossification:																
Hyoid	10	15	10	17	9	13	10	16	46	11	31	9	37	10	35	9
Membranous bones	6	10	1	2	5	8	6	9	29	7	3	1	22	6	19	5
Palatine[a]	1	1							4	1						
Non-ossification:																
Hyoid	2	3	1	2	1	2	1	1	13	3	7	2	4	1	4	1
Presphenoid	1	1							4	1						
Total Skull Alterations:	15	23	11	19	13	19	13	21	58	14	35	10	48	13	42	11
Ribs																
Wavy/Knobby							2	3							8	2
Shortened 13th	3	4	6	10	6	9			13	3	24	7	22	6		
Missing 13th					*	1							4	1		
Shortened 9th-13th			1	1							3	1				
14th thoracolumbar (Rudimentary)	2	3			1	1	3	5	13	3			4	1	15	4
Sternebrae																
<4 Ossification sites[c]	2	3	1	1	1	1	2	3	13	3	3	1	4	1	8	2
Bilobed	1	2	1	1	1	1	1	2	8	2	3	1	4	1	4	1
Split							1	1							4	1
Vertebrae																
Thoracic Centrae:																
Partial ossification (#1-3)	18	28	14	24	9	13**	22	35	54	13	45	13	41	11	50	13
Partial ossification (11,12 or 13)							2	3							4	1
Non-ossification (#1-2)	1	1	2	3	2	3	1	1	4	1	10	3	11	3	4	1
Bilobed (mainly #9-13)	37	58	33	57	32	48	43	69	88	21	72	21	78	21	89	23
Split (#10,11,12)	1	1	1	2	1	2	2	3	4	1	7	2	7	2	12	3
Lumbar Arches:																
Partial ossification (#5-6)			1	1			1	1			3	1			4	1
Lumbar Centrae:																
Bilobed (#1)	1	1					1	2	4	1					8	2
Sacral Arches:																
Partial ossification (mainly #3 and 4)	39	60	47	81	41	61	49	79	71	17	69	20	67	18	69	18
Sacral Centrae:																
Partial ossification (mainly #3 and 4)					1	1	1	1					4	1	4	1
Total Vertebral Alterations:	58	90	64	111	56	84	71	114**	88	21	90	26	85	23	96	25
Pelvic Girdle																
Partial ossification (pubis and/or ischium)	3	4	6	10	3	4	4	7	17	4	21	6	15	4	19	5
Non-ossification (pubis)	1	1							4	1						
Extremities																
Partial ossification																
Metacarpals			1	1	1	2	1	2			3	1	7	2	8	2
Metatarsals	1	1	1	1	1	1			4	1	3	1	4	1		
Total Skeletal Alterations:	69	107	68	119	63	94	75	120	92	22	93	27	89	24	100	26

[a]A single fetus may have more than one defect, therefore the sum of the individual defects may not equal the total number of fetuses with defects.
[b]Considered a major malformation.
[c]At least four well ossified sites should be present in the 20 day old rat fetus. Thus, less than 4 sites present is considered abnormal. Partial and non-ossification of individual sternebrae were recorded and no differences were seen between the treated and control groups (see individual data, appendix 6).
*Rounded-off percentage was less than 1.
**Statistically different from control, χ^2 table 2 X 4 and Fisher's Exact Test (two-tailed).

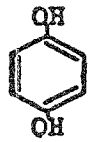
Protocol for a Teratology Study of Hydroquinone in Rats

Introduction

This protocol has been designed to determine the developmental toxicity of hydroquinone in rats.

Test Compound

Hydroquinone (CAS #123-13-9) will be obtained from Kodak Laboratory and Specialty Chemicals in sufficient quantity so that the same batch may be used throughout the study. The batch received will be identified by the batch number, an Eastman Kodak accession number and a Health and Environment Laboratories number. The identity, purity, and stability of the test compound will be determined prior to initiation of the study. Following are some physical-chemical properties of the test compound:

Structural Formula: 

Molecular Formula:	$C_6H_6O_2$
Molecular Weight:	110.1
Melting Point:	174°C
Vapor Pressure:	1 mmHg @ 132.4°C
Form:	White crystalline solid
Solubility:	Soluble in water, ethanol and acetone

Test Animals

Sexually mature male and female albino rats (COBS®CD®(SD)BR) will be purchased from the Charles River Breeding Laboratories, Wilmington, MA. The animals will be identified by metal ear tag and will be housed in suspended wire-bottom cages in a room with the temperature controlled at approximately 22°C, a relative humidity of 50 ± 15% and a photocycle of 12 hours light and dark. The animals will be acclimated to the laboratory for at least two weeks prior to mating.

Males and females will be mated 1:1 over approximately a two-week period in order to obtain 120 inseminated females. Copulation will be verified by daily inspections for the appearance of vaginal plugs and the day a plug is seen will be considered day 0 of gestation.

As the females become inseminated, they will be assigned on the basis of body weight to three test groups and a control group using a computer-generated stratified randomization scheme, until each group contains 30 inseminated females. The inseminated females will be individually housed. Purina Rodent Laboratory Chow 5002 and tap water via an automatic watering system will be available ad lib. throughout the study.

Experimental Design

Route of Administration and Doses

Groups of 30 inseminated females will be given 30, 100 or 300 mg/kg of hydroquinone (chosen based on data from a probe study) on amg/kg basis by gavage (in distilled H_2O) on days 6 through 15 of gestation. A control group of 30 rats will receive a volume of distilled water on day 6-15 of gestation equivalent to the largest volume given a treated animal. The female's body weight on day 6 of gestation will be used to calculate the doses. The stability of hydroquinone in solution (H_2O) will be determined prior to beginning the study and the frequency of test solution preparation will be based on this information. Test solutions prepared and used during the study will be analyzed for concentration of hydroquinone.

Maternal Observations

The dams will be observed twice daily (except week-ends) on non-dosing days and predose (a.m.) and post-dose (p.m.) on treatment days (days 6-15 of gestation) for mortality, morbidity, and clinical signs of toxicity. Animals found dead or moribund will be examined for gross pathologic changes and the condition of the uterus will be noted. Individual body weights of the dams will be recorded on days 0, 6, 9, 12, 16, 19, and 20 (termination) of gestation. Feed consumption will be measured on days 6, 9, 12, and 19 of gestation.

Since data from the probe study indicate that hydroquinone does not affect hematologic and clinical chemistry determinations, the dams will not be bled prior to cesarian sections. At termination, abdominal and thoracic organs of the dams will be examined in situ for gross pathologic changes. Kidneys and livers will be weighed for organ/body weight comparisons and portions of the kidneys and livers and any gross lesions will be collected for histopathologic examination. The uteri of apparently non-pregnant females will be stained with 10% sodium sulfide and examined for implantation sites.[1]

Fetal Observations

On day 20 of gestation the dams will be anesthetized by CO_2 inhalation and the abdominal viscera will be exposed by a mid-line incision through the abdominal wall. Following body weight determinations, the ovaries will be removed, identified as to right or left and the corpora lutea of pregnancy will be counted. The uterine horns will be opened and the implantation sites will be counted and categorized as viable fetus, dead fetus, early resorption or late resorption. A resorption will be classified as "early" when no placeta or conceptus is distinguishable and as "late" when a placenta is present and the embryo is in the process of being resorbed (partially to fully formed). The implantation sites in each uterine horn will be numbered beginning at the ovary and proceeding to the vagina. Thus, the relative positions of the

viable, dead and resorbed fetuses within each horn will be designated. The viable fetuses will be removed from the placentae in sequence according to position, blotted dry, sexed, and examined for external abnormalities, and individually weighed. Approximately one half of the fetuses from each litter will be fixed in Bouin's solution to be later examined for internal soft tissue anomalies using Wilson's free-hand razor blade technique.[2] The other half of the fetuses will be fixed in 95% alcohol for subsequent maceration with potassium hydroxide, stained with Alizarin Red S and cleared in glycerine for examination of the skeletons.[3]

Statistical Analyses

Statistical analyses will compare the test groups to the control group, with the level of significance at $p \leq 0.05$. Maternal data (body weight, feed consumption, organ weights, etc.) and mean number of corpora lutea, implantation sites, viable fetuses and mean fetal body weights will be compared by one way analysis of variance, Bartlett's test for homogeniety of variances, and Duncan's multiple range test when the "F" values are significant. Analyses of other data will be done using appropriate parametric or non-parametric techniques.

Presentation of Results

The following indices will be calculated for all inseminated females and the litters and will be presented for each test group:

Number of pregnant females and percent pregnancy

Corpora lutea per dam (mean ± SD)

Implantation sites per litter (mean ± SD)

Viable fetuses per litter (mean ± SD)

Dead fetuses per litter (mean ± SD)

Resorptions per litter (mean ± SD)

Number of litters with resorptions

Fetal body weights (mean of the litter means ± SD)

Sex ratio of the fetuses (M:F)

Percent pre-implantation loss -

$$\frac{\text{(Number of Corpora Lutea - Number of Implantations)}}{\text{Number of Corpora Lutea}} \times 100$$

Percent post-implantation lost -

$$\frac{\text{(Number of Implantations - Number of Viable Implants)}}{\text{Number of Implantations}} \times 100$$

Maternal body weight, feed consumption and clinical signs of toxicity

Maternal hematologic and clinical chemistry findings, if any

Results of external, internal soft tissue and skeletal examinations of the fetuses

Anomalies will be listed and the incidence in both fetuses and litters involved will be indicated

Absolute and relative organ weight data

Gross pathologic examination of dams and results of histopathologic examinations

Testing Facility and Sponsor

This study will be conducted by the General Toxicology Group in the Toxicological Sciences Section of the Health and Environment Laboratories, Eastman Kodak Company, Rochester, NY. Project manager will be C.J. Terhaar, Ph.D. and study director will be W.J. Krasavage, M.S. The study will be conducted in accordance with Good Laboratory Practices. The sponsor of this study is the Chemical Manufacturers Association, Washington, D.C.

References

1. Kopf, R., Lorenz, D. and Salewski, E. Procedure for staining implantation sites of fresh rat uteri. Naunyn-Schmiedebergs Arch. Exp. Path. Pharmacol. 247:121-135, 1964

2. Wilson, J. G. and Warkany, J., Teratology: Principles and Techniques, University of Chicago Press, Chicago, IL, 1965, pp. 262-277

3. Walker, D. G. and Wirtschafter, L. T., The Genesis of the Rat Skeleton, Charles C. Thomas, Springfield, IL, 1957, p. 2

Title: Protocol for a Teratology Study of Hydroquinone in Rats

Project No. 83-0155G3 Accession No. 900356

Change and Rationale

Page 4 - Experimental Design - Fetal Observations

Add: The gravid uterus of each female will be removed and weighed prior to being opened.

Rationale: This endpoint was not being measured when the protocol was written, but is now a routine observation in our developmental toxicity studies.

Amendment No. 1 Reviewed and Approved by:

Walter J. Krasavage
Walter J. Krasavage, M.S. Teratologist
Study Director

3-13-85
Date

M. Susan James
M. S. James, Coordinator
Quality Assurance Unit

3/13/85
Date

C J Terhaar
C. J. Terhaar, Ph.D., Supervisor
Toxicological Sciences

15 March '85
Date

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 14 1983

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

C. J. Terhaar, Ph.D.
Kodak Park
Building 320
Rochester, New York 14650

Dear Dr. Terhaar:

As discussed by telephone, I am submitting to you the results of the OTS review of protocols for the following studies; reproductive effects, teratology, dominant lethal, and toxicokinetics. Once you and your staff have reviewed these, if there are further questions, please contact me to set up a meeting with the appropriate staff.

Reproductive Effects - Teratology

While the protocols themselves are adequate, we believe that the results of the probe study with the rationale for dose level section should be provided for Agency review. In this way we may ensure complete acceptability of data generated from these studies.

Dominant Lethal

1. Treatment and mating schedule. The treatment schedule for the dominant lethal assay is generally a single administration followed by 6-8 weeks of sequential mating. Your proposal is to treat for 8-10 weeks followed by 2 weeks of mating. While such deviations from the normal schedule are acceptable, the rationale behind their selection should be presented.

2. Positive control. The activity of Apholate in the dominant lethal assay should be documented either by reference or by (submission) of data from the laboratory which will perform the assay.

Protocol Amendment No. 2

Title: Protocol for a Teratology Study of Hydroquinone in Rats

Project No. 83-0155G3 Accession No. 900356

Reason for Amendment

Although this protocol was reviewed and deemed adequate by the office of Toxic Substances (OTS) of the United States Environmental Protection Agency (USEPA), (see attached copy of page 1 of EPA letter dated September 14, 1983), the following additions are being made at the request of our Quality Assurance Unit in order to bring the protocol more in-line with Good Laboratory Practices requirements.

Additions: Page 2, paragraph 1 - Add that the rat was selected as the test species, because it is commonly used in teratology studies and it is the primary rodent species recommended in EPA guidelines for teratology testing.

Page 2, paragraph 3 - Test Animals - Add that the manufacturer's analysis of the basal diet and periodic analyses of the drinking water indicate that no contaminants should be present in the food or water that may compromise the results of the study.

Page 3, paragraph 1 - Route of Administration - Add that gavage was chosen as the route of administration because of the low vapor pressure and minimal dermal absorption of hydroquinone.

Page 7 - Testing Facility - Add that the start date of the study will be the date on which breeding begins and that a final report will be issued within 9 months following the start date.

Amendment No. 2 reviewed and approved by:

Walter J. Krasavage — 8-20-85
Walter J. Krasavage, M.S. Teratologist — Date
Study Director

M. S. James — August 22, 1985
M. S. James, Coordinator — Date
Quality Assurance Unit

C J Terhaar — 21 Aug '85
C. J. Terhaar, Ph.D., Supervisor — Date
Toxicological Sciences

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 7 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Dr. C. J. Terhaar
Health and Environmental Laboratories
Eastman Kodak Company
1669 Lake Avenue
Rochester, N.Y. 14650

Dear Dr. Terhaar:

The Agency has completed its review of the Kodak study entitled "Hydroquinone: Teratology Probe Study in Rats", to examine the doses you are selecting for the main teratology study. As I indicated in our telephone conversation on March 5, 1984, the Health and Environmental Review Division agrees that 200 mg/kg appears to be the threshold for maternal toxicity and believes that your suggested high dose of 300 mg/kg should show overt maternal toxicity. However, HERD believes that since 100 mg/kg was non-toxic, that testing below this level (you suggest 30 mg/kg) will not produce useful data. The Agency is suggesting that the dose levels be adjusted to bring them into closer conformity to the Office of Pesticides and Toxic Substances testing guidelines. Please find the HERD review enclosed and contact me of your wish to discuss this matter further.

Sincerely,

David J. Price

David J. Price
Project Manager
Test Rules Development Branch
Office of Pesticides
and Toxic Substances

Enclosure

Toxicokinetics

1. Methodologies for metabolic and toxicokinetic testing should adequately characterize these areas of concern. However there are problems with the protocol submitted for percutaneous absorption. First, the choice of beagle dogs is poor since dog skin is not a good predictor for human skin kinetics. A better choice for a test species would be the rat, guinea pig or miniature pig. Also in the dog study, a statement is made about "sufficient evidence of skin penetration", Specifically, if there is "sufficient evidence" of skin penetration after a 60 minute exposure, then additional tests would be run at 30 and 15 minute exposures. The meaning of "sufficient evidence" is not stated.

2. Second, the protocol states that 55 cm^2 will be the size of the topical application site. A good percutaneous penetration study will specify a test area which would be approximately equal to 10 percent of the total body surface area. Using a small test area could significantly reduce the amount of hydroquinone absorbed.

3. While Kodak itself, can conduct toxicokinetic studies with human volunteers, be advised that EPA cannot become a party to such testing through review of/or the approval of any testing protocols using humans.

Richard Troast
Team Leader
Test Rules Development Branch

cc: Steven D. Newburg-Rinn
David Price
Carl Morris

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 29 1984

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: HERD Review of Teratology Probe Study in Rats: Hydroquinone

FROM: Myron S. Ottley, Ph.D.
Pharmacologist
Toxic Effects Section
Toxic Effects Branch
Health and Environmental
Review Division (TS-796)

TO: David Price, Ph.D.
Project Manager
Test Rules Development Branch
Existing Chemical
Assessment Division (TS-778)

THRU: Angela Auletta, Ph.D.
for Section Chief
Toxic Effects Section
Toxic Effects Branch
Health and Environmental
Review Division (TS-796)

Upon review of the Kodak letter to Mr. Troast (February 3, 1984) and the accompanying data from the probe teratology study conducted by Kodak, we concur with their conclusion that the 200 mg/kg/day dose level "may be near the threshold dose" for maternal toxicity, with the two lower doses (100 and 50 mg/kg/day) showing no effects. However, we feel that the dose levels chosen for the main study, 30, 100 and 300 mg/kg/day may not be entirely appropriate.

OTS guidelines recommend that the highest dose administered show signs of maternal toxicity, that the mid-dose level show "minimal observable toxic effects" in the conceptus, and that the low-dose level be non-toxic. We agree that since 200 mg/kg/day appeared to be a "threshold" for maternal toxicity, 300 mg/kg/day should show overt maternal toxicity; we feel, however, that since 100 mg/kg/day was non-toxic in both the mother and the conceptus, testing below this level will not produce useful data. As such, it well may be an appropriate low-dose level. It is suggested, therefore, that dose levels for the main teratology study be selected such that the dose-toxicity profile is in closer conformity to the OTS guidelines.

NOV 5 1984

CMA

CHEMICAL MANUFACTURERS ASSOCIATION

GERALDINE V. COX, Ph.D.
Vice President
Technical Director

October 16, 1984

Dr. David J. Price
Project Manager
Test Rules Development Branch
Office of Pesticides and Toxic Substances
U. S. Environmental Protection Agency
Washington, D.C. 20460

Dear Dr. Price:

On behalf of the CMA Hydroquinone/Quinone Program Panel, I would like to request a meeting to discuss initiating teratology testing of hydroquinone. The Panel has reviewed the teratology probe study and protocol submitted to EPA by Eastman Kodak Company. In addition, the Panel reviewed your letter of March 7, 1984, and the comments offered by EPA's Health and Environmental Review Division (HERD) on dose levels suggested by Kodak.

The Panel believes that the protocol modifications suggested below adequately address the comments offered by HERD. In their comments, HERD wrote, "We agree that since 200 mg/kg/day appeared to be 'threshold' for maternal toxicity, 300 mg/kg/day should show overt maternal toxicity; we feel, however, that since 100 mg/kg/day was non-toxic in both the mother and the conceptus, testing below this level will not produce useful data. As such, it may well be an appropriate low-dose level. We suggest, therefore, that dose levels for the main teratology study be selected such that the dose-toxicity profile is in closer conformity to the OTS guidelines."

To be consistent with HERD's suggestions, and to ensure that time and resources are not wasted, the Panel suggests that the following dosages be used (mg/kg/day): 300, 175, 100, 55, and 0. A dose level of 55 mg/kg/day is suggested because there is no assurance that a dose level of 100 mg/kg/day, which was apparently non-toxic to both mother and conceptus in the probe study, will be non-toxic in the main study. If satisfactory to EPA, the Panel will begin the teratology study on rats, at the Health and Environment Laboratories of Eastman Kodak Company.

Robert J. Fensterheim of my staff will contact you to schedule a meeting for addressing any further concerns with this study or other health effects of hydroquinone.

Sincerely yours,

Geraldine V. Cox

Geraldine V. Cox, Ph.D.
Vice President-Technical Director

cc: Gary Timm

RECEIVED JAN - 9 1985

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 8 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Robert Fensterheim
Chemical Manufacturer's Association
2501 M Street, N.W.
Washington, D.C. 20037

Dear Bob:

This letter is to inform you of the Agency's acceptance of Kodak's suggested hydroquinone dose levels for a teratology study in rats. Based on the results of the probe study submitted by Kodak, the Agency finds that dose levels of 30, 100 and 300 mg/kg are acceptable for the main teratology study.

Richard Troast
Test Rules Development Branch

QUALITY ASSURANCE FINAL REPORT
INSPECTION STATEMENT

[Reference 21 CFR 58-35 (b) (7)]

Industrial Laboratory EE5H031
HAEL #83155
Accession #900356

Title: Hydroquinone Assay lot A-13 and 5% Water Solution Predoses, L.C. Method and Final Report

The data, records and methods for the final report of above analyses were audited on March 22, 1985.

The audit showed that there were adequate written procedures for conducting the tests and that the equipment used in these tests was in good working order, and calibrated according to schedule.

Further the audit showed that the laboratory notebooks had been kept in a manner consistent with good laboratory practices, that the equipment was of the proper design for the test, and that the personnel engaged in the tests had the necessary training and expertise in these analyses.

A report of the findings was submitted to the Study Director and to the Management of the Eastman Kodak Health and Environment Laboratories on March 27, 1985.

ESW:nla
3/27/85

E. S. Whitehead
Quality Assurance
Industrial Laboratory

0408a/0005a

QUALITY ASSURANCE FINAL REPORT
INSPECTION STATEMENT

[FR vol 48 #230 11/29/83]

Industrial Laboratory #EE5H024
HAEL #83-155
Accession #900356

Title: Hydroquinone Assay by GC & HPLC

The data, records and methods for the final report of the above analyses were audited on September 17, 1985.

A report of the findings was submitted to the group director and to the Quality Assurance Unit of the Eastman Kodak Health and Environment Laboratories on September 20, 1985.

ESW:nla
9/20/85

Everett S. Whitehead
Quality Assurance
Quality Systems Services

doc. 0033n

INDUSTRIAL LABORATORY REPORT FOR : Toxicological Sciences HAEL

REQUESTED BY: L. Bernard

DATE RECEIVED: 1/25/85
DATES ANALYZED: 1/29/85 and 2/ 7/85

IND. LAB. FILE # : EE5H024

DATE: 7/31/85

TITLE: Hydroquinone Lot A13 Assay by GC/FID and HPLC

AUTHOR: Linda K. Tersegno

SAMPLES:(LABELS AND DESCRIPTION) Hydroquinone Lot A13

FOR ADDITIONAL INFORMATION OR FURTHER WORK CONTACT:
Linda Tersegno or Donna Nichols (ex. 85035) for GC data
Karen Burgess (ex. 85010) for HPLC data

REPORT:

A sample of hydroquinone (Lot A13) was submitted for purity analysis by GC/FID and HPLC. For the GC/FID assay, the sample was found to be 99+% pure by area percent. Labelled GC/FID chromatograms are attached (p.1). The GC/FID conditions listed below were used for the assay.

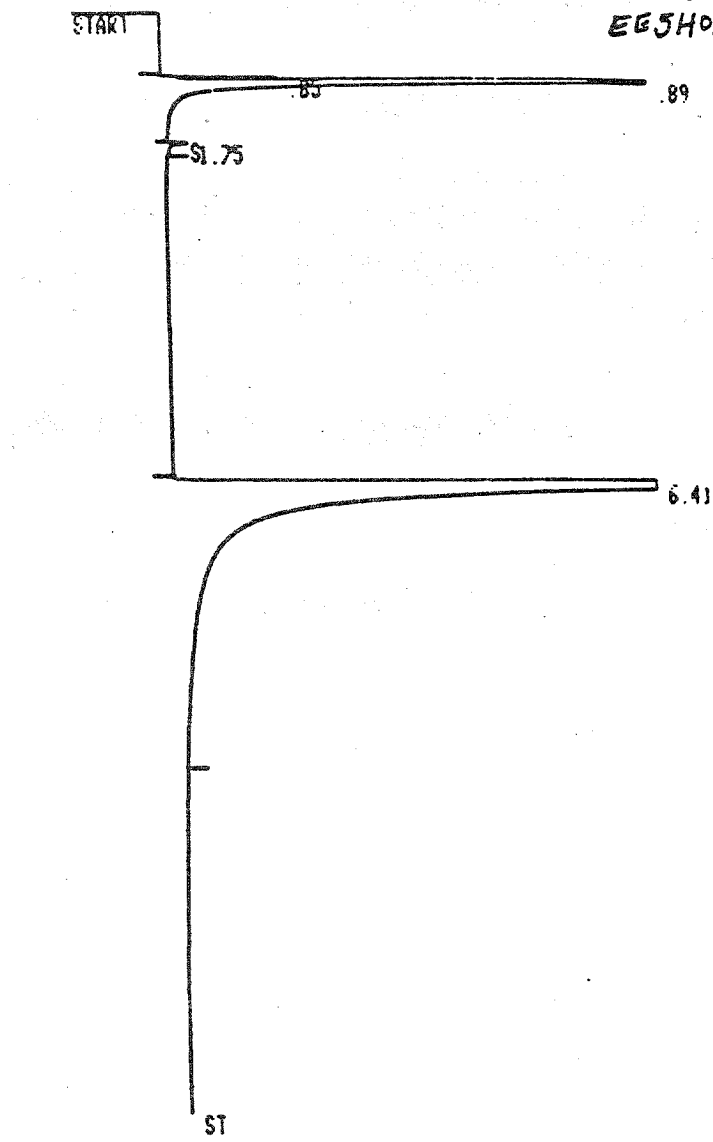
column: DB-1, 30m, 1.0 um film, 0.32 mm ID, FSOT
oven temp.: 100 C to 280 C at 8 C/min
injection: 0.8 uL splitless at 250 C
carrier: helium at 15 psi

The HPLC assay was performed using the method described in Industrial Laboratory Test (ILT) #EH83-124. The sample was found to be 99+% pure by area percent. A labelled chromatogram is attached (p.2).

Linda Tersegno
Karen Burgess

073185

0.8ul D. topping sample
EG5H028 4
L.T.



RUN # 312 JAN/29/85 12:40:46
WORKFILE ID: C
WORKFILE NAME:
SAMPLE # 9

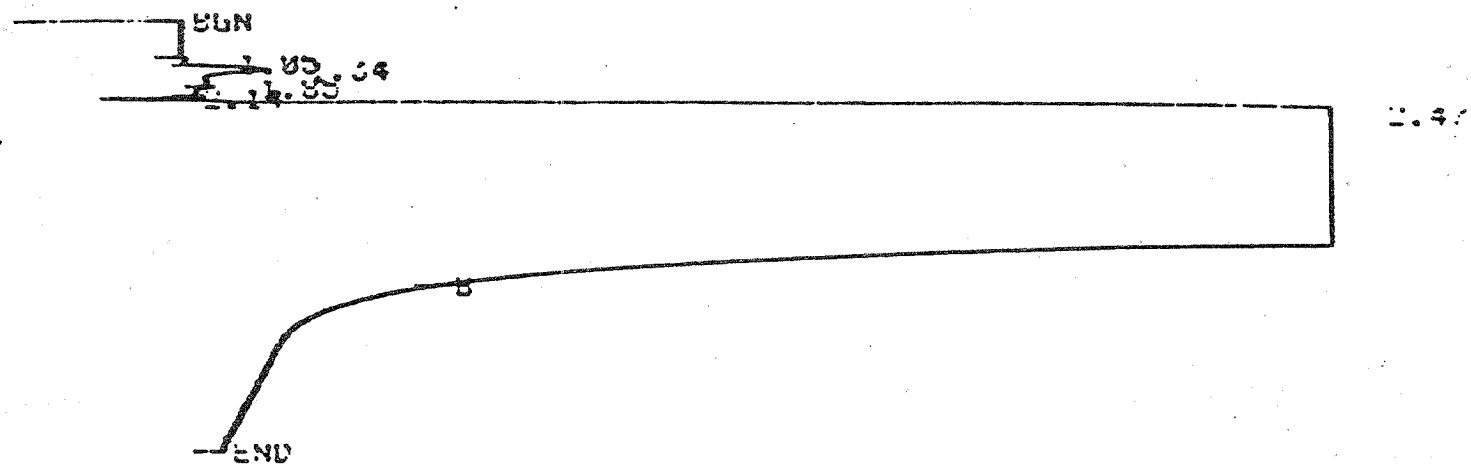
AREA%

RT	AREA	TYPE	AR/HT	AREA%
0.85	121060	D BH	0.018	0.278 } solvent
0.89	2.6117E+07	↑SHB	0.053	60.046
1.75	51012	BB	0.044	0.117 - 0.3%
6.41	1.7286E+07	SBB	0.187	39.559 - 99.7%

TOTAL AREA= 4.3496E+07
MUL FACTOR= 1.0000E+00

RUN 4 HW HSSHY REPEHT 2-7-85

SENSITIVITIES 500 30 HQ in MeCN



INJ: 1 METH 10 FILE 286

RUN 4 HW HSSHY REPEHT 2-7-85 11 : 33.1 2 / / / 85

SENSITIVITIES 500 30

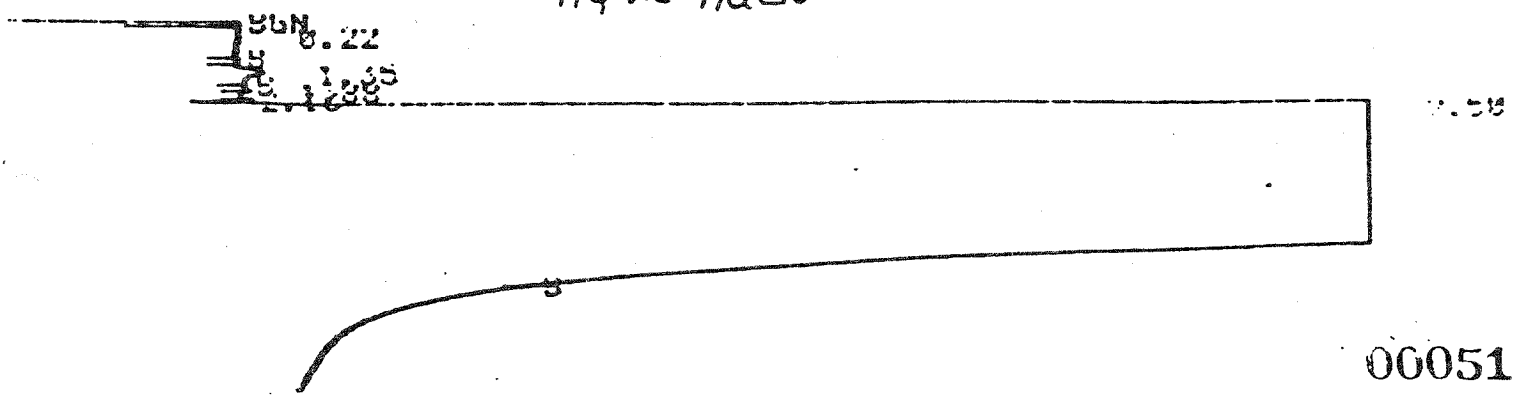
TIME	HREH	BC	RRT	RF	%	NAME
1.06	0.1022	T	0.106	1.000	0.0058	?
1.35	1.1236	T	0.135	1.000	0.0633	?
1.96	0.4431	T	0.196	1.000	0.0250	?
2.15	0.3598	V	0.215	1.000	0.0203	?
2.49	1773.9137		0.248	1.000	99.8858	?

INJ: 1 METH 10 FILE 285

RUN 5 HW HSSHY REPEHT 2-7-85

SENSITIVITIES 500 30

HQ in MeCN



EE 5H031 | 31115 | Appendix - Page 6 of 16

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

REGISTRATION NO. | ACT. NO.

REPORT RESULTS TO

NAME: John Mosher | DEPT NO.: 549 | BLDG: 320

REVIEW POINT 8

DEPT: HAEL (Tox) | PHONE NUMBER: 22756

REFERENCE NO.: Lot A-13 | CHARGE NUMBER: 549-9159

SAMPLE DESCRIPTION: (900356-L11) Hydroquinone

PRODUCT NO. | ACCESSION NO.: 900356 | NO. OF SAMPLES THIS REQUEST | ALL SAMPLES MUST HAVE R&S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
1	6
2	7
4	8
3	9
5	0

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Hydroquinone Assay

REPORT OF RESULTS AS FOLLOWS:

The submitted chemical (labelled Acc. # 900356, Lot A-13, conc. 100 %) was assayed according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{X}$ = 99.7 %

n = 4

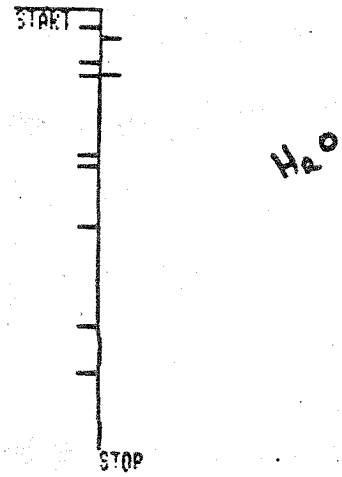
s = 0.33

C. B. Langdon
REPORTED BY

3/13/85
DATE

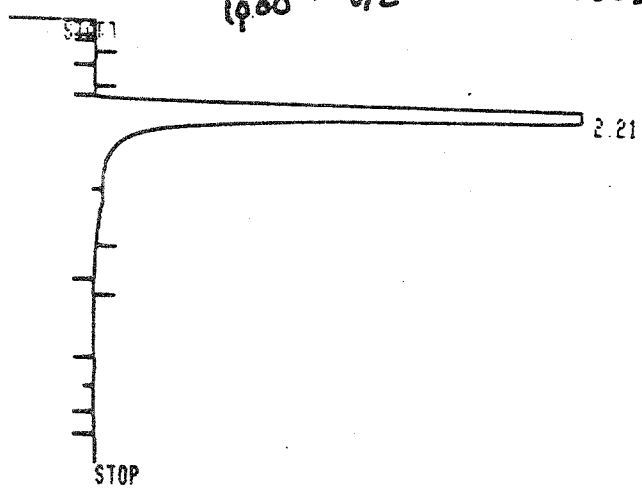
INDUSTRIAL LABORATORY FILE COPY

0005



RUN # 15 MAR/08/85 13:22:27
WORKFILE ID: C
WORKFILE NAME:
SAMPLE # 14
NO RUN PER

1900 mg/L acc# 900356

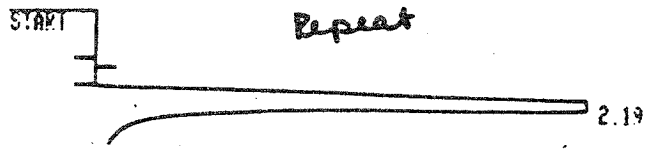


RUN # 16 MAR/08/85 13:36:27
WORKFILE ID: C
WORKFILE NAME:
SAMPLE # 11

AREA%

RT	AREA	TYPE	AR/HT	AREA%
2.21	4.0946E+07	SBB	8.198	100.000

TOTAL AREA= 4.0946E+07
MUL FACTOR= 1.0000E+00



INDUSTRIAL LABORATORY

DATE RECEIVED	ASSIGNED TO:	REGISTRATION NO.	ACT. NO.
MO 2 DAY 25 YR 85 WEEK	CBL		

REPORT RESULTS TO:

NAME	DEPT NO.	BLDG	REVIEW POINTS
John Moisheri	549	320	

DEPT	PHONE NUMBER
HAEL	22756

EKR NO.	REFERENCE NO.	CHARGE NUMBER
	Lot A-13	549-9159

SAMPLE CODE	SAMPLE DESCRIPTION
	(990356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.	ACCESSION NO.	NO. OF SAMPLES THIS REQUEST	ALL SAMPLES MUST HAVE R&S RATINGS
	900356	1	

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
①	⑥
②	⑦
③	⑧
④	⑨
⑤	⑩

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze for concentration of Hydroquinone

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124.The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ % Hydroquinone = 5.0
n = 4
s = 0.41

C. B. Langdon
REPORTED BY

2/25/85
DATE

946-5239-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

JOB NUMBER #	REQUEST NO.
EE5H031	31107

DATE RECEIVED	ASSIGNED TO:	REGISTRATION NO.	ACT. NO.
MO 2 DAY 26 YEAR 85 WEEK	CBL		

REPORT RESULTS TO:

NAME	DEPT NO.	BLDG	REVIEW POINT $
John Mosher	549	320	

DEPT	PHONE NUMBER
HAEL	22756

EKR NO.	REFERENCE NO.	CHARGE NUMBER
	Lot A-13	549-91559

SAMPLE CODE	SAMPLE DESCRIPTION
	(900356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.	ACCESSION NO.	NO. OF SAMPLES THIS REQUEST
	900356	1

ALL SAMPLES MUST HAVE R & S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
1	6
2	7
3	8
4	9
5	10

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze for Concentration of Hydroquinone

Batch 2

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ = 5.0 % Hydroquinone
s = 0.21
n = 4

Carol Langdon KB
REPORTED BY

2/26/85
DATE

946-6230-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

JOB NUMBER: EE5H031
REQUEST NO.: 31108

DATE RECEIVED: 3 Qtr 1 1985 WEEK
ASSIGNED TO: CBL
REGISTRATION NO.:
ACT. NO.:

REPORT RESULTS TO:
NAME: John Mosheir
DEPT NO.: 549
BLDG: 320
REVIEW POINTS:
DEPT: HAEL (Tox)
PHONE NUMBER: 22756
EKR NO.:
REFERENCE NO.: LOT A-13
CHARGE NUMBER: 549-9159

SAMPLE CODE:
SAMPLE DESCRIPTION: (990356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.:
ACCESSION NO.: 900356
NO. OF SAMPLES THIS REQUEST: 1
ALL SAMPLES MUST HAVE R&S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
1	6
2	7
3	8
4	9
5	10

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.:

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze for concentration of Hydroquinone

Batch 5 Preclose

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ = 5.1 % Hydroquinone
s = 0.25
n = 4

Carol B. Langdon CBL
REPORTED BY

3/1/8
DATE

846-6230-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

JOB NUMBER: EE54031
REQUEST NO.: 31109

DATE RECEIVED: MO 3 DAY 1 YR 85 WEEK
ASSIGNED TO: CBL
REGISTRATION NO.:
ACT. NO.:

REPORT RESULTS TO:
NAME: John Moshier
DEPT NO.: 549
BLDG: 3210
REVIEW POINTS:
DEPT: HAEL (Tox
PHONE NUMBER: 22756
EKR NO.:
REFERENCE NO.: Lot A-13
CHARGE NUMBER: 549-91597

SAMPLE CODE:
SAMPLE DESCRIPTION: (900356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.:
ACCESSION NO.: 900356
NO. OF SAMPLES THIS REQUEST: 1
ALL SAMPLES MUST HAVE R&S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS
SPEC. OR STD. TEST NO.:
VENDOR:
PURCHASE ORDER NO.:
1. 2. 3. 4. 5. 6. 7. 8. 9. 10.

USE THIS SECTION FOR ALL OTHER REQUESTS
IDENTIFICATION NO.:
DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY
Analyze for concentration of Hydroquinone

Batch 5 Post Rinse

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ = 4.7 % Hydroquinone
s = 0.13
n = 4

Carol B. Langdon
REPORTED BY

3/1/8
DATE

846-5236-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

EE5H031 | 31111

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

DATE RECEIVED: MO 3 DAY 4 YEAR 85 WEEK	ASSIGNED TO: CBL	REGISTRATION NO.	ACT. NO.

REPORT RESULTS TO:

NAME	DEPT NO.	BLDG	REVIEW POINTS
John Moisher	549	320	

DEPT	PHONE NUMBER
HAEL (Tox)	22756

EKR NO.	REFERENCE NO.	CHARGE NUMBER
	Lot A-13	549-9159

SAMPLE CODE	SAMPLE DESCRIPTION
	(900356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.	ACCESSION NO.	NO. OF SAMPLES THIS REQUEST
	900356	1

ALL SAMPLES MUST HAVE R & S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
1	6
2	7
3	8
4	9
5	10

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze For Concentration of Hydroquinone

Batch 8 Pre dose

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{X}$ = 5.0 % Hydroquinone
s = 0.04
n = 3

C. B. Langdon — REPORTED BY

KB 3/4/85 — DATE

840-6238-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

JOB NUMBER	REQUEST NO.
EE5H031	31110

DATE RECEIVED	ASSIGNED TO:	REGISTRATION NO.	ACT. NO.
MO 3 DAY 4 85 WEEK	CBL		

REPORT RESULTS TO:

NAME	DEPT NO.	BLDG	REVIEW POINT $
John Mosher	549	320	

DEPT	PHONE NUMBER
HAEL (Tox)	22756

EKR NO.	REFERENCE NO.	CHARGE NUMBER
	Lot A-13	549-9159

SAMPLE CODE	SAMPLE DESCRIPTION
	(900356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.	ACCESSION NO.	NO. OF SAMPLES THIS REQUEST	ALL SAMPLES MUST HAVE R& S RATINGS
	900356	1	

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
1	6
2	7
3	8
4	9
5	10

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze For Concentration of Hydroquinone

Batch 8 Post dose

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH-83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ = 5.0 % Hydroquinone
s = 0.05
n = 4

C. B. Langdon
REPORTED BY

KB 3/4/85
DATE

849-5236-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

EES H031 | 31112 | Appendix 2 Page 14 of 16

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

W/K 4/4/85 X-4 Order

DATE RECEIVED	ASSIGNED TO:	REGISTRATION NO.	ACT. NO.
MO 3 DAY 25 YEAR 85 WEEK	CBL		

REPORT RESULTS TO:

NAME	DEPT NO.	BLDG	REVIEW POINTS
John Mosher	549	320	

DEPT	PHONE NUMBER
HAEL (Tox)	22756

EKR NO.	REFERENCE NO.	CHARGE NUMBER
	Lot A-13	549-9159

SAMPLE CODE	SAMPLE DESCRIPTION
	(990356-111) 5% Hydroquinone in Distilled Water

PRODUCT NO.	ACCESSION NO.	NO. OF SAMPLES THIS REQUEST
	900356	1

ALL SAMPLES MUST HAVE R&S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
1	6
2	7
3	8
4	9
5	10

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze for Concentration of Hydroquinone

Batch 10 Predose

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ = 4.8 % Hydroquinone
s = 0.16
n = 4

Carol B. Langdon — REPORTED BY

KB 3/6/85 — DATE

046-5236-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

JOB NUMBER	REQUEST NO.
EE5H031	31113

DATE RECEIVED	ASSIGNED TO:	REGISTRATION NO.	ACT. NO.
MO 3 DAY 6 YEAR 85 WEEK	CBC		

REPORT RESULTS TO:

NAME	DEPT NO.	BLDG	REVIEW POINTS
John Mosher	549320		

DEPT	PHONE NUMBER
HAEL (Tox)	22756

EKR NO.	REFERENCE NO.	CHARGE NUMBER
	Lot A-13	549-9159

SAMPLE CODE	SAMPLE DESCRIPTION
	(990356-411) 5% Hydroquinone in Distilled Water

PRODUCT NO.	ACCESSION NO.	NO. OF SAMPLES THIS REQUEST
	900356	1

ALL SAMPLES MUST HAVE R& S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR	PURCHASE ORDER NO.
①	⑥
②	⑦
③	⑧
④	⑨
⑤	⑩

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze for concentration of Hydroquinone

Batch 10 Postdose

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x}$ = 4.9 % Hydroquinone
s = 0.05
n = 4

Carol B. Langdon — REPORTED BY

KB 3/6/85 — DATE

846-5236-000 (8/82)

INDUSTRIAL LABORATORY REPORT COPY

REQUEST FOR ANALYSIS
INDUSTRIAL LABORATORY

EE5H031

REQUEST NO. 31114

DATE RECEIVED: MO 3 DAY 8 YEAR 85 WEEK

ASSIGNED TO: CBL

REGISTRATION NO.

ACT. NO.

REPORT RESULTS TO:

NAME: John Mosher

DEPT NO. 549

BLDG 320

REVIEW POINTS

DEPT: HAEL (Tox)

PHONE NUMBER

EKR NO.

REFERENCE NO. Lot A-13)

CHARGE NUMBER 549-9159

SAMPLE CODE

SAMPLE DESCRIPTION (990356-L11) 5% Hydroquinone in Distilled Water

PRODUCT NO.

ACCESSION NO. 900356

NO. OF SAMPLES THIS REQUEST 1

ALL SAMPLES MUST HAVE R&S RATINGS

USE THIS SIDE FOR SPECIFICATION AND STD. TEST REQUESTS

SPEC. OR STD. TEST NO.:

VENDOR

PURCHASE ORDER NO.

1 6
2 7
3 8
4 9
5 10

USE THIS SECTION FOR ALL OTHER REQUESTS

IDENTIFICATION NO.

DESCRIBE PROBLEM AND ACTION YOU REQUEST. ATTACH SEPARATE SHEET IF NECESSARY

Analyze for concentration of Hydroquinone

Batch 12 predose

REPORT OF RESULTS AS FOLLOWS:

The submitted sample was analyzed for Hydroquinone concentration according to ILT # EH83-124. The original data will be kept on file in the Ind. Lab. The results are as follows:

$\bar{x} = 5.0$
$n = 4$
$s = 0.09$

C.B. Langdon VB 3/8/85
REPORTED BY DATE

INDUSTRIAL LABORATORY REPORT COPY

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Body Weights and Body Weight Gains of Pregnant Rats

Dose Level: Control

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Maternal Body Weight (g) Day(s) of Gestation 0	6	9	12	16	19	Maternal Body Weight Gain (g) 0-6	6-9	9-12	12-16	16-19	6-19
1	C4909	220.5	256.8	276.1	297.4	329.0	367.6	36.3	19.3	21.3	31.6	38.6	72.2
2	C5030	202.1	237.1	247.8	270.0	285.9	332.7	35.0	10.7	22.2	15.9	46.8	48.8
4	C5025	192.3	214.6	225.0	244.8	273.1	307.6	22.3	10.4	19.8	28.3	34.5	58.5
5	C5013	228.6	263.9	277.6	297.1	324.2	358.0	35.3	13.7	19.5	27.1	33.8	60.3
6	C5049	222.6	268.6	275.6	301.1	335.0	379.3	46.0	7.0	25.5	33.9	44.3	66.4
8	C5036	203.5	242.3	255.0	275.9	312.6	354.2	38.8	12.7	20.9	36.7	41.6	70.3
9	C5028	220.2	251.9	265.9	280.2	310.2	343.1	31.7	14.0	14.3	30.0	32.9	58.3
10	C5010	228.8	262.7	271.1	300.6	333.8	377.7	33.9	8.4	29.5	33.2	43.9	71.1
11	C5005	210.0	251.5	255.1	279.3	317.1	345.0	41.5	3.6	24.2	37.8	27.9	65.6
12	C5001	222.1	263.1	275.0	297.6	330.1	368.2	41.0	11.9	22.6	32.5	38.1	67.0
13	C5621	204.6	235.3	244.3	259.3	294.1	329.5	30.7	9.0	15.0	34.8	35.4	58.8
14	B1098	227.6	256.8	272.1	288.1	320.8	358.1	29.2	15.3	16.0	32.7	37.3	64.0
15	C4908	200.2	227.1	241.9	253.0	280.5	311.8	26.9	14.8	11.1	27.5	31.3	53.4
16	C5029	209.8	241.5	258.6	242.2	234.9	293.6	31.7	17.1	-16.4	-7.3	58.7	-6.6
17	C5003	211.9	255.0	265.5	281.6	313.5	347.9	43.1	10.5	16.1	31.9	34.4	58.5
18	C5052	220.4	260.4	277.1	293.5	311.7	330.6	40.0	16.7	16.4	18.2	18.9	51.3
19	C4953	211.8	252.0	261.5	279.4	305.8	335.2	40.2	9.5	17.9	26.4	32.4	53.8
20	C5085	216.7	259.9	270.6	288.6	323.0	351.6	43.2	10.7	18.0	34.4	28.6	63.1
21	C5032	235.8	284.2	295.7	304.5	330.8	361.6	48.4	11.5	8.8	26.3	30.8	46.6
22	C4915	228.7	260.6	276.4	284.1	299.2	336.9	31.9	15.8	7.7	15.1	37.7	38.6
23	C5021	212.3	232.0	247.3	258.5	282.3	318.2	19.7	15.3	11.2	23.8	35.9	50.3
24	C4939	198.2	223.2	234.7	249.2	276.4	309.5	25.0	11.5	14.5	27.2	33.1	53.2
27	C5066	212.0	247.7	261.9	273.9	305.0	341.2	35.7	14.2	1.2	31.1	36.2	57.3
29	C5060	221.2	257.7	258.9	267.9	293.4	329.3	36.5	1.2	9	25.5	35.9	35.7
Mean		215.1	248.7	262.1	277.8	305.1	341.1	35.1	11.9	15.3	27.3	36.2	54.9
SD		11.2	14.3	16.2	18.8	24.1	22.7	7.3	4.2	9.3	9.5	7.6	16.1

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Body Weights and Body Weight Gains of Pregnant Rats

Dose Level: 30 mg/kg

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Maternal Body Weight (g) Day(s) of Gestation 0	6	9	12	16	19	Maternal Body Weight Gain (g) 0-6	6-9	9-12	12-16	16-19	6-19
32	C5069	197.8	223.0	241.8	253.2	264.2	280.5	25.2	18.8	11.4	11.0	16.3	41.2
33	C5054	219.7	250.7	264.1	286.3	314.1	351.7	31.0	13.4	22.2	27.8	37.6	63.4
34	C5006	191.0	232.5	248.2	263.2	288.8	326.4	41.5	15.7	15.0	25.6	37.6	56.3
35	C5026	248.6	287.6	299.6	318.4	352.4	395.5	39.0	12.0	18.8	34.0	43.1	64.8
36	C5073	237.2	276.8	297.2	323.2	353.2	397.4	39.6	20.4	26.0	30.0	44.2	76.4
37	C5079	232.4	269.9	278.6	295.8	323.9	353.5	37.5	8.7	17.2	28.1	29.6	54.0
38	C4919	220.2	249.8	259.5	272.4	305.0	336.7	29.6	9.7	12.9	32.6	31.7	55.2
39	C4897	205.6	235.6	245.5	258.4	287.5	319.8	30.0	9.9	12.9	29.1	32.3	51.9
40	C5007	220.4	258.7	273.1	284.9	313.2	349.6	38.3	14.4	11.8	28.3	36.4	54.5
41	C5043	224.5	261.3	272.7	288.4	321.6	363.2	36.8	11.4	15.7	33.2	41.6	60.3
42	C5008	212.6	258.6	271.7	287.8	324.1	364.0	46.0	13.1	16.1	36.3	39.9	65.5
43	C5053	180.8	206.4	215.0	225.4	246.7	286.7	25.6	8.6	10.4	21.3	40.0	40.3
44	B1099	221.3	246.9	258.9	274.5	306.6	351.5	25.6	12.0	15.6	32.1	44.9	59.7
45	C4996	216.2	256.5	280.9	298.8	347.1	390.5	40.3	24.4	17.9	48.3	43.4	90.6
46	C5009	227.1	260.4	247.8	290.3	308.8	330.4	33.3	-12.6	42.5	18.5	21.6	48.4
47	C4994	207.5	242.4	257.4	270.8	312.5	359.0	34.9	15.0	13.4	41.7	46.5	70.1
48	C4965	215.3	247.2	257.3	279.7	307.5	347.1	31.9	10.1	22.4	27.8	39.6	60.3
49	C5016	216.1	250.7	264.5	272.6	305.2	323.5	34.6	13.8	8.1	32.6	18.3	54.5
50	C5623	195.4	243.4	263.0	277.8	313.2	342.0	48.0	19.6	14.8	35.4	28.8	69.8
51	C4902	219.4	251.9	268.5	288.5	313.0	351.1	32.5	16.6	20.0	24.5	38.1	61.1
52	C5624	204.4	225.8	242.4	253.9	274.5	295.6	21.4	16.6	11.5	20.6	21.1	48.7
53	C5087	231.2	260.4	283.4	297.6	322.5	367.1	29.2	23.0	14.2	24.9	44.6	62.1
54	C4966	236.1	277.7	295.0	308.4	342.3	383.6	41.6	17.3	13.4	33.9	41.3	64.6
55	C4947	196.4	225.6	241.8	255.4	277.8	312.3	29.2	16.2	13.6	22.4	34.5	52.2
56	C5012	212.1	258.6	264.9	275.6	299.0	333.6	46.5	6.3	10.7	23.4	34.6	40.4
57	C5075	210.3	245.4	257.2	265.4	283.1	303.8	35.1	11.8	8.2	17.7	20.7	37.7
58	C5048	236.9	271.5	288.4	304.4	324.6	355.9	34.6	16.9	16.0	20.2	31.3	53.1
59	C4914	217.1	256.2	266.7	278.6	312.2	353.3	39.1	10.5	11.9	33.6	41.1	56.0
60	C5011	188.3	221.0	230.4	245.4	269.9	306.9	32.7	9.4	15.0	24.5	37.0	48.9
Mean		215.3	250.1	263.3	279.1	307.4	342.5	34.8	13.2	15.8	28.3	35.1	57.3
SD		15.1	18.6	19.9	21.8	25.9	30.9	6.6	6.6	6.6	7.7	8.6	11.4

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Body Weights and Body Weight Gains of Pregnant Rats

Dose Level: 100 mg/kg

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Maternal Body Weight (g) Day(s) of Gestation 0	6	9	12	16	19	Maternal Body Weight Gain (g) 0-6	6-9	9-12	12-16	16-19	6-19
61	C5050	212.9	249.6	260.3	279.6	304.9	335.8	36.7	10.7	19.3	25.3	30.9	55.3
62	C5067	214.2	244.3	250.5	264.8	293.8	333.8	30.1	6.2	14.3	29.0	40.0	49.5
63	C4954	232.8	282.4	291.8	318.1	339.4	357.4	49.6	9.4	26.3	21.3	18.0	57.0
64	C4984	214.2	252.3	266.3	284.0	316.0	354.6	38.1	14.0	17.7	32.0	38.6	63.7
65	C4931	196.4	238.0	250.5	267.8	288.5	321.4	41.6	12.5	17.3	20.7	32.9	50.5
66	C5074	218.4	248.4	260.4	280.9	305.3	338.7	30.0	12.0	20.5	24.4	33.4	56.9
67	C4943	231.3	270.5	280.1	289.9	320.1	355.5	39.2	9.6	9.8	30.2	35.4	49.6
68	C5024	207.0	238.2	241.0	252.2	285.3	330.9	31.2	2.8	11.2	33.1	45.6	47.1
69	C5017	216.8	250.8	263.4	280.0	290.5	304.7	34.0	12.6	16.6	10.5	14.2	39.7
70	C5018	229.6	267.3	272.1	286.1	316.4	358.1	37.7	4.8	14.0	30.3	41.7	49.1
71	C5002	221.3	249.8	257.0	276.3	302.5	332.3	28.5	7.2	19.3	26.2	29.8	52.7
72	C4992	213.9	238.8	251.4	257.0	280.0	312.9	24.9	12.6	5.6	23.0	32.9	41.2
73	C4929	193.8	221.8	230.4	247.7	268.7	307.5	28.0	8.6	17.3	21.0	38.8	46.9
76	C5004	231.7	274.1	285.0	301.5	332.6	364.3	42.4	10.9	16.5	31.1	31.7	58.5
77	C4920	234.4	271.1	286.2	301.8	331.6	371.4	36.7	15.1	15.6	29.8	39.8	60.5
78	C4896	208.4	237.4	250.9	261.3	280.6	315.0	29.0	13.5	10.4	19.3	34.4	43.2
79	C5059	228.7	271.7	282.4	295.6	332.4	371.9	43.0	10.7	13.2	36.8	39.5	60.7
80	C5083	210.2	246.2	259.3	269.7	287.1	305.0	36.0	13.1	10.4	17.4	17.9	40.9
81	C4977	206.5	240.0	251.5	264.7	287.7	320.8	33.5	11.5	13.2	23.0	33.1	47.7
82	C5015	172.2	206.2	216.4	226.8	242.5	266.2	34.0	10.2	10.4	15.7	23.7	36.3
83	C5051	230.6	266.0	278.3	297.7	324.3	359.8	35.4	12.3	19.4	26.6	35.5	58.3
84	C5020	218.8	257.4	271.6	286.8	310.4	349.4	38.6	14.2	15.2	23.6	39.0	53.0
85	C4959	217.8	259.1	278.2	296.7	309.2	330.1	41.3	19.1	18.5	12.5	20.9	50.1
86	C4890	216.2	250.1	257.1	Died 3/5/85			33.9	7.0	Died 3/5/85			
87	C4979	196.0	230.5	243.4	257.0	277.1	314.7	34.5	12.9	13.6	20.1	37.6	46.6
88	C4957	200.8	237.0	243.2	246.1	263.0	281.9	36.2	6.2	2.9	16.9	18.9	26.0
89	C4918	230.6	259.4	267.9	282.9	319.0	364.3	28.8	8.5	15.0	36.1	45.3	59.6
90	C5072	217.6	261.1	271.0	287.5	310.6	353.0	43.5	9.9	16.5	23.1	42.4	49.5
Mean		215.1	250.7	261.3	277.0	300.7	333.8	35.6	10.6	14.8	24.4	33.0	50.0
SD		14.4	17.0	17.7	21.0	23.7	27.2	5.7	3.5	4.8	6.8	8.8	8.5

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Body Weights and Body Weight Gains of Pregnant Rats

Dose Level: 300 mg/kg

Experiment No. 83-0155G3

-Animal Number-		Maternal Body Weight (g)						Maternal Body Weight Gain (g)					
		Day(s) of Gestation											
Study	Ear Tag	0	6	9	12	16	19	0-6	6-9	9-12	12-16	16-19	6-19
91	C5038	201.8	236.8	243.9	262.7	288.4	331.0	35.0	7.1	18.8	25.7	42.6	51.6
92	C4941	201.4	228.5	226.6	241.5	263.6	294.5	27.1	-1.9	14.9	22.1	30.9	35.1
93	C4961	192.1	220.2	220.9	240.0	263.1	304.4	28.1	0.7	19.1	23.1	41.3	42.9
94	C5076	195.1	232.4	243.1	257.9	285.7	330.1	37.3	10.7	14.8	27.8	44.4	53.3
95	C4948	224.9	259.6	263.7	290.8	323.7	365.4	34.7	4.1	27.1	32.9	41.7	64.1
96	C4985	232.4	268.5	274.8	288.8	319.7	362.1	36.1	6.3	14.0	30.9	42.4	51.2
97	B1090	210.4	238.1	229.6	248.7	267.5	301.4	27.7	-8.5	19.1	18.8	33.9	29.4
98	C5078	214.6	238.4	249.2	262.7	284.3	321.1	23.8	10.8	13.5	26.6	36.8	45.9
99	C5061	224.6	262.6	269.3	281.8	309.1	345.5	38.0	6.7	12.5	27.3	36.4	46.5
101	C5068	213.8	248.4	254.8	269.4	285.0	328.5	34.6	6.4	14.6	15.6	43.5	36.6
102	C5047	214.4	240.0	245.5	256.7	273.3	302.6	25.6	5.5	11.2	16.6	29.3	33.3
103	C4942	238.3	265.6	268.6	281.3	295.1	315.9	27.3	3.0	12.7	13.8	20.8	29.5
105	C4893	229.5	256.5	270.2	284.4	320.6	360.5	27.0	13.7	14.2	36.2	39.9	64.1
106	B1097	224.5	257.1	271.3	268.6	303.2	335.5	32.6	14.2	-2.7	34.6	32.3	46.1
107	C5086	217.5	255.1	258.5	269.4	290.3	300.1	37.6	3.4	10.9	20.9	9.8	35.2
108	C5039	209.3	241.6	256.7	268.2	298.5	330.5	32.3	15.1	11.5	30.3	32.0	56.9
109	C4933	210.7	240.2	256.9	267.9	288.9	325.4	29.5	16.7	11.0	21.0	36.5	48.7
110	C5034	228.8	259.2	260.4	260.1	285.9	327.9	30.4	1.2	-0.3	25.8	42.0	26.7
112	C4991	213.2	257.9	263.2	279.6	311.2	347.6	44.7	5.3	16.4	31.6	36.4	53.3
113	C5019	217.3	258.1	269.0	283.6	306.6	346.2	40.8	10.9	14.6	23.0	39.6	48.5
114	C5041	217.7	252.9	259.6	272.1	286.6	322.9	35.2	6.7	12.5	14.5	36.3	33.7
116	C4907	217.3	258.9	265.9	280.2	313.0	357.6	41.6	7.0	14.3	32.8	44.6	54.1
117	C4999	234.2	260.1	265.5	283.3	300.8	347.2	25.9	5.4	17.8	17.5	46.4	40.7
118	C5044	226.9	252.9	252.3	268.4	292.9	340.9	26.0	-0.6	16.1	24.5	48.0	40.0
119	C5070	213.2	250.3	256.3	263.1	281.4	315.4	37.1	6.0	6.8	18.3	34.0	31.1
120	C5057	190.2	226.0	229.9	249.2	278.5	323.9	35.8	3.9	19.3	29.3	45.4	52.5
Mean		215.9	248.7	254.8	268.5	293.0	330.2	32.8	6.1	13.6	24.7	37.2	44.3
SD		12.7	13.1	14.9	14.1	17.0	20.2	5.6	5.6	5.9	6.5	8.3	10.7

000669

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Feed Consumption of Pregnant Rats

Dose Level: Control

Experiment No. 83-0155G3

Maternal Feed Consumption (g/day)

Day(s) of Gestation

-Animal Number- Study	Ear Tag	0-6	6-9	9-12	12-16	16-19	6-16
1	C4909	21.9	24.6	26.7	28.6	31.1	26.8
2	C5030	21.3	21.3	23.4	24.6	29.2	23.3
4	C5025	16.1	18.3	19.4	20.6	24.1	19.5
5	C5013	23.0	24.3	27.9	28.9	32.1	26.8
6	C5049	26.1	27.2	29.9	32.0	34.3	29.9
8	C5036	22.2	23.1	26.6	27.5	31.0	25.9
9	C5028	20.8	24.8	29.3	25.6	28.8	26.0
10	C5010	21.5	23.0	26.0	25.5	29.2	24.9
11	C5005	23.2	25.8	30.2	29.0	30.9	28.4
12	C5001	23.4	25.3	28.7	28.7	31.5	27.7
13	C5621	18.7	20.8	23.2	23.5	27.4	22.6
14	B1098	20.8	24.3	25.4	26.8	29.6	25.6
15	C4908	19.8	22.1	22.8	24.0	25.2	23.1
16	C5029	21.2	24.4	15.5	3.75	27.8	13.5
17	C5003	23.1	24.4	25.2	27.8	28.9	26.0
18	C5052	22.3	25.8	28.6	26.3	28.7	26.8
19	C4953	21.2	21.6	24.8	25.5	27.7	24.1
20	C5085	22.7	25.0	28.0	28.1	29.8	27.1
21	C5032	22.0	24.5	26.7	26.3	30.0	25.9
22	C4915	21.3	23.0	24.6	25.3	26.1	24.4
23	C5021	18.7	19.4	22.0	24.1	26.3	22.1
24	C4939	19.6	20.2	23.1	24.9	24.1	22.6
27	C5066	21.5	4.5	44.1	27.2	27.4	25.5
29	C5060	22.5	19.6	23.2	24.7	27.2	22.7
Mean		21.2	22.4	26.1	25.4	28.7	24.6
SD		2.7	4.5	5.1	5.2	2.5	3.3

00067900

HYDROQUINONE: LOPMENTAL TOXICITY STUDY

Individual Feed Consumption of Pregnant Rats

Dose Level: 30 mg/kg

Experiment No. 83-0155G3

Maternal Feed Consumption (g/day)

Day(s) of Gestation

-Animal Number- Study	Ear Tag	0-6	6-9	9-12	12-16	16-19	6-16
32	C5069	19.1	21.1	22.2	22.8	25.9	22.1
33	C5054	23.7	25.2	27.0	29.0	31.6	27.3
34	C5006	21.2	23.6	26.0	24.8	26.6	24.8
35	C5026	24.3	27.3	28.3	28.6	31.0	28.1
36	C5073	23.9	26.7	29.5	29.7	34.0	28.7
37	C5079	23.1	25.3	26.9	26.1	29.1	26.1
38	C4919	19.4	21.3	23.0	24.6	28.5	23.2
39	C4897	26.6	20.4	24.4	25.4	28.4	23.6
40	C5007	23.1	28.4	27.9	25.5	29.5	27.1
41	C5043	20.4	23.1	25.3	26.0	27.1	24.9
42	C5008	24.6	25.1	26.4	27.9	30.1	26.6
43	C5053	18.4	19.3	21.1	20.6	25.8	20.3
44	B1099	19.4	22.4	25.2	24.8	31.7	24.2
45	C4996	23.5	26.4	28.7	31.3	36.1	29.1
46	C5009	22.6	22.1	25.4	25.3	28.3	24.4
47	C4994	20.0	22.1	24.5	26.8	30.8	24.7
48	C4965	19.4	18.9	25.3	24.4	30.3	23.0
49	C5016	21.1	22.6	24.4	25.4	27.2	24.2
50	C5623	20.3	21.9	27.5	29.5	34.0	26.6
51	C4902	21.9	25.0	28.9	26.4	26.9	26.7
52	C5624	17.4	20.2	21.3	24.1	25.8	22.1
53	C5087	23.2	28.5	29.5	29.5	31.5	29.2
54	C4966	25.3	27.8	29.9	31.0	33.3	27.9
55	C4947	19.6	21.2	22.5	25.1	27.1	23.2
56	C5012	24.4	23.4	24.4	25.4	26.8	24.5
57	C5075	22.7	17.3	29.5	24.2	22.3	23.7
58	C5048	23.8	26.0	27.2	27.2	31.2	26.8
59	C4914	23.3	24.5	27.2	29.0	31.9	27.1
60	C5011	19.9	21.3	24.2	24.0	25.9	23.2
Mean		22.3	23.4	26.0	26.4	29.3	25.3
SD		3.5	3.0	2.5	2.5	3.1	2.3

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Feed Consumption of Pregnant Rats

Dose Level: 100 mg/kg Experiment No. 83-0155G3

Maternal Feed Consumption (g/day)

Day(s) of Gestation

-Animal Number- Study	Ear Tag	0-6	6-9	9-12	12-16	16-19	6-16
61	C5050	26.2	23.1	25.9	28.5	30.8	26.1
62	C5067	21.3	19.7	24.0	25.3	29.1	23.2
63	C4954	28.8	26.5	31.2	33.3	34.6	30.7
64	C4984	23.7	24.5	26.5	27.3	29.5	26.2
65	C4931	19.7	21.2	23.8	24.8	27.7	23.4
66	C5074	20.7	22.5	25.3	26.5	29.4	24.9
67	C4943	23.2	24.4	26.9	26.3	29.5	25.9
68	C5024	20.6	19.3	22.6	23.3	28.7	21.9
69	C5017	21.8	24.3	26.5	25.6	27.7	25.5
70	C5018	23.6	22.5	23.7	23.4	29.2	23.2
71	C5002	20.1	21.1	25.5	24.1	28.5	23.6
72	C4992	21.4	21.1	22.0	24.8	29.2	22.9
73	C4929	17.6	19.9	22.7	23.0	26.9	22.0
76	C5004	21.3	20.8	25.2	26.2	26.6	24.3
77	C4920	24.6	25.0	28.4	24.9	30.3	26.6
78	C4896	19.8	20.9	23.5	22.2	25.3	22.2
79	C5059	24.8	24.7	27.9	28.0	30.0	27.0
80	C5083	23.2	20.1	23.3	23.4	26.0	22.4
81	C4977	21.5	21.1	23.3	23.5	27.4	22.8
82	C5015	18.0	18.1	19.6	18.3	26.6	18.6
83	C5051	24.6	24.6	27.6	29.4	30.1	27.4
84	C5020	20.9	21.5	24.4	24.6	28.6	23.6
85	C4959	23.4	26.8	29.7	28.9	30.9	28.5
86	C4890	21.7	20.8	Died 3/5/85			
87	C4979	20.4	21.3	23.1	23.6	26.2	22.8
88	C4957	21.8	20.7	22.7	23.1	24.6	22.3
89	C4918	20.8	19.7	24.2	27.4	30.4	24.1
90	C5072	23.2	24.8	27.7	27.6	31.0	26.8
Mean		22.1	22.2	25.1	25.5	28.5	24.4
SD		2.4	2.3	2.6	2.9	2.6	2.5

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Feed Consumption of Pregnant Rats

Dose Level: 300 mg/kg Experiment No. 83-0155G3

Maternal Feed Consumption (g/day)

Day(s) of Gestation

-Animal Number- Study	Ear Tag	0-6	6-9	9-12	12-16	16-19	6-16
91	C5038	22.3	20.1	21.9	24.6	29.8	22.4
92	C4941	21.2	14.8	20.4	23.8	26.4	20.1
93	C4961	17.7	16.2	19.7	22.0	25.9	19.6
94	C5076	20.1	20.8	23.5	23.5	29.4	22.7
95	C4948	26.7	22.8	27.1	30.7	35.8	27.3
96	C4985	22.8	21.3	22.5	26.1	31.9	23.6
97	B1090	20.2	14.4	20.1	20.9	26.6	18.7
98	C5078	20.0	20.1	23.5	22.1	28.1	21.9
99	C5061	22.5	19.7	24.9	25.8	29.6	23.7
101	C5068	23.4	20.7	25.0	20.7	28.5	22.0
102	C5047	19.2	19.5	23.1	23.5	29.4	22.2
103	C4942	22.0	20.1	18.4	23.6	30.2	22.8
105	C4893	19.8	18.9	24.6	25.9	30.3	23.4
106	B1097	20.1	21.9	18.5	23.1	28.1	21.4
107	C5086	21.8	18.9	23.6	24.1	26.9	22.4
108	C5039	22.5	21.5	25.0	25.6	30.1	24.2
109	C4933	21.1	22.7	24.4	23.2	28.1	23.4
110	C5034	22.1	18.7	20.4	19.8	28.7	19.6
112	C4991	24.9	21.5	26.6	28.5	31.1	25.8
113	C5019	23.8	19.7	24.5	26.0	31.5	23.6
114	C5041	23.0	18.6	25.1	23.9	27.4	22.7
116	C4907	25.3	21.8	26.2	26.8	29.0	25.1
117	C4999	21.2	19.7	24.4	23.2	29.2	22.5
118	C5044	23.1	17.3	23.0	24.7	29.4	22.0
119	C5070	22.7	19.8	23.0	22.2	26.1	21.7
120	C5057	21.7	18.2	24.5	24.7	29.1	22.7
Mean		22.0	19.6	23.2	24.2	29.1	22.6
SD		2.0	2.1	2.4	2.4	2.1	1.9

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HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Terminal Body and Organ Weights of Pregnant Rats

Dose Level: Control

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Terminal Body Weight (g)	-Liver- Weight (g)	% B.W.	-Kidneys- Weight (g)	% B.W.
1	C4909	323.4	11.1764	3.4556	1.8579	0.5744
2	C5030	288.9	9.3285	3.2285	1.6271	0.5631
4	C5025	272.0	9.1377	3.3592	1.6171	0.5945
5	C5013	312.6	11.1074	3.5537	2.0304	0.6496
6	C5049	337.4	11.7836	3.4923	2.0454	0.6062
8	C5036	312.8	10.7764	3.4447	1.7666	0.5647
9	C5028	309.0	11.0742	3.5840	1.9481	0.6305
10	C5010	341.1	11.7775	3.4525	1.9840	0.5816
11	C5005	306.6	10.4543	3.4096	1.6918	0.5518
12	C5001	328.8	12.7328	3.8729	2.1168	0.6439
13	C5621	296.1	10.2545	3.4631	1.8897	0.6382
14	B1098	327.0	12.1841	3.7255	2.0003	0.6116
15	C4908	274.4	9.6370	3.5119	1.9014	0.6929
16	C5029	258.0	8.8077	3.4136	1.5516	0.6013
17	C5003	312.6	12.3303	3.9443	1.9508	0.6240
18	C5052	293.5	10.4717	3.5676	1.7541	0.5976
19	C4953	308.5	10.3500	3.3544	1.9137	0.6202
20	C5085	321.8	10.2114	3.1735	2.0378	0.6333
21	C5032	328.3	11.4958	3.5016	2.1187	0.6454
22	C4915	299.9	9.5028	3.1682	1.7516	0.5840
23	C5021	290.1	9.8924	3.4095	1.9970	0.6883
24	C4939	274.4	9.0155	3.2851	1.8141	0.6610
27	C5066	314.1	10.4198	3.3171	1.9894	0.6333
29	C5060	296.1	10.4333	3.5231	1.8980	0.6409
Mean		305.3	10.5981	3.4671	1.8856	0.6180
SD		21.7	1.0840	0.1888	0.1583	0.0376

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Terminal Body and Organ Weights of Pregnant Rats

Dose Level: 30 mg/kg

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Terminal Body Weight (g)	-Liver- Weight (g)	% B.W.	-Kidneys- Weight (g)	% B.W.
32	C5069	245.8	9.6069	3.9092	1.7867	0.7270
33	C5054	311.2	11.1208	3.5731	1.8118	0.5821
34	C5006	288.3	11.0356	3.8278	1.8357	0.6367
35	C5026	359.4	12.0159	3.3435	2.1527	0.5990
36	C5073	350.3	13.7674	3.9298	2.2630	0.6460
37	C5079	318.7	10.6294	3.3357	1.8079	0.5673
38	C4919	296.1	10.7149	3.6184	2.1530	0.7271
39	C4897	286.8	10.7460	3.7475	2.1536	0.7510
40	C5007	313.4	10.2491	3.2708	1.7369	0.5543
41	C5043	322.4	10.6468	3.3023	2.2048	0.6838
42	C5008	319.3	11.1807	3.5016	2.0008	0.6266
43	C5053	253.9	9.8844	3.8932	1.6093	0.6339
44	B1099	312.1	10.9421	3.5064	1.6834	0.5394
45	C4996	351.5	13.5002	3.8404	2.0415	0.5807
46	C5009	292.2	10.1745	3.4819	2.1665	0.7414
47	C4994	315.4	10.8647	3.4445	2.2037	0.6987
48	C4965	311.1	11.2401	3.6134	1.9498	0.6268
49	C5016	291.4	10.3141	3.5395	1.9129	0.6565
50	C5623	303.9	12.0486	3.9644	1.9580	0.6442
51	C4902	317.5	11.2596	3.5464	1.9250	0.6063
52	C5624	257.8	9.5506	3.7051	1.8309	0.7103
53	C5087	330.4	11.5506	3.4956	1.9206	0.5812
54	C4966	341.4	11.4884	3.3652	1.9414	0.5687
55	C4947	273.7	9.6290	3.5176	1.6646	0.6081
56	C5012	301.6	10.6122	3.5189	1.9470	0.6456
57	C5075	268.3	9.6402	3.5933	1.8771	0.6997
58	C5048	316.0	11.6794	3.6962	2.3424	0.7413
59	C4914	310.1	10.9935	3.5456	2.0522	0.6619
60	C5011	272.6	9.2067	3.3771	1.9129	0.7017
Mean		304.6	10.9066	3.5864	1.9602	0.6465
SD		28.8	1.0605	0.1981	0.1878	0.0620

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HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Terminal Body and Organ Weights of Pregnant Rats

Dose Level: 100 mg/kg

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Terminal Body Weight (g)	-Liver- Weight (g)	% B.W.	-Kidneys- Weight (g)	% B.W.
61	C5050	293.4	11.6730	3.9783	2.0335	0.6930
62	C5067	296.0	10.4424	3.5278	1.9802	0.6690
63	C4954	313.1	12.7647	4.0773	2.1669	0.6921
64	C4984	314.0	10.2385	3.2611	2.0169	0.6424
65	C4931	279.4	10.5348	3.7700	1.8707	0.6694
66	C5074	298.1	10.0703	3.3779	1.8653	0.6257
67	C4943	320.6	10.8296	3.3776	2.0268	0.6321
68	C5024	288.0	9.7335	3.3793	1.7330	0.6017
69	C5017	262.8	9.4671	3.6029	1.9432	0.7395
70	C5018	321.8	11.5349	3.5843	2.2990	0.7144
71	C5002	296.9	10.5545	3.5550	1.9648	0.6618
72	C4992	271.8	9.9866	3.6742	1.8058	0.6644
73	C4929	271.1	9.7932	3.6128	1.8103	0.6678
76	C5004	325.7	11.0725	3.3995	2.1683	0.6657
77	C4920	335.8	11.9097	3.5471	1.8979	0.5653
78	C4896	278.4	9.6592	3.4692	1.6522	0.5934
79	C5059	329.1	11.2983	3.4327	1.9774	0.6008
80	C5083	270.2	10.7403	3.9745	1.9043	0.7047
81	C4977	284.7	9.1443	3.2116	1.5092	0.5300
82	C5015	242.6	8.2179	3.3874	1.2971	0.5347
83	C5051	320.9	11.2750	3.5139	1.8638	0.5809
84	C5020	304.8	10.5542	3.4628	2.0300	0.6660
85	C4959	291.9	11.2331	3.8483	2.2728	0.7786
86	C4890	Animal died 3/5/85	--	--	--	--
87	C4979	283.8	10.0080	3.5266	1.9102	0.6731
88	C4957	248.4	8.7903	3.5391	1.7616	0.7092
89	C4918	324.9	11.2919	3.4751	2.0647	0.6354
90	C5072	314.7	11.0341	3.5067	1.8488	0.5876
Mean		295.7	10.5130	3.5582	1.9139	0.6481
SD		25.1	1.0065	0.2125	0.2143	0.0601

HYDROQUINONE: DEVELOPMENTAL TOXICITY STUDY

Individual Terminal Body and Organ Weights of Pregnant Rats

Dose Level: 300 mg/kg

Experiment No. 83-0155G3

-Animal Number- Study	Ear Tag	Terminal Body Weight (g)	-Liver- Weight (g)	% B.W.	-Kidneys- Weight (g)	% B.W.
91	C5038	292.3	11.3780	3.8923	2.1829	0.7468
92	C4941	255.5	9.5329	3.7305	1.6674	0.6525
93	C4961	266.0	9.4778	3.5628	1.7632	0.6628
94	C5076	289.6	10.8542	3.7476	1.9400	0.6698
95	C4948	318.7	12.9411	4.0602	2.2629	0.7100
96	C4985	320.0	11.6681	3.6458	2.0693	0.6466
97	B1090	263.4	9.8400	3.7363	1.8946	0.7194
98	C5078	284.0	9.8049	3.4518	1.8594	0.6546
99	C5061	306.8	10.5994	3.4552	1.8927	0.6170
101	C5068	290.3	9.9335	3.4223	1.7949	0.6184
102	C5047	263.3	9.4011	3.5701	1.5430	0.5860
103	C4942	271.3	10.2951	3.7942	2.0948	0.7720
105	C4893	318.8	11.9754	3.7560	2.0920	0.6561
106	B1097	300.3	10.7336	3.5741	2.0478	0.6819
107	C5086	260.4	9.6396	3.7014	1.8214	0.6994
108	C5039	291.6	10.8366	3.7164	1.8739	0.6426
109	C4933	289.7	10.1707	3.5109	1.7933	0.6190
110	C5034	293.7	11.2948	3.8461	1.9714	0.6713
112	C4991	308.5	10.5434	3.4180	1.8871	0.6118
113	C5019	306.0	10.4123	3.4030	1.9045	0.6224
114	C5041	286.3	9.9312	3.4694	1.7086	0.5969
116	C4907	325.6	11.2375	3.4515	1.9491	0.5987
117	C4999	312.1	10.9660	3.5141	2.0929	0.6707
118	C5044	301.1	11.1992	3.7197	2.0810	0.6912
119	C5070	280.5	9.9625	3.5516	1.8497	0.6594
120	C5057	278.1	9.8426	3.5395	1.8785	0.6755
Mean		291.3	10.5566	3.6246	1.9199	0.6597
SD		20.1	0.8659	0.1687	0.1646	0.0458

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Individual Litter Data Collected at Cesarian Section

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 830155G3
Start Date: 2/19/85 Route: Gavage Dose: Control

Dam's Study	Number Ear Tag	Number Corpora Lutea	Implantations No.	Viable Fetuses No.	-Resorptions- Early No.	Late No.	Dead Fetuses No.	Post Implantation Loss No.	No. Males	Sex No. Females	M:F Ratio	Mean Fetal Body Weight Male	Female	M+F	Gravid Uterine Wt. Grams	Corrected Body Wt.(g)
1	C4909	14	14	14	0	0	0	0	7	7	50:50	3.47	3.11	3.29	69.28	254.15
2	C5030	15	14	12	2	0	0	2	4	8	33:67	3.63	3.48	3.53	65.94	223.00
3	C5065	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
4	C5025	12	12	12	0	0	0	0	6	6	50:50	3.23	3.24	3.23	58.52	213.50
5	C5013	14	13	8	4	1	0	5	6	2	75:25	3.13	3.60	3.25	44.78	267.78
6	C5049	17	16	15	1	0	0	1	11	4	73:27	3.42	3.26	3.38	80.00	257.42
7	C5071	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
8	C5036	17	17	16	1	0	0	1	5	11	31:69	3.27	3.11	3.16	78.39	234.45
9	C5028	17	14	12	2	0	0	2	4	8	33:67	3.71	3.34	3.47	65.40	243.59
10	C5010	18	15	15	0	0	0	0	6	9	40:60	3.34	3.16	3.23	80.68	260.45
11	C5005	14	13	13	0	0	0	0	11	2	85:15	3.30	3.24	3.29	67.30	239.31
12	C5001	19	17	15	2	0	0	2	7	8	47:53	2.95	2.64	2.79	69.94	258.83
13	C5621	14	16	16	0	0	0	0	9	7	56:44	3.03	2.98	3.01	75.46	220.65
14	B1098	16	16	15	0	1	0	1	7	8	47:53	3.47	3.31	3.38	79.95	247.10
15	C4908	17	12	12	0	0	0	0	3	9	25:75	3.36	3.38	3.38	64.12	210.29
16	C5029	14	16	14	2	0	0	2	3	11	21:79	3.03	2.71	2.80	65.90	192.12
17	C5003	12	14	12	2	0	0	2	4	8	33:67	3.34	3.30	3.31	63.96	248.65
18	C5052	15	10	5	3	2	0	5	3	2	60:40	3.88	3.37	3.68	31.92	261.60
19	C4953	12	13	12	0	1	0	1	6	6	50:50	3.34	3.22	3.28	63.62	244.93
20	C5085	17	14	14	0	0	0	0	7	7	50:50	2.93	2.68	2.81	64.57	257.20
21	C5032	17	15	14	1	0	0	1	10	4	71:29	3.10	3.00	3.07	66.99	261.31
22	C4915	14	13	13	0	0	0	0	2	11	15:85	3.28	3.17	3.19	63.48	236.46
23	C5021	13	13	12	1	0	0	1	8	4	67:33	3.23	3.04	3.16	61.22	228.92
24	C4939	11	12	12	0	0	0	0	5	7	42:58	2.84	2.81	2.82	58.08	216.36
25	C4923	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
26	C4987	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
27	C5066	15	14	14	0	0	0	0	9	5	64:36	2.97	2.90	2.95	64.76	249.36
28	C5077	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
29	C5060	19	17	15	2	0	0	2	5	10	33:67	2.91	2.98	2.97	68.47	227.67
30	C5058	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
	Mean	15.1	14.2	13.0	1.0	0.2	0	1.2	6.2	6.8	48:52	3.26	3.13	3.18	65.53	239.80
	SD	2.3	1.8	2.5	1.2	0.5	--	1.4	2.5	2.8	--	0.26	0.25	0.24	10.75	19.71

Individual Litter Data Collected at Cesarian Section

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 830155G3
Start Date: 2/19/85 Route: Gavage Dose: 30 mg/kg

Dam's Study	Number Ear Tag	Number Corpora Lutea	Implantations No.	Viable Fetuses No.	-Resorptions- Early No.	Late No.	Dead Fetuses No.	Post Implantation Loss No.	No. Males	Sex No. Females	M:F Ratio	Mean Fetal Body Weight Male	Female	M+F	Gravid Uterine Wt. Grams	Corrected Body Wt.(g)
31	C4955	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
32	C5069	13	10	2	8	0	0	8	1	1	50:50	3.96	3.80	3.88	14.85	230.90
33	C5054	12	13	12	1	0	0	1	5	7	42:58	3.36	3.46	3.42	64.08	247.19
34	C5006	16	14	14	0	0	0	0	4	10	29:71	3.17	3.00	3.05	68.38	219.92
35	C5026	17	17	17	0	0	0	0	10	7	59:41	3.27	3.25	3.26	84.63	274.75
36	C5073	16	16	15	0	1	0	1	9	6	60:40	3.57	3.21	3.42	83.32	266.51
37	C5079	19	18	13	5	0	0	5	8	5	62:38	2.99	3.12	3.04	64.07	254.59
38	C4919	11	13	11	2	0	0	2	7	4	64:36	3.04	3.26	3.12	57.07	239.05
39	C4897	14	12	12	0	0	0	0	5	7	42:58	3.14	3.24	3.20	59.04	227.71
40	C5007	15	14	13	1	0	0	1	7	6	54:46	2.94	3.25	3.08	63.39	249.96
41	C5043	15	16	16	0	0	0	0	9	7	56:44	3.00	2.88	2.95	75.54	246.87
42	C5008	15	16	13	3	0	0	3	5	8	38:62	3.06	2.92	2.97	62.44	256.86
43	C5053	10	10	10	0	0	0	0	4	6	40:60	3.60	3.65	3.63	56.67	197.22
44	B1099	15	16	16	0	0	0	0	7	9	44:56	3.16	3.24	3.20	79.24	232.82
45	C4996	18	17	17	0	0	0	0	10	7	59:41	3.40	3.26	3.34	88.53	263.00
46	C5009	12	9	7	2	0	0	2	5	2	71:29	3.15	3.00	3.11	36.89	255.32
47	C4994	16	17	16	1	0	0	1	8	8	50:50	3.05	3.01	3.03	76.33	239.09
48	C4965	17	16	13	3	0	0	3	6	7	46:54	3.48	3.13	3.29	70.23	240.84
49	C5016	14	12	10	2	0	0	2	5	5	50:50	3.69	3.41	3.55	55.83	235.57
50	C5623	16	12	8	4	0	0	4	4	4	50:50	4.29	3.74	4.02	49.61	254.31
51	C4902	13	14	13	1	0	0	1	4	9	31:69	3.54	3.14	3.26	67.11	250.38
52	C5624	12	8	4	4	0	0	4	3	1	75:25	3.30	3.69	3.40	23.17	234.60
53	C5087	13	16	15	1	0	0	1	6	9	40:60	3.13	2.98	3.04	71.78	258.65
54	C4966	13	13	13	0	0	0	0	9	4	69:31	3.08	2.95	3.04	62.80	278.59
55	C4947	12	12	12	0	0	0	0	6	6	50:50	3.28	3.08	3.18	61.35	212.39
56	C5012	13	13	13	0	0	0	0	4	9	31:69	2.97	2.88	2.90	61.49	240.09
57	C5075	14	15	7	8	0	0	8	2	5	29:71	3.31	3.27	3.28	39.19	229.09
58	C5048	15	8	8	0	0	0	0	6	2	75:25	3.72	3.41	3.64	46.69	269.29
59	C4914	14	14	14	0	0	0	0	4	10	29:71	3.42	3.06	3.16	70.41	239.65
60	C5011	16	15	15	0	0	0	0	5	10	33:67	3.31	3.14	3.20	74.94	197.68
	Mean	14.3	13.7	12.0	1.6	.03	0	1.6	5.8	6.2	49:51	3.32	3.21	3.26	61.69	242.86
	SD	2.1	2.8	3.8	2.3	0.2	--	2.3	2.3	2.6	--	0.32	0.25	0.27	17.12	20.16

000768

Individual Litter Data Collected at Cesarian Section

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 830155G3
Start Date: 2/19/85 Route: Gavage Dose: 100 mg/kg

Dam's Study	Number Ear Tag	Number Corpora Lutea	Implantations No.	Viable Fetuses No.	-Resorptions- Early No.	Late No.	Dead Fetuses No.	Post Implantation Loss No.	No. Males	Sex No. Females	M:F Ratio	Mean Fetal Body Weight Male	Female	M+F	Gravid Uterine Wt. Grams	Corrected Body Wt.(g)
61	C5050	23	10	9	1	0	0	1	4	5	56:44	2.79	2.89	2.85	42.66	250.76
62	C5067	14	12	10	2	0	0	2	8	2	80:20	3.18	3.18	3.18	55.07	240.93
63	C4954	12	5	5	0	0	0	0	1	4	20:80	3.53	3.40	3.43	29.71	283.36
64	C4984	14	15	15	0	0	0	0	8	7	53:47	2.92	3.10	3.00	73.66	240.30
65	C4931	12	12	9	3	0	0	3	7	2	78:22	3.17	3.25	3.19	44.85	234.59
66	C5074	13	12	12	0	0	0	0	5	7	42:58	3.03	3.12	3.08	58.49	239.63
67	C4943	16	16	14	2	0	0	2	9	5	64:36	2.92	2.89	2.91	67.32	253.31
68	C5024	16	15	14	1	0	0	1	6	8	43:57	3.35	3.35	3.35	72.53	215.53
69	C5017	11	3	3	0	0	0	0	0	3	0:100	—	3.72	3.72	18.66	244.10
70	C5018	15	15	15	0	0	0	0	6	9	40:60	3.15	3.03	3.08	72.91	248.91
71	C5002	12	12	10	1	1	0	2	5	5	50:50	3.52	3.22	3.37	52.07	244.82
72	C4992	14	14	12	2	0	0	2	4	8	33:67	2.74	2.74	2.74	54.80	217.00
73	C4929	12	12	11	1	0	0	1	5	6	45:55	3.76	3.39	3.56	62.57	208.50
74	C4913	Not Pregnant		—	—	—	—	—	—	—	—	—	—	—	—	—
75	C5088	Not Pregnant		—	—	—	—	—	—	—	—	—	—	—	—	—
76	C5004	13	15	13	2	0	0	2	6	7	46:54	3.24	3.20	3.22	70.90	254.81
77	C4920	18	15	14	1	0	0	1	6	8	43:57	3.26	2.88	3.04	69.69	266.07
78	C4896	15	15	11	4	0	0	4	6	5	55:45	3.24	2.95	3.11	55.64	222.79
79	C5059	14	14	14	0	0	0	0	8	6	57:43	3.37	3.41	3.39	71.62	257.52
80	C5083	11	6	6	0	0	0	0	2	4	33:67	3.55	3.34	3.41	33.58	236.65
81	C4977	16	16	13	3	0	0	3	4	9	31:69	3.04	2.85	2.91	61.27	223.46
82	C5015	13	11	11	0	0	0	0	4	7	36:64	3.03	2.88	2.93	50.36	192.24
83	C5051	12	12	12	0	0	0	0	6	6	50:50	3.24	3.21	3.22	60.40	260.47
84	C5020	18	13	13	0	0	0	0	5	8	38:62	3.34	2.93	3.08	63.08	241.71
85	C4959	8	5	5	0	0	0	0	2	3	40:60	3.84	3.25	3.49	27.44	264.46
86	C4890	Died 3/5/85		—	—	—	—	—	—	—	—	—	—	—	—	—
87	C4979	15	14	13	1	0	0	1	9	4	69:31	3.12	2.97	3.07	65.01	218.78
88	C4957	15	4	4	0	0	0	0	3	1	75:25	3.33	3.02	3.26	21.50	226.88
89	C4918	16	16	14	2	0	0	2	3	11	21:79	3.21	3.06	3.09	69.95	254.99
90	C5072	14	16	13	3	0	0	3	7	6	54:46	3.47	3.32	3.40	68.52	246.14
	Mean	14.1	12.0	10.9	1.1	.04	0	1.1	5.1	5.8	46:54	3.24	3.13	3.19	55.34	240.32
	SD	2.8	4.0	3.5	1.2	0.2	—	1.2	2.3	2.4	—	0.27	0.23	0.23	16.60	20.01

000077

Individual Litter Data Collected at Cesarian Section

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 830155G3
Start Date: 2/19/85 Route: Gavage Dose: 300 mg/kg

Dam's Study	Number Ear Tag	Number Corpora Lutea	Implantations No.	Viable Fetuses No.	-Resorptions- Early No.	Late No.	Dead Fetuses No.	Post Implantation Loss No.	No. Males	Sex No. Females	M:F Ratio	Mean Fetal Body Weight Male	Female	M+F	Gravid Uterine Wt. Grams	Corrected Body Wt.(g)
91	C5038	13	14	13	1	0	0	1	6	7	46:54	2.91	3.00	2.96	63.62	228.70
92	C4941	16	11	9	2	0	0	2	3	6	33:67	2.39	2.76	2.64	40.50	215.04
93	C4961	13	14	14	0	0	0	0	10	4	71:29	2.78	2.83	2.79	65.28	200.74
94	C5076	15	15	14	1	0	0	1	7	7	50:50	3.29	3.15	3.22	71.63	218.00
95	C4948	13	15	13	1	1	0	2	6	7	46:54	3.30	3.25	3.27	68.82	249.91
96	C4985	12	13	12	1	0	0	1	5	7	42:58	3.65	3.30	3.45	65.57	254.47
97	B1090	14	14	13	1	0	0	1	6	7	46:54	2.61	2.47	2.54	57.10	206.26
98	C5078	16	13	11	1	1	0	2	4	7	36:64	3.06	3.07	3.06	55.55	228.50
99	C5061	13	12	12	0	0	0	0	6	6	50:50	3.17	2.97	3.07	62.04	244.73
100	C4894	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
101	C5068	17	15	15	0	0	0	0	6	9	40:60	3.11	2.80	2.93	66.93	223.33
102	C5047	13	13	7	6	0	0	6	5	2	71:29	2.90	2.82	2.88	35.98	227.35
103	C4942	6	5	4	1	0	0	1	2	2	50:50	3.32	3.14	3.23	22.90	248.44
104	C4935	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
105	C4893	13	15	15	0	0	0	0	6	9	40:60	2.90	2.71	2.78	70.35	248.48
106	B1097	21	16	14	2	0	0	2	6	8	43:57	3.17	2.86	2.99	67.21	233.11
107	C5086	11	10	3	7	0	0	7	2	1	67:33	3.81	3.46	3.69	18.95	241.48
108	C5039	11	11	11	0	0	0	0	2	9	18:82	3.39	3.34	3.35	60.63	230.96
109	C4933	13	12	12	0	0	0	0	7	5	58:42	2.72	2.65	2.69	54.18	235.51
110	C5034	16	16	15	1	0	0	1	9	6	60:40	2.75	2.54	2.68	64.93	228.74
111	C5622	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
112	C4991	12	12	12	0	0	0	0	5	7	42:58	3.67	3.49	3.56	64.62	243.85
113	C5019	15	15	14	1	0	0	1	6	8	43:57	3.18	2.86	2.99	66.70	239.27
114	C5041	15	13	13	0	0	0	0	3	10	23:77	3.10	2.67	2.77	57.45	228.80
115	C4982	Not Pregnant		--	--	--	--	--	--	--	--	--	--	--	--	--
116	C4907	17	17	17	0	0	0	0	6	11	35:65	3.03	2.97	2.99	82.38	243.20
117	C4999	17	16	16	0	0	0	0	7	9	44:56	2.97	2.77	2.86	75.40	236.66
118	C5044	18	16	16	0	0	0	0	14	2	88:12	2.76	2.78	2.76	73.46	227.62
119	C5070	17	14	14	0	0	0	0	5	9	36:64	3.09	2.94	2.99	65.72	214.79
120	C5057	12	12	12	0	0	0	0	6	6	50:50	3.26	3.05	3.15	60.02	218.06
	Mean	14.2	13.4	12.3	1.0	.08	0	1.1	5.8	6.6	47:53	3.09	2.95	3.01	59.92	231.38
	SD	2.9	2.5	3.4	1.7	0.3	--	1.8	2.6	2.6	--	0.33	0.27	0.29	15.00	13.77

Individual Litter Data - External, Internal Soft Tissue and Skeletal Alterations

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 83-0155G3

Start Date: 2-19-85 Route Gavage Dose Control

Dam's Ear Tag No.	C 4 9 0 9	C 5 0 3 0	C 5 0 6 5	C 5 0 2 5	C 5 0 1 3	C 5 0 4 9	C 5 0 7 1	C 5 0 3 6	C 5 0 2 8	C 5 0 1 0	C 5 0 0 5	C 5 0 0 1	C 5 6 2 1	B 1 0 9 8	C 4 9 0 8	C 5 0 2 9	C 5 0 0 3	C 5 0 5 2	C 4 9 5 3	C 5 0 8 5	C 5 0 3 2	C 4 9 1 5	C 5 0 2 1	C 4 9 3 9	C 4 9 2 3	C 4 9 8 7	C 5 0 6 6	C 5 0 7 7	C 5 0 6 0	C 5 0 5 8	Total Fetuses	Total Litters
Dam's Study No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30		
NO. FETUSES EXAMINED:																																
External	14	12	NP	12	8	15	NP	16	12	15	13	15	16	15	12	14	12	5	12	14	14	13	12	12	NP	NP	14	NP	15	NP	312	24
Soft Tissue	7	6	-	6	4	8	-	8	6	7	7	8	8	7	6	7	6	2	6	7	7	7	6	6	-	-	7	-	7	-	156	24
Skeletal	7	6	-	6	4	7	-	8	6	8	6	7	8	8	6	7	6	3	6	7	7	6	6	6	-	-	7	-	8	-	156	24
EXTERNAL ALTERATIONS:																																
Hematoma								1																							1	1
SOFT TISSUE ALTERATIONS:																																
Dilated Renal Pelvis																																
Unilateral					2																										2	1
Bilateral																																
Hydronephrosis																																
Unilateral																																
Bilateral															1																1	1
Hydroureter																																
Unilateral																																
Bilateral																																
Right Subclavian Artery Mispositioned																																
Diaphragmatic Hernia																																
SKELETAL ALTERATIONS:																																
Skull																																
Partial Ossification																																
Hyoid	1									2	1	1		1	2		2		2	1		1	1								15	11
Premaxilla																																
Parietal											1			1																	2	2
Interparietal		1									1											1		2							5	4
Supraoccipital		1									1																				2	2
Basooccipital																	1				1										2	2
Palatine																								1							1	1
Non-Ossification																																
Hyoid											1								1					1							3	3
Presphenoid																								1							1	1
Enlarged Fontanelles																																
Micrognathia																								1							1	1
Vertebrae																																
Thoracic Centrae																																
Partial Ossification																																
First	1			2	1							5		4		1			1	3	1		3	3			1		1		27	13
Second																																
Third																								1							1	1

Dam's Ear Tag No.	C 4 9 0 9	C 5 0 3 0	C 5 0 6 5	C 5 0 2 5	C 5 0 1 3	C 5 0 4 9	C 5 0 7 1	C 5 0 3 6	C 5 0 2 8	C 5 0 1 0	C 5 0 0 5	C 5 0 0 1	C 5 6 2 1	B 1 0 9 8	C 4 9 0 8	C 5 0 2 9	C 5 0 0 3	C 5 0 5 2	C 4 9 5 3	C 5 0 8 5	C 5 0 3 2	C 4 9 1 5	C 5 0 2 1	C 4 9 3 9	C 4 9 2 3	C 4 9 8 7	C 5 0 6 6	C 5 0 7 7	C 5 0 6 0	C 5 0 5 8	Total	
Dam's Study No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	Fetuses	Litters
Vertebrae (Cont'd)																																
Thoracic Centrae																																
Non-Ossification																																
First																								1							1	1
Second																								1							1	1
Bilobed																																
First																																
Fourth																																
Seventh														1							1										2	2
Eighth																			1					1							2	2
Ninth	1									1						1			1		1										5	5
Tenth											1	1		1	1				2	2	1	2	1	3					1		16	11
Eleventh	3			3	1									2	3	1		1	3	3	2	1	3	2					1		29	14
Twelfth	2			2		1					1		1				3	1	2	2	1		1	2			1		1		21	14
Thirteenth						1								1			1		3				1	1			1		1		10	8
Split																																
Ninth																																
Eleventh																1															1	1
Twelfth																																
Thirteenth																																
Lumbar Arches																																
Partial Ossification																																
Fifth																																
Sixth																																
Lumbar Centrae																																
Bilobed																																
First																			1												1	1
Sacral Arches																																
Partial Ossificaion																																
First																																
Second																																
Third	1				1					5							1				1			1					1		11	7
Fourth	3			1	3	2				8		7		3		1	2	3	2	7	4	1		3			5		5		60	17
Sacral Centrae																																
Partial Ossification																																
First																																
Second																																
Third																																
Fourth																																
PELVIC GIRDLE:																																
Pubis																																
Partial Ossif.	1										1								1								1				4	4
Non-ossification																								1							1	1
Ischium																																
Partial Ossification																																
EXTREMITIES:																																
Metacarpals																																
Partial Ossification																																
Metatarsals																																
Partial Ossification																								1							1	1

00080

Dam's Ear Tag No.	C490	C503	C506	C502	C501	C504	C507	C503	C502	C501	C500	C500	C562	B109	C490	C502	C500	C505	C495	C508	C503	C491	C521	C493	C495	C498	C506	C507	C506	C505	Total	
Dam's Study No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	Fetuses	Litters
RIBS:																																
Wavy																																
14th Thoracolumbar																																
Rudimentary									1		1													1							3	3
Shortened 13th																																
Right																																
Left																	1														1	1
Pair						1															2										3	2
9th,10,11,&13th																																
Missing																																
13th																																
Left																																
Pair																																
STERNEBRAE:																																
<4 Ossified												1										1		1							3	3
Partial Ossification																																
First													1											1							2	2
Second										1	2	1	2	1					1	3		1		1					2		15	10
Third																								1							1	1
Fourth										5		4			2					1				1							13	5
Fifth	4	5		2	1	4		4	6	3	3		6	1	1	4	2	1	2	1		2	2	2			4				60	21
Sixth	7	5		6	4	7		6	6	8	5	6	6	4	3	3	5	3	5	7	7	3	1	2			7		4		120	24
Non-Ossification																																
First																																
Second																																
Third																																
Fourth												1										1									2	2
Fifth	3			4	3	3		4		4	3	7		6	5	3	3	2	4	6	7	4	3	4			3		8		89	21
Sixth								2			1	1	2	4	3	4			1			3	4	4					4		33	12
Bilobed																																
First																																
Second																																
Third																																
Fourth																																
Fifth																			1												1	1
Split													1																		1	1
Fifth																																

NP = Not Pregnant

Individual Litter Data - External, Internal Soft Tissue and Skeletal Alterations

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 83-0155G3

Start Date: 2-19-85 Route Gavage Dose 30 mg/kg

Dam's Ear Tag No.	C 4 9 5 5	C 5 0 6 9	C 5 5 5 4	C 5 0 0 0	C 5 0 2 6	C 5 0 7 3	C 5 0 7 9	C 4 9 1 9	C 4 8 9 7	C 5 0 0 7	C 5 0 4 3	C 5 0 0 8	C 5 0 5 3	B 1 0 9 9	C 4 9 9 6	C 5 0 0 9	C 4 9 9 4	C 4 9 6 5	C 5 0 1 6	C 5 6 2 3	C 4 9 0 2	C 5 6 2 4	C 5 0 8 7	C 4 9 6 6	C 4 9 4 7	C 5 0 1 2	C 5 0 7 5	C 5 0 4 8	C 4 9 1 4	C 5 0 1 1	Total	
Dam's Study No.	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	Fetuses	Litters
NO. FETUSES EXAMINED:																																
External	NP	2	12	14	17	15	13	11	12	13	16	13	10	16	17	7	16	13	10	8	13	4	15	13	12	13	7	8	14	15	349	29
Soft Tissue	-	1	6	7	8	8	7	6	6	6	8	6	5	8	8	4	8	7	4	4	6	2	8	6	6	7	4	4	7	8	175	29
Skeletal	-	1	6	7	9	7	6	5	6	7	8	7	5	8	9	3	8	6	6	4	7	2	7	7	6	6	3	4	7	7	174	29
EXTERNAL ALTERATIONS:																																
Hematoma																														1	1	1
SOFT TISSUE ALTERATIONS:																																
Dilated Renal Pelvis																															1	1
Unilateral														1																	6	4
Bilateral				1		1	3				1																					
Hydronephrosis																															2	2
Unilateral						1									1																1	1
Bilateral															1																	
Hydroureter																															2	2
Unilateral				1		1																									1	1
Bilateral				1																											1	1
Right Subclavian Artery Mispositioned											1																					
Diaphragmatic Hernia																																
SKELETAL ALTERATIONS:																																
Skull																																
Partial Ossification																																
Hyoid					1		2		2								2		4	2	2								1	1	17	9
Premaxilla																																
Parietal																																
Interparietal																																
Supraoccipital																			2												2	1
Basooccipital																																
Palatine																																
Non-Ossification																																
Hyoid															1															1	2	2
Presphenoid																																
Enlarged Fontanelles																																
Micrognathia																																
Vertebrae																																
Thoracic Centrae																																
Partial Ossification																																
First							2		3	2	1		1		5		1				2	1	1	1				1	2		23	13
Second																													1		1	1
Third																																

00082

Dam's Ear Tag No.	C495	C569	C505	C506	C502	C503	C507	C419	C489	C500	C504	C500	C503	B109	C496	C509	C494	C495	C501	C563	C490	C562	C587	C496	C494	C501	C507	C584	C491	C501	Total	
Dam's Study No.	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	Fetuses	Litters
Vertebrae (Cont'd)																																
Thoracic Centrae																																
Non-Ossification																																
First																					1		1						1		3	3
Second																																
Bilobed																																
First													1																		1	1
Fourth									1																						1	1
Seventh																																
Eighth									1																						1	1
Ninth							1		1																				1		3	3
Tenth						2	2	1	1	1		1			1					1	2		1	1					1		15	12
Eleventh			3			3	4	1	4	2	1	1	1	1	2			1	3		6	1	2			2			1	1	39	18
Twelfth			1			3	2	2	2					2	3				2	2	3	1							1		24	12
Thirteenth						2			2													1						1			6	4
Split																																
Ninth																																
Eleventh																																
Twelfth									1																					1	2	2
Thirteenth																																
Lumbar Arches																																
Partial Ossification																																
Fifth																			1												1	1
Sixth																			1												1	1
Lumbar Centrae																																
Partial Ossification																																
First																																
Sacral Arches																																
Partial Ossificaion																																
First																			1												1	1
Second									1									1	1										1		4	4
Third							1		3	2		1			3	1		3	4		1	1				1		2	3		26	13
Fourth					1	1	3	5	5	3	4	7			6	3	3	6	6		5	2	6			5	1	4	5		81	20
Sacral Centrae																																
Partial Ossification																																
First																																
Second																																
Third																																
Fourth																																
PELVIC GIRDLE:																																
Pubis																																
Partial Ossif.									1			1						1	4		1							2			10	6
Non-ossification																																
Ischium																																
Partial Ossif.																			1		1										2	2
EXTREMITIES:																																
Metacarpals																																
Partial Ossification																			1												1	1
Metatarsals																																
Partial Ossification																												1			1	1

000083

Dam's Ear Tag No.	C495	C506	C505	C500	C502	C507	C507	C491	C489	C500	C504	C500	C505	B109	C499	C500	C499	C496	C501	C562	C490	C562	C508	C496	C494	C501	C507	C504	C491	C501	Total	
Dam's Study No.	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	Fetuses	Litters
RIBS:																																
Wavy																																
14th Thoracolumbar																																
Rudimentary																																
Shortened 13th																																
Right																																
Left				1											1														1		2	2
Pair																									1						2	2
9th,10,11,&13th																										4	1	1			6	3
Missing																			1												1	1
13th																																
Left																																
Pair																																
STERNEBRAE:																																
<4 Ossified																																
Partial Ossification														1																	1	1
First					1					1				1			1	1				1						2	1		9	8
Second					1					2				1	2							1			3						10	6
Third																									1				1		2	2
Fourth							1		1					2	1	1						2	1	1	2			1	1		14	11
Fifth	1	4	3	6	5		2	3	4	3	5	4	3	2	6	1	4	3	3	1	5		1	2	4	5		1	4	3	88	27
Sixth	1	6	7	9	5		1	5	5	7	8	7	2	7	9	3	8	6	6	1	7	2	7	7	6	6	3		7	7	155	28
Non-Ossification																																
First																																
Second																																
Third																													1		1	1
Fourth														1																		
Fifth			4	3			4	2	2	4	3	3	1	6	3	2	4	3	3		2	2	6	5	2	1	3	3	3	4	1	1
Sixth							5		1					1														4			78	25
Bilobed																															11	4
First									1																							
Second									1																						1	1
Third									1																						1	1
Fourth									1																						1	1
Fifth																															1	1
Split																																
Fifth																																

NP = Not Pregnant

0008

Individual Litter Data - External, Internal Soft Tissue and Skeletal Alterations

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 83-0155G3

Start Date: 2-19-85 Route Gavage Dose 100 mg/kg

Dam's Ear Tag No.	C 5 0 5 0	C 5 0 6 7	C 4 9 5 4	C 4 9 8 4	C 4 9 3 1	C 5 0 7 4	C 4 9 4 3	C 5 0 2 4	C 5 0 1 7	C 5 0 1 8	C 5 0 0 2	C 4 9 9 2	C 4 9 2 9	C 4 9 1 3	C 5 0 8 8	C 5 0 0 4	C 4 9 2 0	C 4 8 9 6	C 5 0 5 9	C 5 0 8 3	C 4 9 7 7	C 5 0 1 5	C 5 0 0 1	C 5 0 0 2	C 4 9 5 9	C 4 8 9 0	C 4 9 7 9	C 4 9 5 7	C 4 9 1 8	C 5 0 7 2	Total	
Dam's Study No.	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	Fetuses	Litters
NO. FETUSES EXAMINED:																																
External	9	10	5	15	9	12	14	14	3	15	10	12	11	NP	NP	13	14	11	14	6	13	11	12	13	5	Died	13	4	14	13	295	27
Soft Tissue	5	5	2	8	4	6	7	7	1	7	5	6	5	-	-	7	7	5	7	3	7	6	6	6	2	-	6	2	7	7	146	27
Skeletal	4	5	3	7	5	6	7	7	2	8	5	6	6	-	-	6	7	6	7	3	6	5	6	7	3	-	7	2	7	6	149	27
EXTERNAL ALTERATIONS:																																
Hematoma																							1								1	1
SOFT TISSUE ALTERATIONS:																																
Dilated Renal Pelvis																																
Unilateral	1		1															2							1		1				6	5
Bilateral																							1								1	1
Hydronephrosis																																
Unilateral							1									1											1				3	3
Bilateral																			2												2	1
Hydroureter																																
Unilateral							1																								1	1
Bilateral																																
Right Subclavian Artery Mispositioned																																
Diaphragmatic Hernia																																
SKELETAL ALTERATIONS:																																
Skull																																
Partial Ossification																																
Hyoid				1	1			1		2						1						2		1	2		1			1	13	10
Premaxilla		1																													1	1
Parietal																									1						1	1
Interparietal																								1	1						2	2
Supraoccipital		1																						1	1						3	3
Basooccipital	2															1												1			4	3
Palatine																																
Non-Ossification																																
Hyoid		2																													2	1
Presphenoid																																
Enlarged Fontanelles																									1						1	1
Micrognathia																																
Vertebrae																																
Thoracic Centrae																																
Partial Ossification																																
First	2				1	2		1		1						1						1	1	1	1		1				13	11
Second																																
Third																																

00085

Dam's Ear Tag No.	C505	C506	C495	C448	C493	C507	C493	C502	C501	C501	C502	C499	C492	C491	C508	C504	C492	C489	C505	C508	C497	C501	C515	C550	C495	C489	C497	C495	C491	C507	Total	
Dam's Study No.	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	Fetuses	Litters
Vertebrae (Cont'd)																																
Thoracic Centrae																																
Non-Ossification																																
First	1																															
Second																1							1								3	3
Bilobed																																
First																																
Fourth																																
Seventh																																
Eighth																							1								1	1
Ninth						1	1																1								1	1
Tenth			1	1		1																	1								3	3
Eleventh		2	3		2	2			1	4		1				2						1	3	1							10	7
Twelfth	3	1	1			1				1	2					1				2		1	2		1		1		2	1	26	15
Thirteenth		1																		3		1	2	1			1	1	1		19	13
Split																				1											2	2
Ninth																																
Eleventh																				1											1	1
Twelfth																																
Thirteenth																							1								1	1
Lumbar Arches																																
Partial Ossification																																
Fifth																																
Sixth																																
Lumbar Centrae																																
Partial Ossification																																
First																																
Sacral Arches																																
Partial Ossificaion																																
First																																
Second	1																															
Third	4									2		1				2									1						2	2
Fourth	4	1			2	5		1	1	7		5				6	1					1 4	1	3 5	2 3		6 7	1 1	1 5	2	23 61	10 18
Sacral Centrae																																
Partial Ossification																																
First	1																															
Second	1																														1	1
Third	1																														1	1
Fourth	1																														1	1
PELVIC GIRDLE:																															1	1
Pubis																																
Partial Ossif.	1																															
Non-ossification																1									1					1	4	4
Ischium																																
Partial Ossification																														1	1	1
EXTREMITIES:																																
Metacarpals																																
Partial Ossif.	1																															
Metatarsals																									1						2	2
Partial Ossification																																

000086

Dam's Ear Tag No.	C 505 0	C 506 7	C 495 4	C 498 4	C 493 1	C 507 4	C 494 3	C 502 4	C 501 7	C 501 8	C 500 2	C 499 2	C 499 2 9	C 491 3	C 508 8	C 500 4	C 492 0	C 489 6	C 505 9	C 508 3	C 497 7	C 501 5	C 505 1	C 502 0	C 495 9	C 489 0	C 499 7	C 495 7	C 491 8	C 507 2	Total	
Dam's Study No.	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	Fetuses	Litters
RIBS:																																
Wavy																																
14th Thoracolumbar																																
Rudimentary																																
Shortened 13th																		1													1	1
Right								1																								
Left				1																									1		2	2
Pair	1																1												1		3	3
9th,10,11,&13th																													2	1	4	3
Missing																																
13th																																
Left																																
Pair																	1														1	1
STERNEBRAE:																																
<4 Ossified							1																									
Partial Ossification																																
First																															1	1
Second				2			1					1										2		1							1	1
Third																								1						1	8	6
Fourth	2			2			1	1				2				2					2	3		1							1	1
Fifth		3	2	1	4	1		1	2	5	4	2	5			1	3	2	1	2	2	2	3	2	1		1	1		1	21	13
Sixth	4	3	2	2	4	6	7	5		6	3	6	6			6	7	6	6	2	6	5	5	4	2		7	2	5	6	60	23
Non-Ossification																															123	26
First																																
Second							1																								1	1
Third																																
Fourth				1			1																								3	3
Fifth	4	1	1	6	1	5	7	6		3	1	4	1			5	4	4	6	1	4	3	3	1	3		1		6	3	87	25
Sixth		1		5	1			2															1	3	1						14	7
Bilobed																																
First																																
Second																																
Third																																
Fourth												1																			1	1
Fifth																																
Split																																
Fifth																																

NP = Not Pregnant

00087

Individual Litter Data - External, Internal Soft Tissue and Skeletal Alterations

Compound: Hydroquinone HAEL No. 83-0155 Accession No. 900356 Experiment No. 83-0155G3

Start Date: 2-19-85 Route Gavage Dose 300 mg/kg

Dam's Ear Tag No.	C	C	C	C	C	C	B	C	C	C	C	C	C	C	C	B	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C		
	5	4	4	5	4	4	1	5	5	4	5	5	4	4	4	1	5	5	4	5	5	4	5	5	4	4	4	5	5	5		
	0	9	9	0	9	9	0	0	0	8	0	0	9	9	8	0	0	0	9	0	0	9	0	0	9	9	9	0	0	0		
	3	4	6	7	4	8	9	7	6	9	6	4	4	3	9	9	8	3	3	3	2	9	1	4	8	0	9	4	7	5		
Dam's Study No.	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	Total Fetuses	Total Litters
NO. FETUSES EXAMINED:																																
External	13	9	14	14	13	12	13	11	12	NP	15	7	4	NP	15	14	3	11	12	15	NP	12	14	13	NP	17	16	16	14	12	321	26
Soft Tissue	7	5	7	7	6	6	6	4	6	-	8	4	2	-	8	7	1	6	6	8	-	6	7	6	-	8	8	8	7	6	160	26
Skeletal	6	4	7	7	7	6	7	7	6	-	7	3	2	-	7	7	2	5	6	7	-	6	7	7	-	9	8	8	7	6	161	26
EXTERNAL ALTERATIONS:																																
Hematoma							1									1														1	3	3
Soft Tissue Alterations:																																
Dilated Renal Pelvis																																
Unilateral											2									1											3	2
Bilateral																													3		3	1
Hydronephrosis																																
Unilateral																													2		2	1
Bilateral																													1		1	1
Hydroureter																																
Unilateral																																
Bilateral											2																				2	1
Right Subclavian Artery Mispositioned																																
Diaphragmatic Hernia						1																									1	1
SKELETAL ALTERATIONS:																																
Skull																																
Partial Ossification																																
Hyoid	1	1				2	1									1				2			3	3						2	16	9
Premaxilla																																
Parietal																								1							1	1
Interparietal																								1							1	1
Supraoccipital																																
Basooccipital	1	1											2			1								4							9	5
Palatine																																
Non-Ossification																																
Hyoid			1																												1	1
Presphenoid																																
Enlarged Fontanelles																																
Micrognathia																																
Vertebrae																																
Thoracic Centrae																																
Partial Ossification																																
First	2	5		3			1				1					1		3	2	1			3	3			4	5			34	13
Second		1																													1	1
Third																								1							1	1
Eleven							1																								1	1
Twelve							1																								1	1
Thirteen							1																								1	1

00088

Dam's Ear Tag No.	C503	C494	C496	C507	C494	C498	B109	C507	C506	C489	C506	C504	C494	C493	C483	B109	C508	C503	C493	C503	C562	C491	C501	C504	C498	C497	C499	C504	C507	C505	Total	
Dam's Study No.	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	Fetuses	Litters
Vertebrae (Cont'd)																																
Thoracic Centrae																																
Non-Ossification																																
First			1																												1	1
Second																																
Bilobed																																
First																																
Fourth																																
Seventh																																
Eighth								1																							1	1
Ninth									1							1				1											3	3
Tenth	1		1		2		1																1	2						1	9	7
Eleventh		1	1		6	1	1	2	4		1		1			3						2	2	3		1	2	6	2	1	40	18
Twelfth		1	1		4		1	2				2			2	2		1		2		1	2	3			1	3	1	2	31	17
Thirteenth		1	1		2								1															3			8	5
Split																																
Ninth																																
Eleventh					1																									1	2	2
Twelfth																																
Thirteenth																													1		1	1
Lumbar Arches																																
Partial Ossification																																
Fifth																								1							1	1
Sixth																								1							1	1
Lumbar Centrae																																
Bilobed																																
First		1						1																							2	2
Sacral Arches																																
Partial Ossificaion																																
First																								1							1	1
Second			1				1				1													1			1			1	6	6
Third		2	5	1			4	1			2		1						2	1			2	5			7	7		2	42	14
Fourth		3	6	7	1		6	2			6	2	2			1		1	2	6			7	7			8	8		4	79	18
Sacral Centrae																																
Partial Ossification																																
First																																
Second																																
Third			1																												1	1
Fourth			1																												1	1
PELVIC GIRDLE:																																
Pubis																																
Partial Ossification			1																				1	3			1			1	7	5
Non-ossification																																
Ischium																																
Partial Ossification			1																				1	1						1	4	4
EXTREMITIES:																																
Metacarpals																																
Partial Ossification																								1						1	2	2
Metatarsals																																

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Dam's Ear Tag No.	C503	C491	C491	C507	C494	C495	B109	C508	C506	C489	C508	C504	C494	C493	C489	B109	C508	C503	C493	C503	C562	C491	C501	C504	C489	C490	C499	C504	C507	C505	Total	
Dam's Study No.	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119	120	Fetuses	Litters
RIBS:																																
Wavy		1				2																									3	2
14th Thoracolumbar															1		2									1	1				5	4
Rudimentary																																
Shortened 13th																																
Right																																
Left																																
Pair																																
9th,10,11,&13th																																
Missing																																
13th																																
Left																																
Pair																																
STERNEBRAE:																																
<4 Ossified			1						2																						3	2
Partial Ossification																																
First			1																	1				1				2			5	4
Second			4																	1				4		1	1	4	1		16	7
Third			1																					2							3	2
Fourth	1	2	1	1			5				1								2	3				5			1	2		1	25	12
Fifth	1		6	3	3	3		2	1		3				4	2	1	4	1			4	3	2		2	5	3	2	4	59	21
Sixth	6	3	6	6	7	5	7	3	4		7	3	2		6	7		3	5	5		4	7	7		9	8	8	7	6	141	25
Non-Ossification																																
First			1																												1	1
Second									2		1				1	1															5	4
Third									2																						2	1
Fourth			1						2											1									1		5	4
Fifth	5	4	1	4	3	3	7	5	4		4	3	2		3	5	1	1	5	7		1	4	5		7	3	5	5	2	99	25
Sixth		1	1	1		1		4	2										1	2											13	8
Bilobed																																
First																																
Second																																
Third																																
Fourth								2																							2	1
Fifth																																
Split																																
Fifth									1																						1	1

NP = Not Pregnant

06000

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JAN 14 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Geraldine V. Cox, Ph.D.
Vice President and Technical Director
Chemical Manufacturers Association
2501 M Street, N.W.
Washington, D.C. 20037

Dear Dr. Cox:

This acknowledges your letter of December 11, 1985 providing information to the U.S. Environmental Protection Agency on hydroquinone. Your submission has been screened as part of our current awareness program on existing chemicals and assigned the following FYI (For Your Information) Document Control Number: FYI-AX-1285-0468. In any further communication with the Agency regarding this submission, please refer to the above Document Control Number and address your reply to:

Document Control Officer (TS-793)
ATTN: Mr. Terry O'Bryan
Office of Toxic Substances
U.S. Environmental Protection Agency
Washington, D.C. 20460

Please recall that the Agency previously requested an additional copy of each of three submissions on phthalate esters by CMA to the Agency between December 1, 1982 and February 23, 1983. These submissions have still not been retrieved from within the Agency. A copy of our previous request is enclosed for your information.

The Agency looks forward to continued cooperation with the Chemical Manufacturers Association in its efforts to evaluate potential risks posed by chemicals to health and the environment.

Sincerely,

Frank D. Kover

Frank D. Kover, Chief
Chemical Screening Branch/ECAD

Enclosure

cc: Lee M. Thomas

CHEMICAL MANUFACTURERS ASSOCIATION

January 24, 1986

file with FYI-AX-1285-0468

The Honorable Lee M. Thomas
Administrator
U.S. Environmental Protection Agency
1200 West Tower
401 M Street, S.W.
Washington, D.C. 20460

2/14/86

12/13 PTS-NA

Dear Mr. Thomas:

There was a typographical error noted in Table 6 of the report sent to you on December 11, 1985, entitled "Hydroquinone: A Developmental Toxicity Study in Rats." A copy of the revised Table 6 is attached. This was a typographical error only and the post-implantation losses were calculated using the correct formula. No other changes in Table 6 are necessary.

Sincerely,

Robert J. Fensterheim

Robert J. Fensterheim
Manager
Hydroquinone/Quinone
Program

Table 6

Hydroquinone - Develo .l Toxicity Study in Rats

Summary of Observations at Time of Cesarean Sections

Dose Group (mg/kg)	0	30	100	300
Number of Females Inseminated	30	30	30	30
Number of Females Pregnant	24(80)[a]	29(97)	28(93)[b]	26(87)
Number of Litters Completely Resorbed	0	0	0	0
Number Litters with Resorptions	14(58)	16(55)	15(54)	13(50)
Corpora Lutea Per Dam	15 ± 2[c]	14 ± 2	14 ± 3	14 ± 3
Implantations Per Dam	14 ± 2	14 ± 3	12 ± 4	13 ± 3
Viable Fetuses Per Litter	13 ± 3	12 ± 4	11 ± 4	12 ± 3
Resorptions Per litter	1.2 ± 1.4	1.6 ± 2.3	1.1 ± 1.2	1.1 ± 1.8
Dead Fetuses Per Litter	0	0	0	0
Gravid Uterine Weight (g)	65.5±10.8	61.7±17.1	55.3±16.6	59.9±15.0
Pre-Implantation Loss (%)[d]	7.8 ± 9.4	7.7 ±12.1	16.2±24.2	6.7 ± 8.9
Post-Implantation Loss (%)[e]	8.7 ±12.3	13.0±19.6	7.9 ± 8.6	9.1 ±16.1
Sex Ratio (M:F)	48:52	49:51	46:54	47:53
Fetal Body Weight M & F (g)[f]	3.18±0.24	3.26±0.27	3.19±0.23	3.01±0.29*
Male	3.26±0.26	3.32±0.32	3.24±0.27	3.09±0.33
Female	3.13±0.25	3.21±0.25	3.13±0.23	2.95±0.27*

[a]Numbers in parentheses are percentages. None of the uteri stained with sodium sulfide had implantations.

[b]One dam died immediately following dosing on the 11th day of gestation due to an intubation error.

[c]Mean ± 1 standard deviation.

[d]Calculated for each dam $\frac{\text{(Number of Corpora Lutea - Number of Implantations)X100}}{\text{Number of Corpora Lutea}}$

[e]Calculated for each dam $\frac{\text{(Number of Implantations - Number of Viable Implantations)X100}}{\text{Number of Implantations}}$

[f]Mean of the litter means ± 1 standard deviation).

*Statistically different from controls (Anova and Duncan's Multiple Range T