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

010599

SEP 23 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Phenol/Sodium Phenate: Submission of Data for Reregistration.
Reregisteration Case: 4074

Chemical No: 649 (064001)/786A (064002)
Submission Nos: S-428469/S-429981/
S-429982/S-441617

DP Barcode: D-184258/D-185039/
D-185045/D-191736

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I
Health Effects Division (H7509C)

09-20-93

TO: Kathryn Davis/Thomas Luminello, PM #52
Accelerated Reregistration Branch
Special Review and Reregistration Division (H7508W)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I
Health Effects Division (H7509C)

9/20/93

Registrant: Sporocidin International, Rockville, MD

Request: Review and evaluate FIFRA-88 Phase 2 and Phase 4 submissions proposed to satisfy the TOX DATA GUIDELINE set of generic requirements for phenol and sodium phenate, namely:

81-1 Acute oral LD_{50}
81-2 Acute dermal LD_{50}
81-3 Acute inhalation LC_{50}
81-4 Primary eye irritation
81-5 Primary dermal irritation
82-2 90-Day dermal
83-3(a) Developmental toxicity
84-2(a, b)/(84-4) Mutagenicity battery

Submissions: The registrant has submitted the following documents meant to satisfy toxicology guideline requirements (GDLN No. in parenthesis).

1847

(GDLN No. in parenthesis).

(A) GENERIC DOCUMENTATION SUBMITTED:

(81-4) "Acute Toxicological Properties and

(81-5) Industrial Handling Hazards of Phenol (1% in Alcohol)," Microfiche I.D. No. OTS0515999.

(81-1) U. S. ENVIRONMENTAL PROTECTION AGENCY, OFFICE OF TOXIC SUBSTANCES: "Oral Toxicity of Phenol in Albino Rats," Microfiche I.D. No. OTS0515558.

(81-1) "Acute Toxicity of Phenol," Microfiche I.D. No. OTS0515567

(81-1 to -5) "Acute Oral, Eye, Skin and Inhalation Toxicity, Preliminary Ground Water Assessment, and Characteristics of Plant Effluents of Phenol with Cover Letter Dated 07/27/87," Microfiche I.D. No. OTS0515378.

(85-4 81-5) "Skin Absorption and Irritation-Phenol," Microfiche I.D. No. OTS0515564

(81-1) "Toxicity of Phenol Dissolved in a Mixture of Hexyl and Heptyl Alcohols," Microfiche I.D. No. OTS0517007.

(81-1) "Toxicity Data on Selected Dow Compounds," Microfiche I.D. No. OTS0517164.

(81-1) "LD_{50} for Single Intraperitoneal Dose to Female Rats of Phenol 1%," Microfiche I.D. No. OTS0515578.

(81-5) "Skin Irritation Potential of Six Chemicals: H2S04, HCL, NACH Phenol, Dowtherm A and HCBD," Microfiche I.D. No. OTS0515998.

(83-2) U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH, "Bioassay of Phenol for Possible Carcinogenicity," pgs. 1-2, 95-125, NIH Publication No. 80-1759, August, 1980.

(84-4) U. S. ENVIRONMENTAL PROTECTION AGENCY, "Phenol and Seven Metabolites of Phenol on Metabolic Cooperation Between Chinese Hamster V79," Publication No. PB86-187184.

U. S. ENVIRONMENTAL PROTECTION AGENCY, "Health Effects Assessment for Phenol," Publication No. PB86-134186. 010599

U. S. ENVIRONMENTAL PROTECTION AGENCY, "Health Effects Assessment for Phenol," Publication No. PB90-142472.

U. S. ENVIRONMENTAL PROTECTION AGENCY, "Toxicological Profile for Phenol," Publication No. PB90-181249.

(85-1) "Comparison of the Metabolic Rate of Phenol, Phenyl Glucoside and Phenyl 6-O-Malonyl Glucoside in the Rat," Microfiche I.D. No. OTS0515719.

(85-1 "Determination of Time to Steady-State Level in Blood During Inhalation Exposure of Benzene by Rats and Mice. Part 1 With Attachments and Cover Sheet," Microfiche I.D. No. OTS0516172.

(85-2) "Results of Skin Absorption Toxicity Tests Conducted on Aqueous Solutions of Phenol," Microfiche I.D. No. OTS0517001.

(85-2) "Results of Toxicological Tests Designed to Evaluate Skin Absorption Properties on 1% Aqueous Phenol Solution," Microfiche I.D. No. OTS0517002.

(85-2) "Absorption of Anhydrous Phenol Through Unbroken Skin," Microfiche I.D. No. OTS0517005.

(B) Additionally, registrant requests application of the same reference documents being submitted for phenol to sodium phenate as well, since the latter, which is also being reregistered under Case No. 4074, is a (simple) mineral salt of the former.

[For confirmation of sodium phenate's status as a mineral salt, the registrant suggests the language in the Agency's Office of Water, Criteria and Standards Division document: "Ambient Water Quality Criteria for Phenol," Doc. Ref. No. EPA 440/5-80-066, October 1980, page A-2.]

B. PRODUCT SPECIFIC DATA: In addition, the following product-specific data from acute studies (all conducted by WIL Research) on one end-use formulation (Happy Jack® Mange Medicine,

containing an unspecified concentration of active ingredients) were assessed, as follows:

Study (GDLN.)	WIL Study No/ MRID No.	Date Reported	Reported Results	Probable TOX. CAT
(81-1) Acute Oral LD_{50}	52003/420523-01	01/08/86	LD_{50} > 5000 mg/kg (Slight, transient salivation, limb tone)	IV
(81-2) Acute dermal LD_{50}	52004/420523-02	01/09/86	LD_{50} > 2000 mg/kg (Body weight loss, days 7-14)	III
(81-4) Primary eye irritation	52004/420523-03	11/07/85	P15=7 at 1 hr; 0 at 7 days	III
(81-5) Primary dermal irritation	52005/420523-04	01/08/86	P11=1.9	III
(81-6) Skin sensitization	52007/420523-05	01/29/86	Strong sensitizer	(II)

These data are acceptable to be reviewed for reregistration of phenol EP.

TOXICOLOGY CONCLUSIONS:

The following submissions contain primary generic data and were screened for adequacy for review under FIFRA-88/Phase 5 to support reregistration of the subject chemicals:

(81-1) Acute Oral LD_{50}:

"The Acute Toxicity of Phenol", unpublished report from the University of Pittsburgh's Mellon Institute of Industrial Research, dated 5-6-49 (OTS 0515567/86-870001405).

The acute oral administration of reagent-grade phenol (100%) to young male rats (90-120 g) resulted in a calculated oral LD_{50} = 1030 (940-1120) mg/kg, which would place it in TOX. CAT. III. However, since females were not tested, GDLN requirement 81-1 is not yet satisfied.

(81-2) Acute Dermal LD_{50}:

"RESULTS OF SKIN ABSORPTION TOXICITY TESTS CONDUCTED ON AQUEOUS SOLUTIONS OF PHENOL", unpublished article dated 4-5-63 from the Biochemical Research Laboratory of Dow Chemical (OTS 0517001/86-8700022110.)

Rabbits were acutely exposed topically to increasing concentrations of phenol (5 to 20% in water) without apparent adverse effects.

These data are not acceptable to satisfy requirements under GDLN 81-2 because of too few animals tested per group.

(81-5) Primary Dermal Irritation/(81-4) Primary Eye Irritation:

(i) Skin Absorption and Irritation of Sodium Phenate, unpublished report dated 3/11/48 from the University of Pittsburgh, Mellon Institute of Industrial Research. (OTS0515564/86-070001402.)

A 10% solution of sodium phenate (57%, with base phenol content = 42.6%) was reported to produce mild to marked dermal erythema and marked capillary injection in one-half the rabbits tested. A 15% aqueous solution applied "in excess" to rabbit eyes produced internal congestion, corneal necrosis and conjunctival injury. (Probable TOX. CAT. = II for both skin/eye.) These data are acceptable for satisfying GDLN requirements for dermal and ocular irritation.

(ii) "SKIN IRRITATION POTENTIAL OF SIX CHEMICALS: H_2SO_4, HCl, NaOH, PHENOL, DOWTHERM A, AND HCBD," unpublished report dated June 24, 1977, from Dow Chemical (OTS0515566/86-870002208) not acceptable to satisfy data or requirements for GDLN (81-5), because of insufficient procedural details.

These data are not acceptable to satisfy GDLN 81-5 requirements because of insufficient procedural detail.

[NB: H_2S04 = (Fuming) Sulfuric acid (96.5%)
HCl = (Conc.) Hydrochloric acid (37.6%)
NaOH = (Conc.) Sodium hydroxide (50%)
Dowtherm A = Diphenyl-diphenyl oxide mixture
HCBD = Hexachloro -1,3 - betadiene.]

(83-2) "BIOASSAY OF PHENOL FOR POSSIBLE CARCINOGENICITY", NIH Publication No. 80-1759, dated August 1980.

From this report's summary

[Using the standard protocol of the NCI's carcinogenesis testing program...], a

dose related depression in mean body weight gain was found in rats and mice of each sex given drinking water containing 2500 or 5000 ppm phenol for 103 weeks. Both rats and mice drank less than did the corresponding controls, but a dose-related decrease in water consumption was observed only for mice.

An increased incidence of leukemia or lymphomas was detected in male rats and may have been associated with the administration of phenol. Although the incidence of these tumors in the low-dose

group was significantly higher than that in controls, the incidence in the high-dose group was not. Thus a definitive association with administration of phenol was not established. Under the conditions of this bioassay, phenol is considered not carcinogenic for either male or female F344 rats or male and female B6C3F1 mice.

ACCEPTABLE for review under GDLN 83-2.

(84-4) Mutagenicity:

"EFFECTS OF PHORBOL MYRISTATE ACETATE, PHORBOL DIBUTYRATE, ETHANOL, DIMETHYLSULFOXIDE, PHENOL, AND SEVEN METABOLITES OF PHENOL ON METABOLIC COOPERATION BETWEEN CHINESE HAMSTER V79 LUNG FIBROBLASTS", journal article (Cell Biol. Toxicol.1(4): 269-283, 1985) by A. RUSSELL MALCOLM, LESLEY J. MILLS AND EDWARD J. McKENNA (PB86-187184)

In contrast to strong positive results (defined as the inhibition of metabolic cooperation assessed as a function of mutant cell recovery from populations of cocultivated HGPRT-deficient and HGPRT wild type Chinese hamster V79 cells in culture) expected for the phorbol esters (which are established tumor promoters), phenol and phenyl glucuronide had no effect on metabolic cooperation (i.e., were negative), but five metabolites of phenol (1,4-benzoquinone, catechol hydroxyquinone, quinol, and phenylsulforte) were weakly positive. Thus phenol may be considered a weak tumor promoter by this assay.

ACCEPTABLE for review as satisfying one of the categories for mutagenicity data requirements (GDLN 84).

(85-1) Metabolism:

"A comparison of the Metabolic Fate of Phenol, Phenyl Glucoside and Phenyl-6-O-Malonyl-Glucoside in the Rat, Group Research Report SBGR.85.127, Shell Research, Sittingbourne (UK), dated February 1985 (EPA MRID OTS0515719/85-870001643).

From the investigator's summary:

"The metabolic fats of phenol and its model plant conjugates phenyl glucoside and phenyl 6-O-malonyl-glucoside have been compared following equimolar oral dosing to rats (1.2 mg phenol $kg._1$). Phenol, as expected, was eliminated mainly as phenyl sulphate (68%) and partly as phenyl glucuronide (12%). The fate of phenyl malonyl-glucoside was very similar to that of phenol with the exception that small amounts of phenyl glucoside and phenyl malonyl-glucoside were eliminated. Interestingly, a major part of the dose of phenyl glucoside (68%) was eliminated unchanged."

This study appears adequate (ACCEPTABLE) is defining various aspects of the metabolic fate of orally administered phenol in the rat.

(85-2) Dermal absorption:

(i) "THE ABSORPTION OF ANHYDROUS PHENOL THROUGH THE UNBROKEN SKIN, unpublished article, dated 10/15/83, by Don D. Irish and Edgar M. Adams, Biochemical Research Laboratory of The Dow Chemical Company (OTS0517005/86-870002215).

Anhydrous phenol (99.5% pure), applied topically to the abdomen of rabbits, was rapidly absorbed percutaneously to appear in the circulation, from which significant concentrations were transported to brain.

ACCEPTABLE for review as satisfying data requirements for DERMAL ABSORPTION (GDLN 85-2).

(ii) "RESULTS OF TOXICOLOGICAL TESTS DESIGNED TO EVALUATE SKIN ABSORPTION PROPERTIES OF 1% AQUEOUS PHENOL SOLUTION", unpublished article dated February 6, 1962, from the Biochemical Research Laboratory of The Dow Chemical (OTS0517002/86-870002212).

Large areas of rabbit skin were exposed for 24 hours to 1% phenol (10 to 320 mg/kg), with minor clinical effects (no significant weight loss, and slight transient hyperemia).

(These data are juded CORE-SUPPLEMENTARY--see DER)

NB:

The remainder of the documentation submitted as "generic" data was not reviewed by TOX-I, because it represented secondary and/or summary literature citations, and not original data from primary sources or studies; or was not related to the potential for adverse (toxic) human health effects.

SUMMARY OF DATA REQUIREMENTS: The following data must be submitted to satisfy generic requirements for re-registration of the subject chemicals:

(81-1) Acute oral LD_{50}
(81-2) Acute dermal LD_{50}
(81-3) Acute inhalation LC_{50}
(81-4) Primary eye irritation
(81-5) Primary dermal irritation
(81-6) Skin sensitization
(82-2) 90-Day dermal
(83-3) Developmental toxicity (one species)
(84-2) Mutagenicity: Bacterial gene mutation or
Mammalian cell gene mutation and
Chromosome aberrations

DISK 8:MAUER:PHENOL.SOD:7/14/93

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Reviewed by: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I, HED (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I, HED (H7509C)

8/26/93

9/14/93

DATA EVALUATION RECORD

MRID NUMBER No.: OTS0515567
PC No.: 064001
Tox Chem. No.: 649

I. SUMMARY

STUDY TYPE: (81-1) Acute oral LD_{50}--Rat

CHEMICAL: Phenol

SPONSOR: Union Carbide Corporation

TESTING FACILITY: University of Pittsburgh, Mellon Institute of Industrial Research

TITLE OF REPORT: The Acute Toxicity of Phenol.

AUTHOR(S): C. P.Carpenter

STUDY NUMBER: [None given]

DATE ISSUED: May 6, 1949

CONCLUSIONS: Acute oral administration of reagent-grade-phenol (100%) to males resulted in a calculated LD_{50} = 1030 (940-1130) mg/kg, which would place it in TOX. CAT. III.

TB-I EVALUATION: UNACCEPTABLE since females were not tested.

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II. DETAILED REVIEW

A. TEST MATERIAL: Phenol (Merck; Eimer and Amend)

Description:	Liquid
Batches (Lots):	C. P. (technical)
Purity (%):	100
Solvent/carrier/diluent:	Water

B. TEST ORGANISM: Rodent

Species:	Rat
Strain:	"Albino"
Weights - males:	90-120 g
females:	[Not tested]
Source:	[Not stated]

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the acute toxic potential of the test article when administered by gavage to rats.

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D. PROCEDURES/METHODS OF ANALYSIS: Four groups of ten males each were administered single oral doses of 5% phenol in water and observed for 14 days post-dose.

E. RESULTS: Deaths ensued promptly at doses in excess of the LD_{50} (see Report Table attached here). At autopsy of such animals, congested and hemorrhagic lungs and livers were evident, with pale kidneys and bloated g.i. tract.

TB CONCLUSION: A minimum of procedural detail was provided in this assay, and only males were tested. Hence the study does not satisfy GDLN 81-1, and is judged UNACCEPTABLE

ATTACHMENT: Data Table
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Table 12-70

PHENOL

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Single Doses to Male Albino Rats by Mouth

Fed by Stomach Tube as a Solution in Water. 1 ml. = 0.05 grams.

Rat No.	Date Dosed	Grams Wt.	Weight Change in 14 Days	Dosage; Grams per Kilo	Dose in Grams	Dose in ml. of Solution	Days to Death
41325	3-27-46	114	-	1.26	0.144	2.8	0
41326	"	110	-	1.26	0.139	2.8	0
41310	"	94	-	1.26	0.118	2.4	0
41312	"	100	-	1.26	0.126	2.5	0
41314	"	112	-	1.26	0.141	2.8	0
41317	"	104	-	1.26	0.131	2.6	0
41321	"	106	-	1.26	0.134	2.6	0
41319	"	95	-	1.26	0.120	2.2	0
41311	"	93	+ 49	1.26	0.117	2.3	-
41315	"	101	+ 78	1.26	0.127	2.5	-
41872	4-18-46	99	-	1.12	0.111	2.2	1
41881	"	92	-	1.12	0.103	2.0	1
41891	"	90	-	1.12	0.101	2.0	1
41898	"	90	-	1.12	0.101	2.0	0
41901	"	100	-	1.12	0.112	2.2	1
41911	"	99	-	1.12	0.111	2.2	0
41874	"	98	+ 91	1.12	0.110	2.2	-
41875	"	98	+ 78	1.12	0.110	2.2	-
41877	"	91	+ 74	1.12	0.102	2.0	-
41880	"	100	+ 73	1.12	0.112	2.2	-
40991	3-13-46	104	-	1.00	0.104	2.0	1
40994	"	102	-	1.00	0.102	2.0	1
40997	"	96	-	1.00	0.096	1.9	1
40998	"	95	-	1.00	0.095	1.9	1
41003	"	114	-	1.00	0.114	2.2	1
40984	"	98	+ 38	1.00	0.098	2.0	-
40989	"	111	+ 31	1.00	0.111	2.2	-
40993	"	110	+ 83	1.00	0.110	2.2	-
40999	"	100	+ 68	1.00	0.100	2.0	-
41001	"	103	+ 97	1.00	0.103	2.0	-
41850	4-18-46	97	-	0.89	0.0865	1.7	1
41831	"	90	+ 46	0.89	0.0800	1.6	-
41851	"	96	+ 68	0.89	0.0855	1.7	-
41852	"	94	+ 78	0.89	0.0836	1.6	-
41853	"	96	+ 57	0.89	0.0855	1.7	-
41860	"	100	+ 92	0.89	0.0890	1.8	-
41862	"	96	+ 70	0.89	0.0855	1.7	-
41863	"	93	+ 75	0.89	0.0830	1.6	-
41869	"	93	+ 8	0.89	0.0830	1.6	-
41839	"	93	+ 42	0.89	0.0830	1.6	-

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Reviewed by: Irving Mauer, Ph.D., Geneticist 05-26-93
Toxicology Branch-I, HED (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief 9/12/93
Toxicology Branch-I, HED (H7509C)

DATA EVALUATION RECORD

MRID NUMBER No.: OTS0517001 /17002
PC No.: 064001
Tox Chem. No.: 649

I. SUMMARY

STUDY TYPE: (81-2) Acute Dermal LD_{50} - Rabbit

CHEMICAL: Phenol

SPONSOR: Dow Chemical, Midland, MI

TESTING FACILITY: Dow's Biochemical Research Laboratory

TITLE OF REPORT: Results of Skin Absorption Toxicity Tests Conducted on Aqueous Solutions of Phenol.

AUTHOR(S): Ken Olson

STUDY NUMBER: D002146

DATE ISSUED: April 15, 1963 (Feb. 08, 1962)

CONCLUSIONS: From (minimal) safety evaluation testing, test material was non-toxic up to an aqueous concentration of 5%.

TB-I EVALUATION: UNACCEPTABLE (Both studies)

II. DETAILED REVIEW

A. TEST MATERIAL: Phenol (unstated source)

Description: [Not stated]
Batches (Lots): [Not stated]
Purity (%): [Not stated]
Solvent/carrier/diluent: Water

B. TEST ORGANISM: Lagomorph

Species: Rabbit
Strain: [Not stated]
Age: [Not stated]
Weights - males: [Not stated]
females: [Not stated]
Source: [Not stated]

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the toxic potential of the test article when applied to the skin of depilated rabbits.

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D./E. PROCEDURES/METHODS OF ANALYSIS: Doses ranging from 1.0 to 32.0 cc/kg (0.05-6.4 g/kg) of 1%, 5% and 20% solutions of phenol in water were applied to large areas of the depilated skin of groups of six rabbits, (sex unstated), and held in place under an impervious cuff for 24 hours.

All animals administered 1% phenol topically survived; one death was recorded at 5%, and 3 at 20% phenol (see Summary Report Table attached here). The author concluded that unprotected and/or prolonged contact with concentrations of 5% phenol (and stronger) should be avoided.

F. TB EVALUATION: Does not meet current test guidelines for this type of assay - UNACCEPTABLE.

ATTACHMENT: Summary Data Table

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TOXICITY OF PHENOL BY CUTANEOUS ABSORPTION WHEN APPLIED TO CLIPPED RABBIT SKIN FOR 24 HOURS UNDER AN IMPERVIOUS CUFF

% Phenol	g./kg. phenol	cc/kg. of solution	total cc per rabbit	No. died No. exposed
1% in water (solution)	0.01	1.0	2.75	0/1
1% in water (solution)	0.02	2.0	4.70	0/1
1% in water (solution)	0.04	4.0	9.60	0/1
1% in water (solution)	0.08	8.0	17.4	0/1
1% in water (solution)	0.16	16.0	36.8	0/1
1% in water (solution)	0.32	32.0	85.8	0/1
5% in water (solution)	0.05	1.0	2.85	0/1
5% in water (solution)	0.10	2.0	5.66	0/1
5% in water (solution)	0.20	4.0	12.12	0/1
5% in water (solution)	0.40	8.0	18.00	1/0
5% in water (solution)	0.80	16.0	42.08	0/1
5% in water (solution)	1.60	32.0	69.44	0/1
20% in water (emulsion)	0.2	1.0	2.50	0/1
20% in water (emulsion)	0.4	2.0	5.80	0/1
20% in water (emulsion)	0.8	4.0	10.00	0/1

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(Continued)

% Phenol	g./kg. phenol	cc/kg. of solution	total cc per rabbit	No. died No. exposed
20% in water (emulsion)	1.6	8.0	20.64	1/1*
20% in water (emulsion)	3.2	16.0	33.92	1/1*
20% in water (emulsion)	6.4	32.0	99.84	1/1*

* Animals were dead 2 hours from the beginning of the exposure.

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8/26/93

9/13/93

DATA EVALUATION RECORD 010599

MRID NUMBER No.: OTS0515564
PC No.: 064002
Tox Chem. No.: 786A

I. SUMMARY

STUDY TYPE: (81-2, 81-4, 81-5) Acute dermal LD_{50}; dermal and eye irritation -- rabbit

CHEMICAL: Sodium phenate

SPONSOR: Union Carbide Corp.

TESTING FACILITY :University of Pittsburgh, Mellon Institute of Industrial Research

TITLE OF REPORT: Skin Absorption and Irritation of sodium Phenate

AUTHOR(S): C. P. Carpenter

STUDY NUMBER: [None given]

DATE ISSUED: 05/11/48

CONCLUSIONS: Dermal LD_{50} calculated as 2350 (1880-2940) mg/kg (TOX CAT. III). Mild to marked erythema and marked capillary injection were observed in 50% of a group of animals tested, which would place the test article in TOX. CAT. II. Similarly, an aqueous solution placed in rabbits eyes caused corneal necrosis and conjunctival lesions; TOX. CAT. II

TB-I EVALUATION: UNACCEPTABLE for all three assays, since sex of the test animals was not specified, and too few procedural details were provided.

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II. DETAILED REVIEW

A. TEST MATERIAL: Sodium phenate (Boder Scientific)

Description: [Not stated]
Batches (Lots): [Not stated]
Purity (%): 57 (phenol equivalent = 42.6%)
Solvent/carrier/diluent: Water

B. TEST ORGANISM: Lagomorph

Species: Rabbit
Strain: [Not stated]
Age: [Not stated]
Weights - males: [Not stated]
females: [Not stated]
Source: [Not stated]

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the toxic potential of the test article when administered dermally to rabbits.

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D. PROCEDURES/METHODS OF ANALYSIS: Sodium phenate (as a 50% solution in water) was applied to the clipped trunks of four groups of 10 rabbits each (sex not specified), and held in place under occlusive dressing for 24 hours. Animals were observed for 14 days post-dose. Based on the mortality observed (see attached Report Table), the dermal LD_{50} was calculated as 2350 (1880-2940) mg/kg. Animals manifested marked erythema, edema and necrosis; internal examination revealed lesions (unspecified as to nature, severity or frequency) in kidneys, livers, intestines and lungs.

In irritation studies, a 10% solution produced mild to marked erythema and marked capillary injection in "2, 1, and 2 rabbits" [group sizes not specified], whereas a 15% aqueous solution, "applied in excess" to rabbit eyes [number not specified] produced "internal congestion, dense necrosis of the cornea, and injury to the conjunctiva". [Probable TOX. CAT. II for both assays]

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F. TB EVALUATION: Too few procedural details were provided in these studies to satisfy GDLN Test Requirements: 81-2, 81-4 or 81-5.

Hence all assays are judged UNACCEPTABLE.

ATTACHMENT: Data Tables

Disk 8:064002.MEM:MAUER:08/19/93

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Table 11-46

SODIUM PHENATE

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Single Doses to Rabbits by Skin Absorption

Administered as a 50% Aqueous Solution under "Vinylite" dam for 24 hours

Rabbit No.	Date Clipped	Date Applied	Gm. Wt.	Weight Change in 14 Days	Dosage Ml. per Kilo	Dose in Ml.	Days to Death
60969	10-16-47	10-16-47	2528	-	5.0	25.3	1
62061	"	"	2824	-	5.0	28.2	2
62062	"	"	2640	-	5.0	26.4	1
62063	"	"	2930	-	5.0	29.3	1
62064	"	"	2458	-	5.0	24.6	1
67881	11-20-47	11-20-47	2770	-	5.0	27.7	1
69013	2-12-48	2-12-48	2706	-	5.0	27.1	0
69014	"	"	2014	-	5.0	20.1	0
69015	2-12-48	2-13-48	2306	-	5.0	23.1	1
69016	"	"	2342	-	5.0	23.4	1
67967	2-2-48	2-2-48	2864	-	2.52	14.4	1
67969	"	"	2628	-	2.52	13.2	1
67972	"	"	2280	-	2.52	11.5	2
69006	2-11-48	2-21-48	2062	-	2.52	10.4	5
69001	2-12-48	"	2756	-	2.52	13.9	0
69012	"	"	2626	-	2.52	13.2	1
67968	2-2-48	2-2-48	2330	- 384	2.52	11.7	-
67970	"	"	2260	- 250	2.52	11.4	-
67971	"	"	2380	- 16	2.52	12.0	-
69005	2-11-48	2-12-48	2068	-	2.52	10.4	-
64253	11-20-47	11-20-47	3280	-300	1.26	8.3	-
64255	"	"	2580	+ 250	1.26	6.5	-
64256	"	"	2564	- 230	1.26	6.5	-
64257	"	"	2624	+ 34	1.26	6.6	-
64259	"	"	2508	- 176	1.26	6.3	-
64260	2-11-48	2-12-48	2354	+ 16	1.26	6.7	-
68995	"	"	2256	- 31	1.26	5.7	-
68997	"	"	2920	- 04	1.26	7.4	-
68998	"	"	2194	- 95	1.26	5.5	-
69002	"	"	2426	+ 506	1.26	6.1	-
63675	11-6-47	11-6-47	2598	- 42	0.63	3.3	-
63676	"	"	2278	+ 42	0.63	2.9	-
63677	"	"	2912	- 72	0.63	3.7	-
63678	"	"	2406	+ 198	0.63	3.0	-
63679	"	"	2684	+ 460	0.63	3.4	-
63680	"	"	2604	+ 162	0.63	2.3	-
68921	2-11-48	2-12-48	2546	- 152	0.63	3.2	-
68928	"	"	2412	- 612	0.63	3.0	-
68933	"	"	2366	- 20	0.63	3.0	-
68994	"	"	2510	- 48	0.63	3.2	-

Table 11-47

PHENOL

Single Doses to Male Albino Rabbits by Skin Absorption

Administered as a 10% dispersion under "Vinylite" dam for 24 hrs.

Rabbit No.	Date Clipped	Date Applied	Gm. Wt.	Weight Change in 14 Days	Dosage; ml. per Kilo	Dose in ml.	Days to Death
66599	1-5-48	1-5-48	2474	-	1.0	24.7	0
66604	"	"	2248	-	1.0	22.5	0
64268	11-20-47	11-20-47	2976	-	1.0	29.8	7
64270	"	"	2836	-	1.0	28.4	1
64267	"	"	2470	- 276	1.0	27.5	-
66614	1-5-48	1-5-48	2026	-	0.795	16.1	0
66622	"	"	2182	-	0.795	17.3	0
66623	"	"	2244	-	0.795	17.8	1
666617	1-9-48	1-9-48	2938	-	0.795	23.4	0
66619	"	"	3190	-	0.795	25.4	0
67156	"	"	2120	-	0.795	16.8	0
67155	"	"	2200	-	0.795	17.5	0
67036	1-26-48	1-26-48	2164	-	0.795	17.2	0
67030	"	"	2452	-	0.795	19.5	0
67053	1-14-48	1-14-48	2144	-	0.63	13.5	1
67247	"	"	2112	-	0.63	13.3	0
67257	"	"	2126	-	0.63	13.4	0
67275	1-20-48	1-20-48	2075	-	0.63	13.1	1
67256	1-14-48	1-15-48	1952	+ 284	0.63	12.3	-
67253	1-20-48	1-20-48	2416	- 206	0.63	15.2	-
67634	"	"	2604	- 294	0.63	16.4	-
67647	"	"	3192	- 322	0.63	20.1	-
67653	"	"	2224	- 234	0.63	14.0	-
67649	"	"	2468	- 216	0.63	15.5	-
67872	1-20-48	1-20-48	2388	-	0.50	11.9	5
67661	"	"	2328	- 128	0.50	11.6	-
67662	"	"	2270	+ 74	0.50	11.4	-
67870	1-20-48	1-20-48	2150	+ 140	0.50	10.8	-
67935	1-26-48	1-26-48	2038	- 138	0.50	10.2	-
65779	12-30-47	12-31-47	2710	+ 18	0.50	13.5	-
65780	12-31-47	12-31-47	2444	+ 60	0.50	12.2	-
65784	"	"	2550	+ 156	0.50	12.7	-
65803	"	"	2364	- 22	0.50	11.8	-
65814	"	"	2520	+ 204	0.50	12.6	-

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010599

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Toxicology Branch-I, HED (H7509C)

8-26-93

9/14/93

DATA EVALUATION RECORD

MRID NUMBER No.: OTS-0515998
PC No.: 064001
Tox Chem. No.: 649

I. SUMMARY

STUDY TYPE: (81-5) Primary Skin Irritation - Rabbit

CHEMICAL: Phenol

SPONSOR: Dow Chemical, Midland, MI

TESTING FACILITY: Toxicology Research Laboratory, Dow

TITLE OF REPORT: Skin Irritation Potential of Six Chemicals: H_2SO_4, HCl, NaOH, Phenol, Dowtherm-A. and HCBD.

AUTHOR(S): D. J. Wroblewski

STUDY NUMBER: [Not given]

DATE ISSUED: June 24, 1977

CONCLUSIONS: Only a summary of procedures and results given.

TB-I EVALUATION: UNACCEPTABLE

010599

II. DETAILED REVIEW

A. TEST MATERIAL:

Description: Phenol (source not specified)
Batches (Lots): [Not stated]
Purity (%): [Not stated]
Solvent/carrier/diluent: Water

B. TEST ORGANISM: Lagomorph

Species: Rabbit
Strain: New Zealand White
Age: [Not stated]
Weights - males: [Not stated]
females: [Not stated]
Source: [Not stated]

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the irritation potential of the test article when administered topically to rabbit skin.

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D. PROCEDURES/METHODS OF ANALYSIS: Concentrated (presumably technical) samples of six chemicals were applied for six seconds (H_2SO_4, HCl, NaOH) or 20 seconds (Phenol, Dowtherm-A, HCBD) to the shaved abdominal skin of an unstated number of NZW rabbits (sex not stated), washed off, and observations made 24 and 48 hours, as well as seven days post-exposure.

F. RESULTS: Summary table only was provided, as follows:

Chemicals	Exposure Time	Results
96.5% H_2SO_4	6 seconds	Moderate burn
37.6% HCl	6 seconds	Mild burn
50% NaOH	6 seconds	Mild burn
Phenol	20 seconds	Moderate burn
Dowtherm A	20 seconds	slight redness
HCBD	20 seconds	No reaction

'96.5% Sulfuric acid (H_2SO_4)
37.6% Hydrochloric acid (HCl)
50% Sodium Hydroxide (NaOH)
Phenol
Dowtherm A
HCBD (Hexachloro-1, 3-butadiene)

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F. **TB EVALUATION:** UNACCEPTABLE.

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Disk 8:Mauer:064001.2:MB:8/23/93

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010599

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05-27-93

9/13/93

DATA EVALUATION RECORD 010599

MRID NUMBER No.: [OTS]
PC No.: 064001
RD Record No.: 649

I. SUMMARY

STUDY TYPE: (83-1) Oncogenicity - Mouse/Rat

CHEMICAL: Phenol

SPONSOR: National Cancer Institute (NCI Carcinogenesis Testing Program)

TESTING FACILITY: Hazleton Laboratories, Vienna, VA

TITLE OF REPORT: Bioassay of Phenol for Possible Carcinogenicity

STUDY NUMBER: NIH Publication No. 80-1759

DATE ISSUED: August 1980

CONCLUSIONS: Not carcinogenic in either mice or rats when administered in drinking water at concentrations causing weight loss (5000 ppm)

TB-I EVALUATION: CORE-MINIMUM DATA

II. DETAILED REVIEW

010599

A. TEST MATERIAL: Phenol (Eastman Kodak; Textile Chemical)

Description: Liquid
Lots No: A4X B4A; 79380
Purity (%): 98.47
Solvent/carrier/diluent: Water (drinking water)

B. TEST ORGANISM: Rodents

Species: Rat; mouse
Strain: F344; B6C3F1
Age: 3-4 weeks
Source: NCI Frederick Cancer Research Center (MD)

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the oncogenic potential of the test article when administered in drinking water to rats and mice, according to established (published) procedures and FIFRA Test Guidelines.

A Statement of Quality Assurance measures (inspections/audits) was provided.

A Statement of adherence to Good Laboratory Practice (GLP) was provided.

D. PROCEDURES/METHODS OF ANALYSIS: Following subchronic studies to select dosages for the main study (5 concentrations up to 10,000 ppm), groups of 50 animals of each sex of both species were administered phenol in drinking water containing 2500 and 5000 ppm test article for two years (103 weeks). Matched controls received tap water for the same period of time.

The standard array of tissues were examined for both chronic effects as well as neoplasms.

E. RESULTS: In subchronic (90-day) testing, severe weight loss, but no deaths were recorded at concentrations up to 10,000 ppm in both species.

At 20 weeks of the main study, high-dose (5000 ppm) rats of both sexes weighed less than controls (Report Table 1), and water consumption was slightly reduced (80-90% of controls). However, mortality appeared not to be affected, as determined at the end of the study:

Survival at 2 yrs	Control (%)	2500	5000
Rat: Male	26/50 (52)	22/50 (44)	30/50 (60)
Female	38/50 (76)	39/50 (78)	37/50 (74)

Commonly observed rat tumors were encountered in both treated and control animals (Report Appendix A) in comparable frequency, except for a greater incidence of phaeochromocytomas of adrenal medulla in low-dose (2500 ppm) males (control, 13/50; low-dose, 22/50; high-dose, 9/50). Additionally, leukemia or lymphoma were also increased in treated males: 31/50 low-dose, and 25/50 high-dose, vs 18/50 controls.

Mean body weights in both low-dose and high-dose mice were lower than controls throughout the study, and water consumption was also depressed in a dose-related manner (75% of controls in low-dose; 50-60% high-dose). As with rats, survival was apparently not compromised by treatment:

Survival at 2 yrs	Control (%)	2500	5000
Mouse: Male	42/50 (84)	45/50 (90)	48/50 (96)
Female	41/50 (82)	40/50 (80)	42/50 (84)

No unusual neoplasms were encountered in treated mice. Although the frequency of uterine endometrial stromal polyps was increased in high-dose females (5/48 vs 1/50 in concurrent controls), this increase was stated to be within background [but background data was not provided in this Final Report]

The authors concluded that, under conditions of this bioassay, phenol was not carcinogenic for either male or female F344 rats, or for male or female B6C3F1 mice.

F. TB EVALUATION: Acceptable (CORE-MINIMUM DATA).

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08-26-93

9/13/93

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Toxicology Branch-I, HED (H7509C)

DATA EVALUATION RECORD

MRID NUMBER No.: [OTS]
PC No.: 064001
Tox Chem. No.: 649

I. SUMMARY

STUDY TYPE: (84-4) Mutagenicity - other genotoxicity in vitro.

CHEMICAL: Phenol

TESTING FACILITY: U. S. Environmental Protection Agency, Environmental Research Laboratory, Narragansett, RI

TITLE OF REPORT: [Journal Article] Effects of Phorbol Myristate Acetate, Phorbol Dibutyrate, Ethanol, Dimethylsulfoxide, Phenol, and Seven Metabolites of Phenol on Metabolic Cooperation Between Chinese Hamster V79 Lung Fibroblasts, ... in: Cell Biology and Toxicology, Vol. 1, NO. 4: 269-283 (1985),

AUTHOR(S): A. Russell Malcolm, Lesley J. Mills and Edward J. McKenna

DATE ISSUED: 1985

CONCLUSIONS: Phenol and its metabolites were found to have only weak capacity to inhibit metabolic cooperation, an in vitro indication of tumor promotion.

TB-I EVALUATION: ACCEPTABLE, but only in the absence of exogenous activation.

II. DETAILED REVIEW

A. TEST MATERIAL: Phenol (Aldrich Chemical)

Description: Liquid
Batches (Lots): N/A
Purity (%): 99
Solvent/carrier/diluent: Water

B. TEST ORGANISM: Established mammalian cell line

Species: Chinese hamster lung (V 79)
Strains: HGPRT+, $6TG^S$; and HGPRT-, $6TG^I$
Source: Dr. James Trosko, Michigan State University

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the genotoxic potential of test article when administered in vitro to V79 cells, and determining metabolic cooperation in mixed cultures, which indicates the capacity as a tumor promoter

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D. PROCEDURES/METHODS OF ANALYSIS: Phenol and seven of its metabolites were assayed for their ability to induce metabolic cooperation (as an indication of tumor promotion) in mixed populations of cocultivated hypoxanthine guanine phosphoribosyl transferase-deficient mutant(HGPRT-) and wild-type (HGPRT+) V79 lung fibroblasts. Two phorbol esters (phorbol myristate acetate, and the dibutyrate) served as positive controls. Two solvents commonly used to prepare chemicals for testing, namely, ethanol and dimethylsulfoxide (DMSO), were also tested.

Following cytotoxicity testing 15 parallel cultures of co-cultivated mutant and wild-type cells per dose were exposed for 48 hours to test chemicals and the base-analog 6-thioguanine (TG), cleared in fresh medium for an additional 4-5 days, and visible colonies (reprenserting mutant cell recovery) enumerated, fixed and stained.

E. RESULTS: Phenol and phenylglucuronide had no effect on metabolic cooperation (MC), whereas four oxidative metabolites (1,4-benzoquinone, catechol, hydroxyequinol, and quinol) inhibited MC, as did phenylsulfate.

The authors concluded that phenol and its metabolites have only weak capacity as tumor promoters, as indicated by low MC.

F. TB EVALUATION: Acceptable as an assay for other genotoxic effects, but only in the absence of mammalian activation (as acknowledged by the authors).

Disk 8:MAUER:064001.3:MB:08/24/93

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Reviewed by: Irving Mauer, Ph.D.
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Secondary Review: Karl P.Baetcke, Ph.D., Chief
Toxicology Branch-I/HED (H7509C) 9/13/93

DATA EVALUATION RECORD

MRID: OTS 0515719
PC No.: 064001
Tox Chem.: 649

I. SUMMARY

STUDY TYPE: (85-1) Metabolism --- rat.

CHEMICAL: Phenol

SPONSOR: Shell Oil, Houston TX

TESTING FACILITY: Sittingbourne Research Center (UK)

TITLE OF REPORT: A Comparison of the Metabolic Fate of Phenol, Phenyl Glucoside and Phenyl-o-Malonyl-Glucoside in the Rat.

Author: V. T. Edwards

Study No.: SRCGRM 85 (Report No. SBGR.85.127)

Date Issued: February 15/June 12, 1985

TB EVALUATION: UNACCEPTABLE.

II. DETAILED REVIEW

A. TEST MATERIAL: Radioactive phenol (Shell), plus unlabeled reference compounds (metabolites)

Description: Liquid
Batch (Lot): (Technicals)
Purity (%): (Not stated)
Solvent: Dionized water.

B. TEST ORGANISM: Rodent

Species: Rat
Strain: Fischer-344
Age: 8-10 weeks
Weight - males (only): 200 g

Source: Charles River, Marston (UK)

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the pharmokinetics and metabolism of the test article when administered to rats.

Neither a Statement of Quality Assurance measured, nor a Statement of adherence to Good Laboratory Practice (GLP) was provided in the Final Report.

D. PROCEDURES/METHODS OF ANALYSIS: Groups of male rats (4 per compound) were administered a single low oral dose of the following radioactive compounds: (C-14)

1.2 mg/kg phenol

2.0 mg/kg phenyl-beta-D-glucopyranoside

3.8 (or 5.0) mg/kg phenyl-6-O-malonyl-beta-D-glucop yranoside;

..... and sacrificed 24 to 36 hr later.

Urinary and fecal excretion products were analyzed by HPLC, TLC, or MS.

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E. RESULTS:

An average 80% of the applied radioactivity was excreted in the urine, with a residual 5% found in feces. Four phenol metabolites separated in the urinary samples, and were identified as follows:

phenyl sulfate (68%)
phenyl glucuronide (12%)
phenyl glucoside (trace)
Phenyl-malonyl-glucoside (trace)

F. TE EVALUATION: UNACCEPTABLE.
The study does not include necessary procedures and/or data required by current GDLN 85-1 for this type of assay.

010599

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05-31-93

9/12/93

DATA EVALUATION RECORD

MRID NUMBER No.: OTS 0517005
PC No.: 064001
Tox Chem. No.: 649

I. SUMMARY

STUDY TYPE: (85-2) Percutaneous absorption - rabbit.

CHEMICAL: Phenol

SPONSOR: Dow Chemical, Midland, MI

TESTING FACILITY: Dow's Biochemical Research Laboratory

TITLE OF REPORT: Absorption of Anhydrous Phenol Through the Unbroken Skin

AUTHOR(S): D. D. Irish and E. M. Adams

STUDY NUMBER: D-002150

DATE ISSUED: September 4, 1987

CONCLUSIONS: In animals treated topically with massive doses of test article, both free and conjugated (total) phenol appear in brain tissue shortly after increased concentration are found in circulating blood.

TB-I EVALUATION: UNACCEPTABLE

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II. DETAILED REVIEW

A. TEST MATERIAL: Phenol (anhydrous; Dow)

Description: Liquid
Purity (%): 99.8
Solvent/carrier/diluent: [Not stated]

B. TEST ORGANISM: Lagomorph

Species: Rabbit
Strain: [Not stated]
Age: [Not stated]
Weights - males: [Not stated]
females: [Not stated]
Source: [Not stated]

C. STUDY DESIGN (PROTOCOL): This study was designed to assess the potential of the test article to be absorbed through unbroken skin when administered to the abdominal areas of shaved rabbits, according to established (published) procedures and FIFRA Test Guidelines.

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D. PROCEDURES/METHODS OF ANALYSIS: Anhydrous phenol was applied at the level of 0.015 g/sq. cm. to the shaved abdominal area (10 sq. cm/kg) of groups of five or ten rabbits, and samples of blood taken 5, 10, 20, 60 and 120 minutes later.

"Free" and "total" (conjugated) blood phenol were determined for both control and test animals by the procedure of Theis and Benedict.

Additional groups of animals were treated with equivalent doses, killed 5, 10, 20 and 60 minutes later, and brain phenol determined.

E. RESULTS: It was reported that data from these experiments indicated that the concentration of phenol in brain increased "very rapidly" following increased levels found in blood (Report Tables, attached to this DER).

F. TV EVALUATION: CORE-SUPPLEMENTARY, since many data requirements are lacking

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ATTACHMENTS: Data Tables

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FREE BLOOD PHENOL OF RABBITS RECEIVING LIQUEFIED PHENOL

Time of Bleeding	Blood phenol mg./100cc.							
	#5-48	#5-49	#5-50	#5-51	#5-52	#5-56	#5-57	Average
0	2.47	1.36	1.56	1.46	1.75	2.28	1.66	1.79
5	3.36	2.00	2.53	2.25	2.56	2.62	2.20	2.47
10	3.00	2.10	2.40	2.19		2.62	2.65	2.49
20	3.15	2.21	2.55	2.23	2.20	2.71	2.51	2.36
60	3.28	2.10	2.62	2.17	2.06	2.81	2.31	2.48
120	2.80	1.60	2.28	1.97	1.75	2.48	2.66	2.25

TOTAL BLOOD PHENOL OF RABBITS RECEIVING LIQUEFIED PHENOL

Time of Bleeding	Blood phenol mg./100cc.							
	#5-48	#5-49	#5-50	#5-51	#5-52	#5-56	#5-57	Average
0	3.28	2.67	2.48	2.60	2.95	2.62	2.71	2.76
5	4.61	3.66	3.62	3.46	4.15	3.15	3.11	3.68
10	4.79	4.04	4.28	3.68		3.42	3.46	3.92
20	4.94	4.82	4.98	4.15	4.15	4.25	3.79	3.92
60	5.65	5.03	6.10	4.98	5.05	5.50	4.01	4.44
120	5.40	4.90	5.80	4.95	5.10	4.60	4.29	5.01

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FREE PHENOL VALUES OF CONTROL RABBITS

Time of Bleeding	Blood phenol in mg./100 cc.								
	#5-36	#5-42	#5-47	#5-53	#5-54	#5-55	#5-58	#5-62	Ave.
0	1.50	3.51	3.00	1.34	1.65	1.75	2.60	1.65	2.13
5	1.55	2.56	3.00	1.34	1.54	1.79	2.45	1.64	1.98
10	1.65	2.35	2.85	1.50	1.44	1.64	2.42	1.60	1.97
20	1.65	2.32	2.56	1.30		1.67	2.25	1.57	1.90
60	1.65	2.14	2.62	1.25	1.70	1.64	2.02	1.56	1.81
120		2.00	2.62	1.33	1.54	1.56	1.67	1.57	1.83

TOTAL PHENOL VALUES OF CONTROL RABBITS

Time of Bleeding	Blood phenol in mg./100 cc.								
	#5-36	#5-42	#5-47	#5-53	#5-54	#5-55	#5-58	#5-62	Ave.
0	2.15	4.12	4.29	1.97	2.11	2.68	3.50	1.77	2.80
5	2.33	3.75	4.15	1.93	2.42	2.74	3.13	1.74	2.77
10	2.40	3.36	3.77	2.10	2.00	2.71	3.00	1.74	2.62
20	2.35	3.00	3.66	2.07		2.46	3.00	1.67	2.59
60	2.28	3.23	3.46	1.94	2.13	2.42	2.67	1.60	2.39
120		2.62	3.36	1.80	1.99	2.17	2.28	1.63	2.26

TOTAL BLOOD PHENOL OF RABBITS RECEIVING APPLICATIONS OF ANHYDROUS PHENOL

Time of Bleeding	Blood phenol mg./100 cc.											
	#33	#41	#30	#150	#149	#152	#155	#151	#132	#154	#142	Average
0	1.65	2.50	1;69	2.21	2.41	3.40	3.30	2.92	3.12	3.12	3.46	2.56
5	3.53		3.30	3.06	3.42		3.12	2.95	2.82	3.12	3.53	3.08
10	3.68		2.38	3.64	4.06	4.25	3.79	3.22	3.31	3.46	4.42	3.62
20	4.14	3.53	2.92	4.25	4.38	6.00	4.08	4.00	3.22	4.35	4.42	4.10
60	6.45	3.75	5.20	5.80	5.30	6.00	4.62	6.00	5.05	5.96	6.17	5.48
120	7.55	4.34		4.62	4.98	5.30	4.62	5.76	4.25	5.47	5.70	5.37

FREE BLOOD PHENOL OF RABBITS RECEIVING APPLICATIONS OF ANHYDROUS PHENOL

Time of Bleeding	Blood phenol mg./100 cc.												
	#33	#41	#30	#150	#149	#152	#155	#151	#132	#154	#147	#142	Average
0	1.60	2.45	1.62	1.90	1.68	1.77	1.96		2.12	2.30	2.12	2.56	2.01
5	3.01	2.87	1.67	2.36	2.41			2.12	2.54	2.79	2.72	3.23	2.57
10	2.64		1.62	2.30	2.94	2.65	2.75	2.36	2.69	2.96	2.95	3.40	2.72
20	2.68	2.70	1.96	2.65	2.86	3.30	2.95	2.97	2.38	3.42	3.12	3.05	2.81
60		2.65	2.36	2.52	2.86	2.79	2.75	2.80	3.01	3.30	3.46	3.20	2.65
120	2.26	2.65		1.96	2.16	2.52	2.41	3.32	2.52	2.65	3.30	2.72	2.55

~~SECTION HEAD~~
MICROFICHE

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

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Attachment was not in the original Pkg.

SEP 23 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Phenol/Sodium Phenate: Submission of Data for Reregistration.
Reregisteration Case: 4074

Chemical No: 649 (064001)/786A (064002)
Submission Nos: S-428469/S-429981/
S-429982/S-441617

DP Barcode: D-184258/D-185039/
D-185045/D-191736

FROM: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I
Health Effects Division (H7509C)

09-20-93

TO: Kathryn Davis/Thomas Luminello, PM #52
Accelerated Reregistration Branch
Special Review and Reregistration Division (H7508W)

THRU: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I
Health Effects Division (H7509C)

9/20/93

Registrant: Sporocidin International, Rockville, MD

Request: Review and evaluate FIFRA-88 Phase 2 and Phase 4 submissions proposed to satisfy the TOX DATA GUIDELINE set of generic requirements for phenol and sodium phenate, namely:

81-1 Acute oral LD_{50}
81-2 Acute dermal LD_{50}
81-3 Acute inhalation LC_{50}
81-4 Primary eye irritation
81-5 Primary dermal irritation
82-2 90-Day dermal
83-3(a) Developmental toxicity
84-2(a, b)/(84-4) Mutagenicity battery

Submissions: The registrant has submitted the following documents meant to satisfy toxicology guideline requirements (GDLN No. in parenthesis).

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Reviewed by: Irving Mauer, Ph.D., Geneticist
Toxicology Branch-I, HED (H7509C)
Secondary Reviewer: Karl P. Baetcke, Ph.D., Chief
Toxicology Branch-I, HED (H7509C)

09-27-93
8/27/93

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DATA EVALUATION RECORD

MRID NUMBER No.: OTS-0515719
PC No.: 064001
Tox Chem. No.: 649

I. SUMMARY

STUDY TYPE: (85-1) Metabolism = Rat

CHEMICAL: Phenol

SPONSOR: Shell Oil, Houston, TX

TESTING FACILITY: Sittingbourne Research Centre (UK)

TITLE OF REPORT: A Comparison of the Metabolic Fate of Phenol, Phenyl Glucoside and Phenyl 6-O-Malonyl-Glucoside in the Rat

AUTHOR(S): V. T. Edwards

STUDY NUMBER: SRCGRM85 (Report No. SBGR.85.127)

DATE ISSUED: February 1985 (Final, June 12, 1985)

CONCLUSIONS: Excretion pattern of metabolites identified in urine samples of male rats (only) treated at low (radioactive) doses (only) are described in summary.

TB-I EVALUATION: This study is UNACCEPTABLE in its present form

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II. DETAILED REVIEW

A. TEST MATERIAL: Radioactive phenol (Shell) and unlabelled reference compounds (metabolites)

Description: Liquid
Batches (Lots): (Technicals)
Purity (%): [Not stated]
Solvent/carrier/diluent: Deionized water

B. TEST ORGANISM: Rodent

Species: Rat
Strain: Fischer-344
Age: 8-10 weeks
Weights - males (only): 200 g
Source: Charles River, Mauston (UK)

C. STUDY DESIGN (PROTOCOL): This study was designed to designed to determine the pharmacokinetic and excretion patterns of the test articles administered orally to rats.

A Statement of Quality Assurance measures (inspections/audits) was not provided.

A Statement of adherence to Good Laboratory Practice (GLP) was not provided.

D. PROCEDURES/METHODS OF ANALYSIS: Groups of males (4 per compound) were administered single low oral doses of the following radioactive (14-C) compounds: 1.2 mg/kg phenol; 2.9 mg/kg phenyl-beta-D-glucopyranoside; 3.8 (or 5.0) mg/kg phenyl-6-0-malonyl-beta--D-glucopyransoide, and sacrificed 24-36 hours later.

Urinary and fecal excretion products were analyzed by TLC, HPLC and/or MS.

E. Results: An average 80% of applied radioactivity was excreted in the urine, with a residual (5%) found in feces. Four phenol metabolites separated in urine samples and were identified as follows: phenyl sulfate (68%); phenyl glucuronide(12%); and traces of phenyl glucoside, and phenyl-malonyl-glucoside.

F. TB EVALUATON: (NOT ACCEPTABLE) Core-Supplementary, since study does not include necessary data required by current FIFRA Test GDLN 85-1 for this type of assay.

Disk 8:MAUER:mb:064001.PHE:9/24/93