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MR 269396



September 8, 2003

Hand Delivered

TSCA Document Control Office (7407)
EPA East Building, Room 6428
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Avenue N.W.
Washington, DC 20460-0001

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Attention: TSCA Section 8(e) Coordinator

RE: DCPD/Codimer Concentrate – Mouse Micronucleus Study



Dear Sir or Madam:

The American Chemistry Council Olefins Panel submits this letter on behalf of certain of its members¹ pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA) to inform EPA of certain findings in mice exposed to Dicyclopentadiene/Codimer Concentrate (DPCP/Codimer Concentrate). The Panel has not made a determination as to whether a significant risk of injury to health or the environment is actually presented by the preliminary findings.

DCPD/Codimer Concentrate was tested pursuant to the Olefins Panel's testing plan for the Resin Oils and Cycloalkadiene Concentrates Category under the High Production Volume Chemical Challenge Program.² The CAS Registry number used to identify DCPD/Codimer Concentrate is 68478-10-4 (Naphtha, petroleum, light steam-cracked, debenzenized, C8-16-cycloalkadiene conc.). This stream is isolated by distillation from the C8+ fraction of a thermally processed pyrolysis gasoline. DCPD/Codimer Concentrate typically contains about 40% DCPD, with the balance primarily comprised of codimers of cyclopentadiene with piperylene, butadiene and with methylcyclopentadiene.

¹ The sponsor companies are Chevron Phillips Chemical Company LP, The Dow Chemical Company, Equistar Chemicals, LP, ExxonMobil Chemical Company, The Goodyear Tire & Rubber Company, NOVA Chemicals Inc., Noveon, and Shell Chemical Company LP.

² The test plan is available at <http://www.epa.gov/chemrtk/olefins/olefintp.pdf>.

2003 SEP 23 PM 2:27
OPPT/NCIC



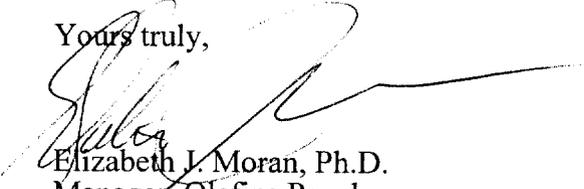
Responsible Care®

A range finding study was conducted using dose groups of 3 male and 3 female CrLCD-1(ICR)BR mice administered DCPD/Codimer concentrate twice at an approximately 24-hour interval daily by gavage in corn oil vehicle. Transient clinical signs including lethargy, hyperreactivity to touch, prostration, incoordination, and minimal reaction to sound were observed in male and female mice, while in addition, spasm, and circling to the left were observed in female animals, during the first 2 hours after receiving a single dose of either 1750 or 1500 mg/kg. No adverse clinical signs were noted at 7 hours post-dosing. Clinical signs were observed in both male and female mice following administration of the second dose of 1750 mg/kg and in addition, temporary total body paralysis in a single male mouse was noted prior to dosing. All female and 5 male mice, including the male mouse exhibiting temporary paralysis, survived until scheduled sacrifice 24 hr after the second dose was administered.

Enclosed are a letter summarizing the finding and a spreadsheet with individual animal data. The final report is not yet available but will be forwarded when received from the laboratory.

If you have any questions, please contact me at 301 924 2006 or Elizabeth_Moran@americanchemistry.com.

Yours truly,



Elizabeth J. Moran, Ph.D.
Manager, Olefins Panel

Attachments

cc: Richard H. Hefter (MC 7403)



DuPont Haskell Laboratory
for Health and Environmental Sciences
Elkton Road, P.O. Box 50
Newark, DE 19714-0050

CC: L. A. Belcher
A. M. Kaplan
M. S. Bogdanffy

DATE: July 6, 2003

TO: Elizabeth Moran, Ph.D.
Managing Director, CHEMSTAR
American Chemistry Council
1300 Wilson Blvd.
Arlington, VA 22209

FROM: Maria Donner, Ph.D. *LAB for Maria Donner*
Senior Research Toxicologist
Genetic Toxicology/Biochemical and Molecular Toxicology

RE: Results of the DCPD/Codimer Concentrate in vivo MN study
ACC Reference Number OLF-92.0-HPV789-DHL

RANGEFINDER

A rangefinder was conducted to determine the dose levels for the definitive study, using groups of 3 male and 3 female Cr1CD-1[®](ICR)BR mice. The test substance was administered twice, at an approximately 24-hour interval, by oral intubation. Initially three mice/sex were administered a dose of the DCPD/Codimer Concentrate at the concentration of 1500 and 2000 mg/kg of body weight. Based on the clinical signs observed after the administration of the first dose, a third dose group at 1750 mg/kg of body weight was added. Corn oil was used as vehicle.

Mortality

At 2000 mg/kg body weight

Day 0 (dosing day 1): Approximately 3-hours post-dosing 1/3 female animals was found dead.

Day 1 (dosing day 2): 1/3 male animals and 1/2 female animals were found dead prior to dosing.

At 1750 mg/kg body weight

Day 1 (dosing day 2): 1/3 male animals was found dead prior to dosing.

Body Weights

Average body weigh losses of approximately 20% were observed for all dose groups over the 3-day observation period.

Clinical Signs Observed on Day 0 (Dosing Day 1)

At 2000 mg/kg body weight

Approximately 40 to 60 minutes post-dosing, male animals exhibited lethargy (1/3 animal), apparent hyperreactivity to touch and minimal reaction to sound (3/3 animals). Female animals exhibited apparent hyperreactivity to touch and minimal reaction to sound (3/3 animals), incoordination (3/3 animals), spasm and circling to the left (1/3 animals).

Approximately 5 hours post-dosing lethargy was observed in all males (3/3 animals) and all females (3/3 animals).

At 1750 mg/kg body weight

Approximately 20 to 30 minutes post-dosing, male animals exhibited lethargy (1/3 animals), hyperreactivity to touch, incoordination, and prostration (3/3 animals). Female animals appeared limp, and exhibited incoordination, prostration, and hyperreactivity to touch (3/3 animals).

Approximately 2 hours post-dosing hyperreactivity to touch was observed in all male (3/3) and female (3/3) animals.

Approximately 7 hours post-dosing no adverse clinical signs were observed in either male (3/3) or female (3/3) animals.

At 1500 mg/kg body weight

Approximately 1 hour post-dosing, male animals exhibited lethargy, hyperreactivity to touch (also to touch of bottom of paw), and minimal reaction to sound (3/3 animals). Female animals exhibited hyperreactivity to touch, incoordination, and minimal reaction to sound (3/3 animals). 1/3 female animals exhibited spasms, circling to the left, and hopping.

Approximately 7 hours post-dosing no adverse clinical signs were observed in either male (3/3) or female (3/3) animals.

Clinical Signs Observed on Day 1 (Dosing Day 2)

At 2000 mg/kg body weight

Approximately 2 hours post-dosing, no adverse clinical signs were observed in all male (2/2) or females (1/1) animals.

At 1750 mg/kg body weight

For approximately 20 seconds prior to dosing, 1/2 males exhibited total body paralysis. Approximately 15 minutes post-dosing, the same male animal exhibited spasms, hyperactivity, resting, wet perineum, ruffled fur excessive grooming and incoordination. Approximately 20 minutes past-dosing 1/2 male animals exhibited hyperreactivity to touch. About 40 minutes post-dosing the only observed sign was wet underbody (1/2 animals). In female animals, no adverse clinical signs were observed in 3/3 animals immediately post-dosing. Approximately 20 minutes post-dosing, 1/3 female animals exhibited hyperreactivity to touch.

At 1500 mg/kg body weight

Approximately 2 hours post-dosing no adverse clinical signs were observed in either male (3/3) or female (3/3) animals.

Clinical Signs Observed on Day 2 (Post-Dosing day 1)

At 2000 mg/kg body weight

Approximately 24 hours post dosing clinical signs in male animals included ruffled fur, hyperreactivity to touch (1/2 animals), and yellow stained perineum (1/2 animals). No adverse clinical signs were observed in 1/1 female animal.

At 1750 mg/kg body weight

Approximately 24 hours post dosing no adverse clinical signs were observed in either male (2/3) or female (3/3) animals. However, no food or feces could be found on the cageboard.

At 1500 mg/kg body weight

Approximately 24 hour post-dosing, the only clinical sign observed was stained perineum (yellow) in 1/3 male animals. No adverse clinical signs were observed in the other males (2/3) or any of the female (3/3) animals

MICRONUCLEUS TEST

Based on the observations from the rangefinder, the dose levels for the micronucleus test were 437.5, 875, and 1750 mg/kg of body weight. The results from the *in vivo* micronucleus test were negative.

Body Weights and Body Weight Gains

Less than 10% body weight losses were observed for male and female animals at the 875 and 1750 mg/kg dose levels.

Clinical Observations and Mortality

Clinical signs of toxicity observed in male and female animals at 1750 mg/kg included ataxia (1/7 males; 1/7 females), lethargy (1/7 males; 3/7 females), and hyperactivity (7/7 males; 1/7 females). In addition, male animals exhibited spasms (1/7), and female animals exhibited ruffled fur (1/7), prostration (1/7), and hyperreactivity (1/7).

No clinical signs were observed in male or female animals at 875 or 427.5 mg/kg. No mortality or morbidity was observed in any dose group in either male or female animals.

No clinical signs were observed in the negative or positive control male or female animals.

HASKELL LABORATORY WORK REQUEST NO.: 14294
HASKELL SAMPLE NO.: 25430
HASKELL SERVICE CODE: 572
TEST SYSTEM: Mice

	A	B	C	D	E	F	G	H	I	J	K	L
1	DuPont-12025											
2												
3		An#	sex	mg/kg	day	Dose Time	Observation Time	Clin. Obs.				
4												
5		3	f	1500	0	8:16	8:41	spasms				
6								circling to left				
7								hopping				
8												
9		1	m	1500	0	8:14	8:51	lethargic				
10								hyperactive when touched on bottom of paw				
11												
12		3	m	1500	0	8:16	8:51	lethargic				
13								hyperactive when touched on bottom of paw				
14												
15		4, 5, 6	m	2000	0	8:21 - 8:23	8:55	more active to touch, minimal reaction to sound				
16												
17		4, 5, 6	f	2000	0	8:24 - 8:27	8:55	more active to touch, minimal reaction to sound				
18												
19		6	f	2000	0	8:27	9:00	spasms				
20								circling to left				
21												
22		6	m	2000	0	8:23	9:02	lethargic				
23												
24		4, 5, 6	f	2000	0	8:24 - 8:27	9:15	incoordination				
25												
26		1, 2, 3	m	1500	0	8:14 - 8:16	9:15	hyperactive to touch				
27												
28		1, 2, 3	f	1500	0	8:17 - 8:19	9:15	hyperactive to touch				
29												
30		1, 2, 3	f	1500	0	8:17 - 8:19	9:15	incoordination				
31												
32		4	f	2000	0	8:24	11:10	FD				
33												
34		4, 5, 6	m	2000	0	8:21 - 8:23	13:00	lethargic				
35												
36		5, 6	f	2000	0	8:24 - 8:27	13:00	lethargic				
37												
38		1, 2, 3	m	1500	0	8:14 - 8:16	15:30	appear normal				
39												
40		1, 2, 3	f	1500	0	8:17 - 8:19	15:30	appear normal				
41												
42		5	m	2000	1	8:22	7:00	FD				
43												
44		5	f	2000	1	8:26	7:00	FD				
45												
46		1, 2, 3	m	1500	1	8:14 - 8:16	10:25	NAD				
47												
48		1, 2, 3	f	1500	1	8:17 - 8:19	10:25	NAD				
49												
50		4, 6	m	2000	1	8:21 - 8:23	10:25	NAD				
51												
52		6	f	2000	1	8:24 - 8:27	10:25	NAD				
53												
54												
55		FD = found dead			NAD = no abnormalities detected							
56												
57												
58												
59		An#	sex	mg/kg	day	Dose Time	Observation Time	Clin. Obs.				
60												
61		7	m	1750	0	8:26	8:42	lethargic				
62												
63		7, 8, 9	f	1750	0	8:29 - 8:31	8:42	limp				
64												
65		7	f	1750	0	8:29	8:44	incoordination				
66												
67		8	f	1750	0	8:30	8:47	incoordination				
68												
69		7, 8, 9	m	1750	0	8:26 - 8:27	8:51	hyperactive to touch				

WR 14294 SC 572 DCPD/Codimer Concentrate

ACC Reference Number OLF-92.0-HPV789-DHL

	A	B	C	D	E	F	G	H	I	J	K	L
70												
71		7, 8, 9	f	1750	0	8:29 - 8:31	8:51	hyperactive to touch				
72												
73		7, 8, 9	m	1750	0	8:26 - 8:27	8:56	incoordination, prostrate				
74												
75		7, 8, 9	f	1750	0	8:29 - 8:31	8:56	incoordination, prostrate				
76												
77		7, 8, 9	m	1750	0	8:26 - 8:27	10:25	hyperactive to touch				
78												
79		7, 8, 9	f	1750	0	8:29 - 8:31	10:25	hyperactive to touch				
80												
81			m & f	1500	1		13:20	all dosed mice NAD				
82												
83			m & f	2000	1		13:20	all dosed mice NAD				
84												
85			m & f	1750	0		13:20	all dosed mice NAD				
86												
87			m & f	1500	1		17:55	all dosed mice NAD				
88												
89			m & f	2000	1		17:55	all dosed mice NAD				
90												
91			m & f	1750	0		17:55	all dosed mice NAD				
92												
93		9	m	1750	1	8:31	6:55	FD				
94												
95		7	m	1750	1	7:55	< 7:55	total body paralysis prior to dosing. front paws crossed across lower chest. Shallow breathing.				
96												
97												
98												
99		7	m	1750	1	7:55	7:55 - 8:10	spasms, hyperactivity, excessive grooming, incoordination				
100												
101												
102		7	m	1750	1	7:55	8:17	resting, perineum wet, ruffled fur				
103												
104		8	m	1750	1	7:58	8:20	hyperreactive to touch				
105												
106		7, 8, 9	f	1750	1	7:59 - 8:01	8:22	NAD				
107												
108		8	f	1750	1	8:00	8:28	hyperreactive to touch but not sound				
109												
110		7	m	1750	1	7:55	8:39	wet underbody				
111												
112												
113												
114												
115												
116						Dose	Observation					
117		An#	sex	mg/kg	day	Time	Time	Clin. Obs.				
118												
119		1, 2	m	1500	2		9:00	NAD				
120												
121		3	m	1500	2		9:00	stained perineum yellow				
122												
123		4, 6	m	2000	2		9:00	ruffled fur, hyperreactive to touch				
124												
125		1, 2, 3	f	1500	2		9:00	NAD				
126												
127		6	f	2000	2		9:00	stained perineum yellow				
128												
129		6	f	2000	2		9:00	NAD				
130												
131		7, 8	m	1750	1	7:55 - 7:58	11:00	NAD				
132												
133		7, 8, 9	f	1750	1	7:59 - 8:01	11:00	NAD				
134												
135		7, 8	m	1750	1	7:55 - 7:58	14:30	no food or feces under cages				
136												
137		7, 8, 9	f	1750	1	7:59 - 8:01	14:30	no food or feces under cages				