

03  
TSCA 8e

BEHQ-100-14816

MR 41011

RECEIVED  
duplicate of OPP  
LO 000585

00 NOV -7 PM 4:21

COURTNEY M. PRICE  
VICE PRESIDENT  
CHEMSTAR

American  
Chemistry  
Council  
Good Chemistry  
Makes It Possible



MR 41011

September 26, 2000

Contain NO CBI

Document Processing Desk (FIFRA 6(a)(2))  
Program Management and Support  
Office of Pesticide Programs  
Mail Code 7510C  
Ariel Rios Building  
1200 Pennsylvania Avenue  
Washington, DC 20460



BEHQ-00-14816

RECEIVED  
00 NOV -7 PM 4:30

RE: Section 6(a)(2) Supplemental Submission by American Chemistry Council's Sodium Chlorite - Chlorine Dioxide Panel on Behalf of Three Sodium Chlorite Registrants



BB010000028

Dear Sir or Madam:

The Sodium Chlorite - Chlorine Dioxide Panel (formerly the Chlorine Dioxide Panel)/(Panel) of the American Chemistry Council (formerly the Chemical Manufacturers Association) submits to EPA the following supplement to the results from its two-generation reproduction study with sodium chlorite (CAS No. 7758-19-2) on behalf of three member companies which are registrants of sodium chlorite. These results are submitted pursuant to Section 6(a)(2) of the Federal Insecticide, Fungicide and Rodenticide Act. These companies (see attached) are sodium chlorite registrants and sponsors of the Sodium Chlorite: Drinking Water Rat Two-Generation Reproductive Toxicity Study.

In connection with EPA's negotiated rulemaking on disinfectants and disinfection byproducts (59 Fed. Reg. 38,668 (July 29, 1994)) the Panel agreed to conduct a 2-generation reproductive developmental neurotoxicity drinking water study on sodium chlorite in rats with developmental and neurotoxicity endpoints to assist EPA in refining the reference dose (RfD) for chlorine dioxide. A Section 6(a)(2) letter (November 28, 1995) was submitted previously by the Panel for this study and supplementary information has been provided subsequently (August 6, 1998). This letter supplements the previous submissions for this study and a copy of the additional data is attached for your information. It should be noted that this additional data does not alter the conclusions identified in the previous submissions.

RECEIVED  
OPPT NCIC  
2000 NOV -9 AM 9:15

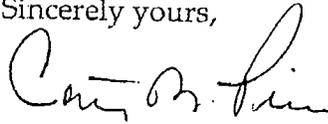


A.04

FIFRA 6(a)(2) Submission  
September 26, 2000  
Page 2

If you have any questions regarding this issue please call John DiLoreto,  
Manager of the Sodium Chlorite - Chlorine Dioxide Panel, at (703) 741-5615.

Sincerely yours,



Courtney M. Price  
Vice President, CHEMSTAR

Attachments: (1) Sodium Chlorite Registrants of the Sodium Chlorite - Chlorine Dioxide  
Panel  
(2) Report from Walter F. Loeb, Veterinary Clinical Pathologist, to the  
Chlorine Dioxide Panel, Chemical Manufacturers Association

cc: TSCA Section 8(e) Docket  
Office of Drinking Water  
Sodium Chlorite - Chlorine Dioxide Panel

Attachment

Sodium Chlorite Registrants of the Sodium Chlorite - Chlorine Dioxide Panel

Vulcan Chemicals  
P.O. Box 385015  
Birmingham, AL 35238  
Panel Representative: Roger Etherington  
Phone: (205) 298-3405  
Fax: (205) 298-2955

Sterling Pulp Chemicals, Ltd.  
302 East Mall  
Suite 200  
Toronto, ONT  
Canada M9B 6C7  
Panel Representative: Gerald Cowley  
Phone: (416) 234-7522  
Fax: (416) 239-8091

ATOFINA Chemicals Inc.  
92091 Paris La Defense Cedex  
Paris France  
Panel Representative: Roland Parsy  
Phone: 1133149008642  
Fax: 1133149008868

Walter F. Loeb V.M.D., Ph.D.  
Veterinary Clinical Pathologist  
Veterinary Pathologist

Client: CHLORINE DIOXIDE PANEL  
CHEMICAL MANUFACTURERS ASSOCIATION  
1300 WILSON BOULEVARD  
ARLINGTON VA 22209  
Attention: Mr. John DiLoreto

17 August 1999

Species: Rat

Study: SODIUM CHLORITE: DRINKING WATER RAT TWO-GENERATION  
REPRODUCTIVE TOXICITY STUDY  
(previously issued, audited, and finalized under the name,  
"TWO GENERATION REPRODUCTIVE STUDY OF CHLORINE DIOXIDE WITH  
NEUROTOXICITY ADD-ON. CMA-14.0-CONS WL")

---

#### INTRODUCTION

Quintiles, Ledbury UK, has performed a TWO GENERATION REPRODUCTIVE STUDY OF CHLORINE DIOXIDE WITH NEUROTOXICITY ADD-ON for CMA. In this study it was noted that hemoglobin, packed cell volume, mean cell volume, and/or mean cell hemoglobin were reduced in some groups of treated animals as compared to the controls. These findings are consistent with the effects of iron deficiency. It was desired by the members of the Chlorine Dioxide Panel to attempt to utilize materials from the Quintiles study to investigate this hypothesis. The histologic evaluation of embedded or fixed liver tissue, stained for iron, appeared to be the only evaluation possible from remaining material from this study. In the study reported by Ani Lytics Inc. on 19 June 1998, high dose animals were compared to controls, and for each generation (F0, F1, F2a, F2b) high dose animals had significantly lower amounts of liver iron than controls. In the investigation described in this report, the same evaluation was performed on the liver sections from the low and mid-dose animals.

#### STUDY

The available liver tissues consisting of paraffin blocks and wet tissues were transferred from Quintiles to EPI for sectioning and staining. Two slides from each tissue were stained for iron with prussian blue (Perl's method), and one was stained with hematoxylin and eosin. The slides were labelled with the animal number but not the treatment group. Each prussian blue stained liver section (4 per animal) was examined and graded as to the amount of stained iron present. Sections were examined by Dr. Walter Loeb at 100x and 200x, and if required, 500x, and iron granules were identified if they were morphologically and tinctorially characteristic. The amount of iron was quantitated as follows: 0.00= none seen; 0.25= 1-3 granules (total) seen in four sections of liver; 0.50= trace amount present, but more than 3 granules in the 4 sections; 0.75=

some iron seen in many but not all 500x fields; 1.00= Iron visible at 100x, and seen in most 500x fields; 1.50= modest amount of iron seen at 100x; 2.00= moderate amount of iron seen at 100x. None of the sections contained more than a moderate amount of iron.

To confirm that the values obtained for the animals in the control group when originally examined as reported in June 1998 were valid for comparison to the low dose and mid-dose animals reported here, slides from 20 control animals were randomly selected and reread without knowledge of the initially reported value. The comparison is shown in Table I. For 15 of the 20 animals, the rereading was identical to the original value, for 4, it differed by one step, and for 1 it differed by two steps.

TABLE I. COMPARISON OF READING OF CONTROLS

<u>Animal Number</u>	<u>Current Reading</u>	<u>Initial Reading</u>
127	1.00	1.00
140	1.00	1.00
149	0.75	0.50
131	1.00	1.00
356/2b	0.50	0.25
346/2b	0.50	0.50
352/6b	0.50	0.50
342/6b	0.50	0.50
356/6b	0.50	0.50
362/6b	1.00	0.50
354/2b	0.50	0.50
344/6b	0.50	0.50
253/2b	0.50	0.50
341/2a	0.50	0.25
357/6a	0.50	0.50
355/6a	0.50	0.50
345/2a	1.00	1.00
363	1.00	0.75
139/8	0.50	0.50
<u>142/4</u>	<u>0.50</u>	<u>0.50</u>
Mean	0.663	0.588

As the data were not normally distributed, they could not be validly tested by the paired t-test. They were tested by the Wilcoxon Signed Rank Test (for nonparametric data) and yielded a p value of 0.999, indicating that the two readings were not significantly different. Therefore the initial readings for the controls were used in this report.

#### RESULTS

Results are tabulated in the attached tables. For 13 week old animals in the F1 generation no sections for males were received from groups 1 and 4; therefore the table for these animals consists of group 2 and 3 only.