

AR 226 - 1447

F

cc: J. Mitchell, Jr., Plastics
J. A. Zapp/G. J. Stopps, Haskell Lab.
J. F. Morgan, Haskell Lab.
C. F. Reinhardt, Haskell Lab.
H. Sherman, Haskell Lab.
F. D. Griffith) In turn, Haskell Lab.
C. S. Hornberger)

May 8, 1970

W. E. HILTON
FLUOROCARBONS DIVISION
WASHINGTON WORKS
PARKERSBURG, W. VA.

TOXICOLOGICAL INFORMATION ON C₈ APFC

I'm sorry for the delay in replying to your recent request for an evaluation of employee hazard from C₈APFC in your polymerization operations. I hope this letter will sufficiently amplify my telephone comments of April 16.

As I understand it, you currently are using C₉APFC, but are phasing it out and will be using C₈APFC for ca. 80 per cent of the Teflon® polymerizing and chlorendic acid for the other 20 per cent. AHT is not used.

I have summarized the available toxicity information on C₈APFC and chlorendic acid in the attached table. We have even less information on C₉APFC and some of it is internally conflicting. The information is inadequate for a complete evaluation of the toxicity of these materials. Your principal exposure is by skin absorption. We have no skin absorption toxicity information on any of the three. C₈APFC and C₉APFC cause liver enlargement, but we don't know what is the lowest repeated oral dosage that will cause it. We have no repeated oral dosage study to indicate if C₈APFC or C₉APFC accumulates in the body to toxic levels. We do not know the eye or skin irritation potential for C₈APFC or C₉APFC and we do not know whether the liver enlargement effect occurs only in rats or in other species as well. Except for the knowledge that chlorendic acid does not cause liver enlargement, our data for this material are similarly sketchy. We have no information on the toxicity of disuccinic acid peroxide.

To answer the initial toxicity questions on C₈APFC, I suggest the following tests:

- I. Determination of lethal concentration by single oral doses and determination of lowest oral dosage causing liver enlargement in rats (histopathology of liver only).

\$600

EID072196

000086

DWS 1036533

00000001

May 8, 1970

II. Accumulation in the rat to cause <u>liver enlargement</u> (two-week subacute, oral dosing).	\$ 750
III. Accumulation in the rat to lethal levels (with histo- pathologic examination of tissues, oral dosing).	\$1400
IV. Recovery study for regression of liver enlargement in the rat after oral dosing.	\$1000
V. Single administration skin absorption toxicity (this is done in the rabbit and can be done with enough rabbits to measure liver enlargement).	\$ 800
VI. Repeated application skin absorption study without histo- pathology but with examination of livers.	\$1500
VII. Primary skin irritation and sensitization (this is done in the guinea pig and can be done with enough guinea pigs to determine if there is significant liver enlargement).	\$1200
VIII. Eye irritation.	300
IX. Repeated (two-week) inhalation administration with histo- pathology.	\$2000
X. Coordination of the above program, interim reports and final evaluation.	+15%

The liver enlargement evaluation in the above studies has not added materially to the cost. In addition, we recommend a 90-day feeding study in rats and dogs including a one-generation reproduction-teratogen study in rats. This would cost ca. \$30,000. This study is recommended because we have no chronic studies on any of these surfactants and no adequate studies in non-rodent species. Depending on the results of this 90-day study, a protracted study in dogs or dogs and rats, might be indicated.

None of the above studies would allow us to set an atmospheric level of CRAPFC that would be hygienically acceptable on a chronic basis. This would require a chronic inhalation study. The exact cost would depend on final test design, but it would be in excess of \$100,000.

EID072197

000087

DWS 1036534

DUP001002

May 8, 1970

If you can eliminate continuous exposure to CgAPFC by inhalation, none of the repeated inhalation studies would be necessary. Similarly, elimination of repeated exposure by skin absorption would eliminate the need for a repeated skin absorption toxicity study. I suggest a visit by our industrial hygienist, Mr. Morgan, as the most beneficial next step to determine the extent of the toxicity testing program. This would also give us better insight into developing the necessary toxicity testing program for chlorendic acid.

RSW

RICHARD S. WARITZ
RESEARCH MANAGER, BIO-SCIENCES GROUP

RSW:ljm
Attachment

EID072198

000088

DWS1036535

DUP001005

SUMMARY OF TOXICITY DATA[§] ON C₈APFC AND CHLORENDIC ACID

<u>Test</u>	<u>C₈APFC</u>	<u>Chlorendic* Acid</u>	<u>Chlorendic* Anhydride</u>
Oral Approximate Lethal Dose	670 mg/kg	5000 mg/kg**	1000 mg/kg not lethal
Oral liver enlargement	60-90 mg/kg	No	No
Oral Subacute	ND	8 x 1000 mg/kg caused seven deaths (10 rats used)	8 x 1000 mg/kg caused six deaths (10 rats used).
Approximate Lethal Dose	0.8 mg/L (caused liver enlargement)	ND	ND (Respiratory irritant in rats).

ND - Not determined

* - Data from Hooker Chemical

** - Haskell Laboratory found 2250 mg/kg

§ - On rats only

EID072199

000089

DW\$ 1036536 ★