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PROTOCOL FOR CONTINUED STUDY OF THE
EFFECTS OF MATERNALLY INHALED VINYL CHLORIDE
ON MOUSE, RAT AND RABBIT
EMBRYONAL AND FETAL DEVELOPMENT

Prepared for the companies sponsoring
The Manufacturing Chemists' Association
Technical Task Group on Vinyl Chloride Research

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I. INTRODUCTION

This protocol describes the second part of a multi-stage teratological study on Vinyl Chloride. In the first stage described in a protocol distributed January 29, 1974 pregnant mice, rabbits and rats were exposed to 500 ppm Vinyl Chloride 7 hours daily throughout the period of organogenesis. A summary of the results of this part is attached to this protocol and complete reports have been previously distributed to the sponsors and submitted as part of the testimony of The Dow Chemical Company at the OSHA hearings in July 1974. As noted in the summary maternal toxicity was not observed in either rats or rabbits but deaths were observed in the mice. No teratogenic effects were observed in any species exposed to Vinyl Chloride alone, based on the external and soft tissue examinations.

One group of mice exposed to Vinyl Chloride was given 15% ethanol in their drinking water as their only source of liquid. This experimental group was included to determine whether or not simultaneous ingestion of ethanol might enhance any teratogenic potential of Vinyl Chloride. This treatment combination did result in an increase in the maternal toxicity as well as an increase in the incidence of cleft palate, a teratogenic response.

II. EXPERIMENTAL PROCEDURES

Based on the above observations, it is recommended that in the second part of this experiment an additional group of mice (large enough to yield at least 40 litters) be exposed to Vinyl Chloride at a concentration of 50 ppm 7 hours/day on days 6-15 of gestation. Half the group of mice will receive 15% ethanol in water while the others will receive tap water and no ethanol.

In addition to the study in mice, additional groups of rats and rabbits will be exposed to 2500 ppm Vinyl Chloride on the same treatment schedule as in the first experiment. In each species, half of the group (enough to produce 15 rabbit or 20 rat litters) will receive 15% ethanol in their drinking water and the remaining half will receive no ethanol. In addition to these groups of rats and rabbits receiving 2500 ppm Vinyl Chloride with and without ethanol, an additional group of rats and rabbits will be given 15% ethanol alone. These groups will serve as controls for the Vinyl Chloride exposed animals that also receive ethanol.

The methods of exposure of the animals and examinations of the fetuses for evidence of teratogenic effect will be the same as those described in the original protocol.

TABLE I
GENERAL DESIGN OF TERATOLOGY STUDIES

<u>Species</u>	<u>Vinyl Chloride Exposure</u>	<u>Percent Ethanol in Water</u>
<u>PART I -- COMPLETED</u>		
Mice	500 ppm	0
Mice	500 ppm	15%
Mice	0	15%
Rats	500 ppm	0
Rabbits	500 ppm	0
Mice,rats,rabbits	0	0
<u>PART II -- PROPOSED</u>		
Rats	2500 ppm	0
Rats	2500 ppm	15%
Rats	0	15%
Rabbits	2500 ppm	0
Rabbits	2500 ppm	15%
Rabbits	0	15%
Mice	50 ppm	15%
Mice	50 ppm	0

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TABLE II
SUMMARY - VINYL CHLORIDE TERATOLOGY STUDIES

	Rats	Rabbits	Mice	
Vinyl chloride, 500 ppm, 7 hr/day	yes	yes	yes	yes
Ethanol - 15% in drinking water	no	no	no	yes
Gestation days of treatment	6-15	6-18	6-15	6-15
No. maternal deaths/No. treated	0/33	0/19	6/30 (20%)	4/30 (13%)
% Pregnancy	94 (control = 96)	95 (control = 100%)	72 (control = 88)	31 (control = 83)
No. litters examined	31	18	19	5
Maternal weight gain	-- ^a	--	sl. dec.	dec.
Maternal food consumption	--	dec.	--	dec.
Maternal liver weight - absolute	--	--	sl. dec.	dec.
- relative	--	--	--	dec.
Implantation sites/dam	--	sl. dec.	--	dec.
% Resorptions	--	--	sl. inc.	--
Litters totally resorbed	0/31	1/19	0/19	2/7
Litter size	--	sl. dec.	sl. dec.	dec.
Fetal body weight	dec.	--	sl. dec.	dec.
Fetal crown-rump length	inc.	--	--	dec.
External malformations	--	--	--	--
Visceral malformations	--	--	--	inc. ^b
Skeletal malformations	--	--	--	--

^a-- = no change, dec. = decrease, inc. = increase, sl. = slight

^bcleft palate

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