

Mr. W. A. Knapp
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INDUSTRIAL BIOLOGY RESEARCH AND TESTING LABORATORIES, INCORPORATED

MORRIS V. SHELANSKI, M.D., C.M.E.D.

14 November 1958

**Mr. W. A. Knapp
Research Consultant
General Chemical Division
Allied Chemical Corporation
Post Office Box #405
Morristown, New Jersey**

Dear Mr. Knapp:

We are pleased to enclose for your kind consideration our protocol of studies for the determination of the safety of use of Vinyl Chloride as a household aerosol propellant. We hope that the information contained therein may be of some use to you in arriving at a decision. If you should desire any information in more detail, at this time, please do not hesitate to call on us.

We are grateful for this opportunity of serving you, and trust that we may be given similar opportunities to bid in the future should you require the type of services we offer.

Sincerely,

**INDUSTRIAL BIOLOGY RESEARCH
AND TESTING LABORATORIES, INC.**

Morris V. Shelanski
**MORRIS V. SHELANSKI, M.D., C.M.E.D.
Director**

**MVS/ld
Enc.**

cc: Mr. P. J. Cambourelis, Solvay Process Division

ASI 000015808

PROTOCOL

SUBACUTE INHALATION STUDIES WITH VINYL CHLORIDE

Part I

I. 1 Purpose:

To determine the safety of use of Vinyl Chloride as a household aerosol propellant.

I. 2 Material:

Vinyl Chloride as supplied by Solvay Process Division of the Allied Chemical Corporation.

I. 3 Procedure:

- I. 31** Albino rats of the Sherman Wistar strain will be used in this study. The rats will be young adult males and females each having an initial weight of 100 - 150 grams.
- I. 32** The procedure will aim to have a population of at least thirty rats surviving the procedure when exposed to the Vinyl Chloride. For each group of animals proposed for this study there will be a group of sixty rats (thirty males and thirty females) subjected to a two week preliminary period (ten exposure days) which will duplicate the experimental regime but omitting actual exposure to the Vinyl Chloride. At the end of this preliminary period, twenty males and twenty females will be selected from each group of sixty on the basis of ability to withstand the physical demands of the regime, using food intake and weight gains as criteria.
- I. 33** The minimum experiment will consist of two such groups of forty animals - one group serving as a control group and the other group serving as the experimental group exposed to the Vinyl Chloride. The animals will be exposed to the Vinyl Chloride eight hours a day five days a week in exposure chambers. Vinyl Chloride will be supplied in a continuous air stream at the desired concentration throughout the entire exposure period. During the exposure period the animals will

Protocol - Subacute Inhalation Studies With Vinyl Chloride

Part I - (Continued from Page 1)

I. 33 (Cont'd.)

not be given any food or water to preclude the possibility of absorption of the experimental material into the food or water thereby defeating the purpose of this inhalation study. Males and females will be housed separately throughout the entire study so as not to compromise the weight gain curves.

I. 34 Analytical procedures will be performed to determine the actual Vinyl Chloride content in the exposure chambers periodically during the exposures. The method of analysis for Vinyl Chloride will be one recommended by Solvay Process Division if such is available. If not, this laboratory will undertake to develop a satisfactory method.

I. 35 Special studies will be performed on the animals as follows:

I. 351 Weight Gain Curves

All animals on the experiment will be weighed at the beginning of the preliminary period and weekly thereafter throughout the course of the experiment. Weight gain curves will be drawn separately for the males and for the females in each group. The weight gain data will be subjected to statistical analysis to determine significance of the differences, if any, among groups.

I. 352 Hematology Studies

Hematology studies will be performed on all animals at the beginning and at the end of the two week preliminary study and at the end of each twenty-five exposure-day period thereafter. These studies will consist of hemoglobin determinations, white blood cell count, red blood cell count, and differential.

I. 353 Pathological Studies

I. 353.1 If the study is only of twenty-five exposure-day duration, ten animals in each group will be sacrificed at the end of the procedure for necropsy. Gross examination of tissues will be performed when the animals are sacrificed. Microscopic studies will

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I. 353.1 (Cont'd.)

be made of the brain, stomach, small intestine, large intestine, liver, pancreas, heart, lung, spleen, kidney, gonads, (spinal cord), adrenals, skin, and skeletal muscle.

The remaining animals in each group will be kept on normal colony diet and regime after the conclusion of the study. If significant pathology is evident in the sacrificed animals, follow-up sacrifices may then be made serial on the surviving animals to determine whether or not such pathology will disappear in time after the animals are taken off exposure.

- I. 353.2 If the study is planned for fifty or seventy-five exposure days, two males and two females in each group will be sacrificed at the end of each twenty-five exposure-day interval. These animals will be selected on the following basis: one male and one female showing highest weight gain, and one male and one female showing least weight gain.

At the end of the procedure five males and five females will be sacrificed for pathological studies. The remaining animals in each group will be kept in reserve for the purpose described above.

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Part IIII. 1 Cost Of Studies:

		<u>Exposure Days</u>		
		<u>25</u>	<u>50</u>	<u>75</u>
II. 11	1 Experimental + 1 Control Group	\$ 8,000.00	\$14,000.00	\$20,000.00
II. 12	2 Experimental + 1 Control Group	11,600.00	20,300.00	29,000.00
II. 13	3 Experimental + 1 Control Group	15,000.00	26,250.00	37,500.00

II. 2 Suggested Schedule Of Payments:

II. 21	25 Exposure Days:	50% in advance. 50% upon submission of Final Report.
II. 22	50 Exposure Days:	Payment for first 25 exposure days in advance. Payment for second 25 exposure days upon submission of Final Report.
II. 23	75 Exposure Days:	Payment for first 25 exposure days in advance. Payment for second 25 exposure days at end of that period. Payment for third 25 exposure days upon submission of Final Report.

II. 3 Interruption Of Studies:

This inhalation study will be undertaken by Industrial Biology Research and Testing Laboratories, Inc. with the understanding that, if the experimental animals are not able to survive the concentration (s) of Vinyl Chloride selected, Allied Chemical Corporation will be notified and will have the right of stopping the study. If the study is stopped, the initial advance payment will be considered a guaranteed minimum payment for Industrial's services. If the study is stopped before the period covered by the advance payment (12.5 exposure days in the twenty-five exposure day study, and twenty-five exposure days in the fifty and seventy-five exposure day studies), the difference between the cost of the actual exposure-days and that covered by the advance payment will be credited to Allied Chemical Corporation for re-

INDUSTRIAL BIOLOGY RESEARCH AND TESTING LABORATORIES, INCORPORATED

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Part II - (Continued from Page 4)

II.3 (Cont'd.)

sumption of this study at lower exposure levels. If the study is stopped after the period covered by the advance payment, Allied Chemical Corporation will pay Industrial an additional fee prorated upon the additional number of actual exposure-days not covered by the advance payment.

This protocol is submitted on a tentative basis and is in no way considered to be final or binding upon either Industrial Biology Research and Testing Laboratories, Inc. or Allied Chemical Corporation pending mutual agreements on performance guarantees, use of reports, and non-exclusive and non-confining basis of performance.

**INDUSTRIAL BIOLOGY RESEARCH
AND TESTING LABORATORIES, INC.**

Morris V. Shelanski
MORRIS V. SHELANSKI, M.D., C.M.
Director

14 November 1958

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ASI 000015813