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1,1,1-TRICHLOROETHANE:
DEVELOPMENT OF A BIOLOGIC STANDARD FOR THE
INDUSTRIAL WORKER BY BREATH ANALYSIS

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DEVELOPMENT OF A BIOLOGIC STANDARD FOR THE
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By

R. P. Stewart, M.D., M.P.H.

C. L. Hake, Ph.D.

A. Wu, Ph.D.

S. A. Graff, B.S.

H. V. Forster, Ph.D.

A. J. Lebrun, M.D.

P. E. Newton, M.S.

R. J. Soto, M.S.

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From the Department of Environmental Medicine, The Medical College of Wisconsin, Milwaukee, Wisconsin, Allen-Bradley Medical Science Laboratory, 8700 West Wisconsin Ave., Milwaukee, Wisconsin, 53226.

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1,1,1-TRICHLOROETHANE

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SYNOPSIS-ABSTRACT

Twenty adults of both sexes were exposed repetitively to 1,1,1-Tri-chloroethane (1,1,1-T) vapor concentrations of 0, 100, 350 and 500 ppm for periods of 1, 3 and 7-1/2 hours in a controlled-environment chamber for two purposes: 1) to develop a practical "biologic" test which would indicate the magnitude of an industrial exposure; 2) to monitor the physiological response of healthy adults to different vapor concentrations and durations of exposure. These studies were designed to simulate the type of exposures encountered in the industrial setting and consisted of both steady, non-fluctuating vapor concentrations as well as widely fluctuating vapor concentrations.

Post-exposure breath analysis proved to be a practical screening method with which to determine the body burden of 1,1,1-T and so provides a Biological Threshold Limit measurement for workmen.

Repetitive vapor exposure to the current TLV of 350 ppm produced no untoward subjective or objective health responses in the healthy subjects other than the objection to the solvent's odor by the majority of the female subjects.

INTRODUCTION

Since the commercial introduction of 1,1,1-Trichloroethane (methyl chloroform; 1,1,1-T) in 1954, this solvent has become increasingly popular, primarily because it is less toxic than the several other chlorinated aliphatic hydrocarbon solvents with comparable physical properties. In 1971, production reached 169.6 million kg of 1,1,1-T for use in metal degreasing, dry-cleaning, and aerosol products⁽¹⁾.

The industrial experience has been excellent from a health standpoint, however, accidental overexposure to high concentrations of the solvent has resulted in sudden death believed due to respiratory center depression, oxygen depletion, or cardiac arrhythmia secondary to epinephrine sensitization of the heart⁽³⁻⁸⁾.

In general, the exposure of healthy adults to the Threshold Limit Value of 350 ppm has not resulted in significant untoward, physiological responses^(2,9). The effects of such exposures upon the performance of cognitive tasks, however, is controversial. Stewart et al⁽¹⁰⁾ and Salvini et al⁽¹¹⁾ noted no decrement in the performance of cognitive tasks performed by volunteers exposed to 1,1,1-T in an environmental chamber. In contrast, Gamberale and Hultengren⁽¹²⁾ reported a decrement in reaction time, perceptual speed, and manual dexterity in subjects exposed to the Threshold Limit Value.

In 1961, Stewart et al⁽¹³⁾ suggested that breath analysis in the post-exposure period could be used as a biologic monitor of exposure, complementing and individualizing the breathing zone data obtained during the traditional industrial hygiene survey. While this has been

confirmed by others, the use of breath analysis to monitor worker exposure has not become popular, perhaps because the data base is too limited⁽¹⁴⁻¹⁵⁾.

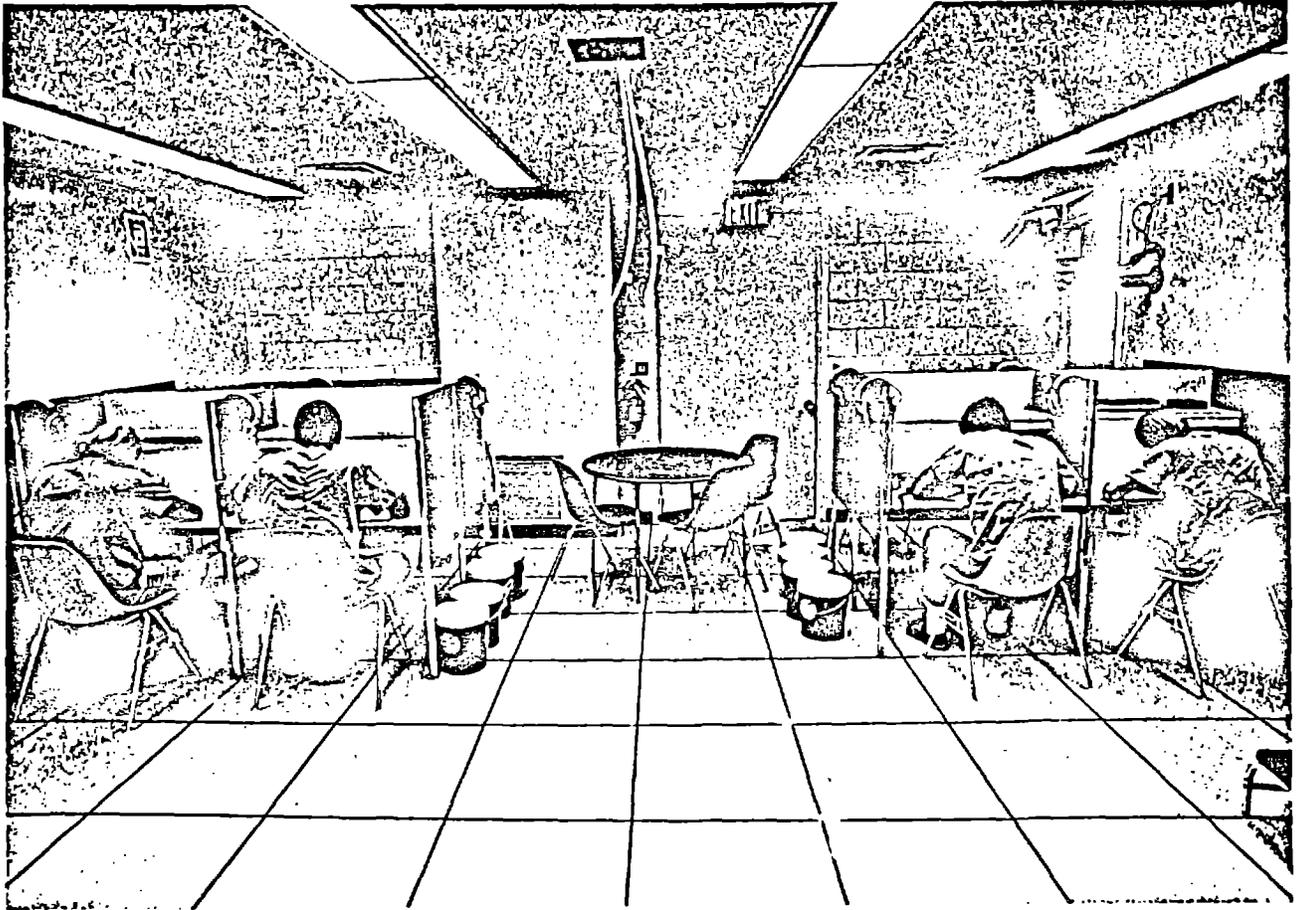
In the series of experiments to be reported, 20 adults of both sexes were exposed to 1,1,1-T, 100, 300, and 500 ppm for varying periods for the purpose of expanding our existing human data base. The goals were: 1) to observe the physiologic response of man to exposure to 1,1,1-T vapor and 2) to develop a practical biologic test useful for estimating the magnitude of exposure to 1,1,1-T.

EXPERIMENTAL

Healthy adults of both sexes were exposed to known concentrations of 1,1,1-T vapor in a controlled-environment chamber (Figure 1). These studies were designed to simulate the type of exposures encountered in the industrial setting and consisted of both steady, non-fluctuating vapor concentrations as well as widely fluctuating vapor concentrations of 1,1,1-T.

Exposure Schedule:

The vapor exposure sequence is presented in Table I. The sequence was initiated with male subjects who were exposed to 1,1,1-T vapor concentrations of 0, 100, 350, and 500 ppm for periods of 1, 3, or 7-1/2 hr. The female subjects were exposed to 0 and 350 ppm for periods of 1, 3, or 7-1/2 hr. The vapor concentrations in the controlled-environment chamber were not permitted to fluctuate widely except for the male



Controlled-environment chamber. This 20' x 20' x 8' room in which eight subjects are performing cognitive tasks features an independent ventilation system and a remotely controlled closed circuit TV camera. The two polyethylene probes in the center of the picture supply chamber air to the two independent analytical systems used to monitor the vapor concentration.

exposure during Week 4 when the wide fluctuation experiment was performed. The female subject exposure sequence occurred subsequent to the exposure of male subjects and duplicated Week 3 for males.

The widely fluctuating concentrations of 1,1,1-T vapor during Week 4 of exposure of male subjects was attained by varying the concentration of 1,1,1-T in the chamber from 200 to 350 to 500 ppm during equal periods of time. The sequence of the up and down concentrations was designed so that the last period of exposure for all subjects was to a vapor concentration of 350 ppm 1,1,1-T.

Subjects:

The subjects were selected from the Caucasian, middle-class, working population of the Milwaukee metropolitan area. They were recruited for this study by a private employment agency. Each subject who completed the study received \$2.50 per hour spent at the laboratory, plus overtime, with a three-hour minimum payment for the Saturday morning medical surveillance check. After the objectives of the study and the nature of the procedures to be used were fully explained to them, all subjects signed an informed consent form, a copy of which is attached as Appendix I.

Ten healthy males volunteered. Their mean age was 23 years with a range of 19 to 26; their mean height was 179.8 cm with a range of 71 to 186; and their mean weight was 76.4 kg with a range of 61.2-93.5 kg. Four of these subjects were assigned to Group I (7-1/2-hr exposure), 3 to Group II (3-hr exposure), and 3 to Group III (1-hr exposure).

The mean age of the ten participating females was 23 years with a range of 18 to 33; their mean height was 162.4 cm with a range of 152 to 170; and their mean weight was 58.2 kg with a range of 49.7 to 70.7. The division of subjects into groups was identical to that of the male study.

All subjects were cautioned to abstain from the use of drugs and to limit their use of alcohol to very moderate amounts. Subjects who were smokers were not allowed to smoke during their stay in the controlled-environment chamber. Subjects who underwent behavioral testing (3-hr and 7-1/2-hr) were asked to refrain from consuming any caffeine prior to the end of each day's study (1-hr post-exposure)..

Most of the subjects had no other wage-earning job during the time of the study, and none experienced any exposure to 1,1,1-T outside of the laboratory.

Exposure Chamber:

All exposures to the vapor of acetone were conducted in a controlled-environment chamber 20 x 20 x 8 ft in size, which contained a 5 x 4 x 8 ft toilet facility and a 5 x 4 x 6-1/2 ft room shielded against electromagnetic radiation. Both the toilet facility and the shielded room were ventilated by air from the chamber. This three-room complex has its independent air handling system and all outside doors are self-sealing when closed. Air flow through the complex was approximately 1500 cu ft per minute and approximately 25% of this flow was exhausted causing a slight negative pressure within the complex at all times. Air temperature was maintained at 72-74° F while relative humidity ranged between

45-55%. The 1,1,1-T vapor was introduced by sweeping the concentrated vapor from a warm flask with a stream of air into the chamber's circulating air. A reciprocal dual-piston pump maintained a steady flow of liquid 1,1,1-T into the flask.

Analysis of Exposure Chamber Atmosphere:

The 1,1,1-T (Aldrich Chemical Co. Inc.) used to contaminate the chamber was inhibited with 3% p-dioxane.

Standards were prepared by filling saran bags with room air pumped in sequence through a charcoal column, a wet test meter, a Drierite column, and a type N all-service gas mask cannister. After filling a bag with a known amount of clean, dry air, a calculated amount of 1,1,1-T was injected into the bag using a microliter syringe. Necessary amounts of 1,1,1-T were calculated taking into account bag volume, ambient temperature and barometric pressure. Calibration of analytical devices was accomplished by attaching the saran bag standard to the necessary probe within the chamber. At least three standards were analyzed prior to allowing subjects to enter the chamber each day and then standards were analyzed at approximately 1-hr intervals throughout the day.

Two completely independent systems were used to monitor the chamber atmosphere. In both cases, air was withdrawn from the chamber through a 1/4" I.D. polyethylene tube at approximately 7 l/min, through or past the analytical device, to a small diaphragm pump which discharged back into the chamber.

A Wilks MIRAN-I was used as the primary monitoring and chamber concentration control device. The 20-m cell was operated at a 0.75-m path-length, and the absorption band at 13.9 μ was used. Voltage output of the MIRAN-I was connected to a strip-chart recorder, and a voltage proportional to the pen position of that recorder was conducted to the analog-to-digital input of a PDP-12 (DEC) computer. The computer sampled pen position voltage each sec, averaged those voltages every 30 sec, recorded the average on magnetic tape, and used the average to present on a scope the concentration over that 30-sec interval and the cumulative or time-weighted average concentration since the beginning of the run.

A gas chromatograph (GC) was used as the "backup" method of chamber air analysis. The Varian Aerograph Model 2700 GC was equipped with a column packed with Poropak Q operated at 185° C. Nitrogen was used as the carrier gas to a hydrogen flame detector operated at 220° C. An automatic device injected a sample of air into the GC every 170 sec. Output of the GC was connected to a strip-chart recorder. Peak-height values read manually were compared to standards and these were compared with the values obtained using the infrared spectrometer. Concentrations found by the two methods were in agreement throughout the study.

Medical Surveillance:

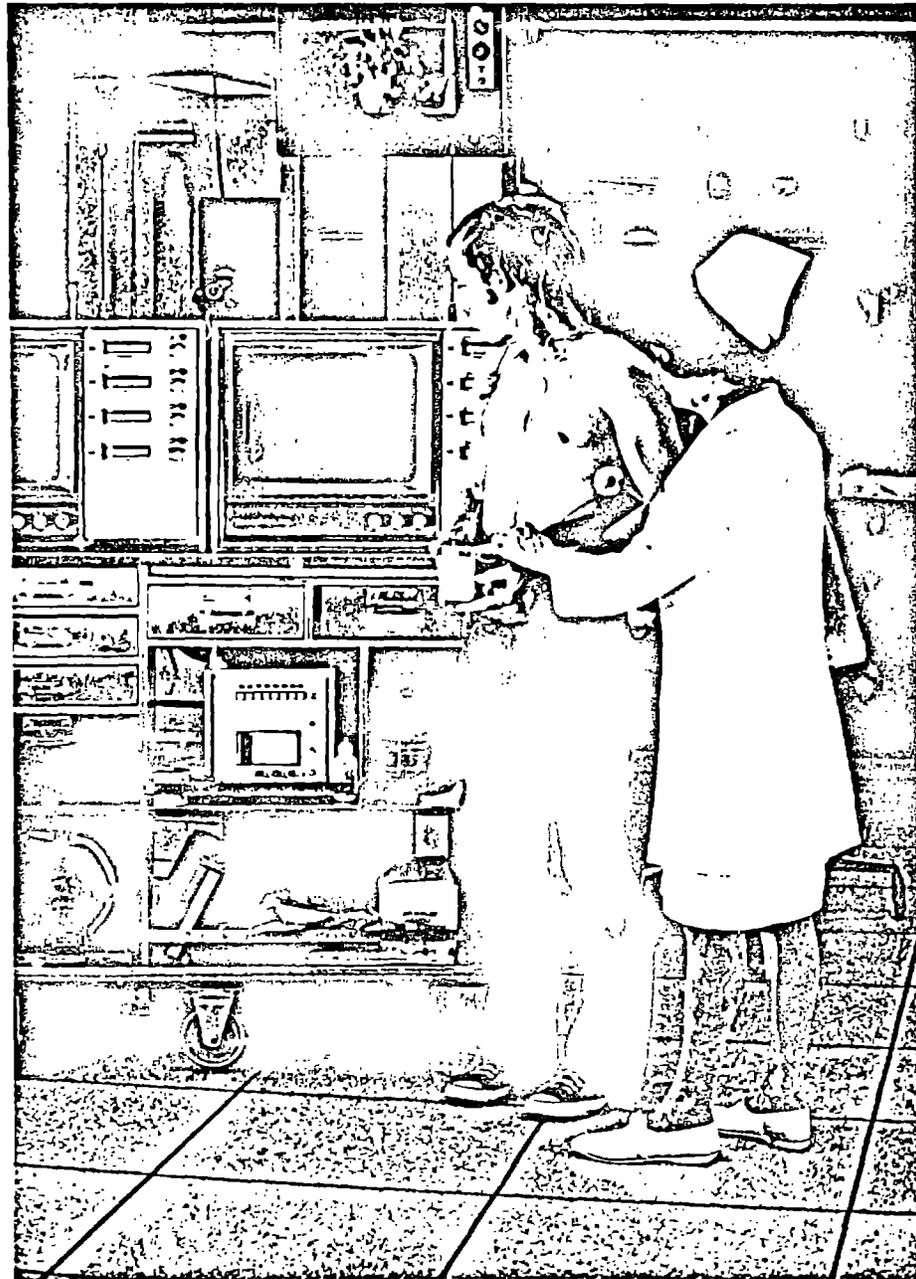
Each subject was given a comprehensive medical examination prior to the study and after the last exposure day of the study. These examinations included a complete history and physical examination with the

following laboratory studies: complete blood count, survey panel of clinical chemistries (SMA-12), and a 12-lead electrocardiogram (EKG). A complete blood count and the panel of clinical chemistries were repeated at least once per week during the weekly exposures. Prior to each day's exposure the subjects were given a brief medical examination which included blood pressure, temperature, subject signs or symptoms, and urinalysis (Combistrix^R). During the time that they were in the environmental chamber, each subject's EKG (lead-II) was continuously monitored by telemetry and recorded at hourly intervals. The subjects were under continual surveillance by medical personnel while they were in the study.

Breath Sample Collection and Analysis:

Alveolar breath samples were obtained daily from each subject prior to entry into the environmental chamber, immediately before exiting from the chamber, and at the following times after exiting the chamber (post-exposure): 1, 15, and 30 min; 1, 2, and 3 hr. These samples were obtained in 40 ml glass tubes which were sealed after filling with screw caps containing saran liners. The breath sample just prior to the end of the vapor exposure was obtained by having the subject breathe into a tube extending through a chamber port-hole and connecting to a 3-l saran bag outside the chamber.

The storage characteristics of the 1,1,1-T breath samples in the glass tubes were determined by filling a series of the tubes with chamber air containing 1,1,1-T and then measuring the remaining solvent concentration at intervals of time thereafter. One set of these tubes was air



Lead II of the electrocardiogram was continuously monitored by telemetry. No abnormalities occurred in any of the subjects during the series of vapor exposures.



The collection of an expired breath sample in a glass pipette. This technique has been previously described in detail in: Stewart, R.D.: "The Use of Breath Analysis in Clinical Toxicology," Essays in Toxicology, Ed. by W. Hayes, Vol. V, Chapt. 5, Academic Press, 1974.



Collection of an expired breath sample in a saran bag.
The subject takes a normal breath, holds it for 20 seconds
and then exhales into the bag.

mailed from Boston, Massachusetts to check on the feasibility of mailing breath samples from remote areas to central laboratories for analysis.

On the fourth day of weeks featuring exposures to concentrations of 350 and 500 ppm, an additional 3- $\frac{1}{2}$ alveolar breath sample was obtained in a saran bag 15 min post-exposure. These samples were scanned by infra-red spectroscopy for any unsuspected compounds which might have been present in the breath.

A Varian Aerograph Model 2700 gas chromatograph (GC) equipped with a hydrogen flame ionization detector was used to determine 1,1,1-T in the breath samples. The GC was fitted with a stainless steel column 2 ft x 1/8 in, packed with Poropak Q, 60/80 mesh. The column was preconditioned at 230° C overnight prior to use. The operating conditions of the GC were as follows: carrier gas (nitrogen) flow rate of 40/ml per min; column temperature of 185° C; injection port, 210° C; and detector, 220° C. Both hydrogen and air flow were kept at the optimum. The sample size was usually kept at 1 ml. Standards at five concentrations to bracket the unknown levels were prepared with clean air as diluent. A single injection from the saran bags was used because of the reproducibility of the analysis. The concentration of 1,1,1-T in the unknowns was obtained by direct comparison of peak heights to the standards. The minimal amount of 1,1,1-T detectable from breath by this method was 0.05 ppm with an accuracy of ± 0.5 ppm.

Blood Sample Collection and Analysis:

Blood samples were withdrawn from an antecubital vein of each subject on Days 2 and 4 of each 1,1,1-T exposure week. The blood samples

were obtained pre-exposure, immediately before exiting from the chamber, and 15 min post-exposure.

Two ml of blood were taken from each subject and introduced into a 4-ml aluminum-capped, glass vial containing 2 ml pure hexane to extract 1,1,1-T. The mixture was shaken for about 30 sec. As demonstrated by experimentation, long agitation (1-1/2 hr) did not improve the efficiency of the extraction. The top hexane layer was withdrawn and analyzed for 1,1,1-T with a gas chromatograph. Samples were analyzed within 24-hr.

A Varian Aerograph Model 2700 Moduline^R gas chromatograph (GC) equipped with a tritium foil electron capture detector was used to determine 1,1,1-T levels in blood for both male and female subjects. The GC was fitted with a stainless steel column, 24 in x 1/8 in packed with Poropak Q, 60/80 mesh. The column was preconditioned at 230° C overnight prior to its use. Throughout the analysis for 1,1,1-T in blood, the column was baked at 200° C when not in use. The operating conditions of the GC were: carrier gas (nitrogen) flow rate of 30 ml/min, column temperature, 185° C; injection port, 230° C; and detector, 210° C. A calibration curve (peak height versus concentration), prepared daily, was constructed with the following concentrations (ppm in hexane): 0.28, 0.55, 1.10, 2.20, 5.40 and 10.80. Samples were injected in duplicate and the concentration of 1,1,1-T in blood was obtained directly from the calibration curve. The detectable limit of 1,1,1-T by this method was 0.005 ppm, while the accuracy reported here was +0.2 ppm.

Analysis of Urinary Metabolites:

Portions of the 24-hr urines from male subjects were frozen for several months before analysis for trichloroethanol and trichloroacetic acid were performed. One ml of urine was introduced into a 5-ml polyethylene vial containing 1 ml β -glucuronidase (500 units, Sigma Chemical Co., St. Louis, Missouri) in 0.15 M phosphate buffer. The resulting mixture was incubated at 37° C for one hour. A control sample was also prepared in an identical manner. Analysis of trichloroethanol was carried out by direct injection of the enzymatic hydrolyzate into a gas chromatograph (GC).

A Varian Aerograph Model 2700 GC equipped with a hydrogen flame ionization detector was used to determine trichloroethanol in the urine of male subjects. The GC was fitted with a stainless steel column, 6 ft x 1/8 in, 25% Apiezon L on Chromosorb W, 45/60 mesh. The column was preconditioned at 200° C for 24 hr prior to its use. The operating conditions were: carrier gas (nitrogen) flow rate 60 ml/min, column temperature, 105° C; injection port, 210° C; and detector, 250° C. Both hydrogen and air were kept at 10 psig. Standards at four concentrations to bracket the unknowns were prepared and trichloroethanol concentrations in urine were obtained by direct comparison of peak heights to the standard. The detectable limit in urine by this method was 0.01 mg/ml with an accuracy of ± 0.01 mg/ml. With exception of the 7-1/2-hr subjects at 500 ppm exposure where trichloroethanol concentration in urine was found to be 0.04 mg/ml, all subjects afforded 0.03 mg/ml or less trichloroethanol concentrations in 24-hr urine collections during exposures to 1,1,1-T.

Because the trichloroethanol peak from the above GC assay with a flame ionization detector was not well resolved, an alternate method was developed and was employed for the analysis of female urine specimens. The urine from female subjects was enzymatically hydrolyzed; applying a procedure similar to above with one exception. After hydrolysis, sodium chloride was added in order to salt out the released alcohol. This was followed by an extraction with one ml of pure hexane.

The gas chromatographic column and conditions were identical to those for studying the male subjects except an electron capture detector was used and column temperature was set at 140° C. A standard curve was prepared daily and the concentration of the trichloroethanol in unknowns was obtained directly from this curve. The usual sample size was 1 µl. The detectable limit by this method was 0.5 µg/ml with an accuracy of ±1 µg/ml.

Attempts to determine the presence of trichloroacetic acid in urine were made. Trichloroacetic acid was not found in the urines of the 7-1/2-hr male and female subjects at 500 ppm and 350 ppm, respectively. As a result, no attempts were made to determine this acid for those subjects with 3-hr and 1-hr exposures.

Neurological Studies:

Within 5 min of entry into the environmental chamber on each exposure day, and within 10 min prior to exit, each subject performed a modified Romberg and heel-to-toe equilibrium test which was videotaped for later inspection if necessary. The test consisted of standing upon each leg singly with arms at the side for a minimum of 3 sec, and

walking heel-to-toe in a straight line for approximately 5 ft. This was first done with the eyes open and then repeated with the eyes shut.

Spontaneous electroencephalograms (EEG) and visual evoked responses (VER) were recorded 4 times each on Monday, Wednesday, and Friday on Group I (7-1/2-hr) subjects. Recordings were normally made once during the first hr and 3 times after the 5th hr of exposure. A complete description and illustration of the EEG-VER monitoring system is found in a previous publication from this laboratory⁽¹⁶⁾. Gold-plated silver disk electrodes were oriented on the scalp according to the 10-20 International Electrode System⁽¹⁷⁾. The paste-filled disk electrode at the inion was cemented with collodion to the scalp to prevent shifting. An 8-channel Grass polygraph fitted with EEG amplifiers was utilized for recording. EEG activity was recorded for 15-30 sec before, periodically during, and 15-30 sec after acquisition of the VER. The EEG recordings were analyzed by visual examination.

The VER was recorded from the electrode at the inion, referred to the left ear. An EEG channel was used to amplify the VER, and the output was fed to an on-line averaging computer (Nuclear Chicago, 7100). The VER was triggered by a strobe flash (3 μ sec) at the rate of 1 per sec for 100 sec. The strobe was operated to deliver 18 million beam candles at 1 m from the subject's eyes, which were closed throughout the period of strobe flashing. Analysis time was 250 msec. Flash delay from the synchronizing pulse which initiated the computer sweep was 25 msec. The computer averaged the response to the 100 flashes, and the resultant VER was recorded on an X-Y plotter for analysis.

It has been shown that VER amplitude can be altered by varying levels of attention, cortical desynchronization, and sleep⁽¹⁸⁻²⁰⁾. Accordingly, standardized conditions were used throughout each exposure day, specifically immediately preceding the actual recordings. After entering the booth, the subject was always allowed 3-5 min to achieve a relaxed state, and then immediately prior to initiating the strobe flash, in an attempt to standardize "attention," the subject clapped his hands 5 times slowly and forcibly.

The most prominent and reproducible portions of the VER complex are the 3rd, 4th, and 5th waves (designation by Gastaut)^(16,19,21). Our analysis was thus restricted to these waves. Wave 3 was identified as proceeding in a positive direction 80-120 msec after initiation of the strobe flash. Waves 4 and 5 were the succeeding negative and positive segments of the VER. Our analysis involved 1) measuring the amplitude of these waves and 2) measuring whether changes had occurred in latency and wave form of the VER complex.

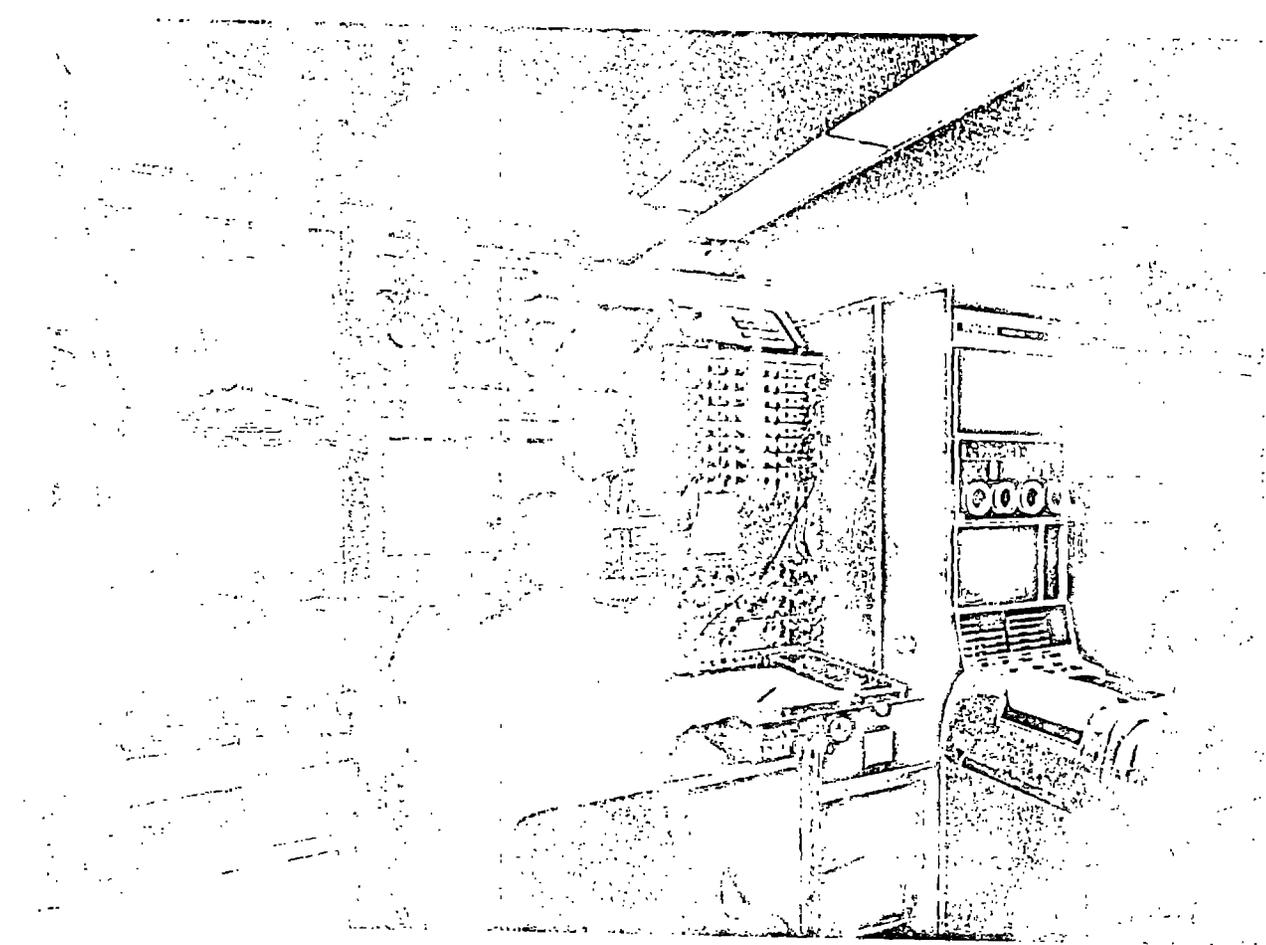
Pulmonary Function Studies:

Measurements designed to evaluate functional integrity of pulmonary airways and alveolar-capillary gas exchange were made on subjects exposed for 7-1/2 or 3 hr. Subjects exposed for 7-1/2 hr were studied between the 5th and 7th hours in the chamber on six occasions in the following sequence: 1) at 0 ppm 4 days before the initial 1,1,1-T exposure 2) 4th day at 100 ppm 3) 4th day at 350 ppm (steady), 4) 4th day at 350 ppm (fluctuating), 5) 4th day at 500 ppm and 6) at 0 ppm 4 days after final exposure to 1,1,1-T. The subjects exposed for 3 hr were studied between

the 1st and 2nd hr of exposure on the two days of 0 ppm exposure. The testing protocol was standardized with the functional integrity of airway assessment always preceding the gas exchange assessments.

Functional integrity of airways was assessed by having the subject perform a forced maximum expiratory maneuver. The subject was seated, erect, and breathing through a mouthpiece connected with wide bore tubing to a Fliesch flow-transducer. The transducer was connected to a Vertek pneumotachograph which sent analog data to the analog-to-digital converter of a PDP-12 computer. Appropriate software was utilized to calculate values for vital capacity (FVC), percent of vital capacity expired in 1 sec (FEV_1), peak expiratory flow rate (PEFR), and flow rate at 50% of FVC (MMEF). This maneuver was performed at least three times, with the data from the two "best" maneuvers being saved on magnetic tape. The mean of the two values was taken as indicative of the function of each specific condition.

Alveolar-capillary gas exchange was assessed by the single breath carbon monoxide diffusion technique (D_{LCO})⁽²²⁾. Computerized systems as noted above were used to calculate inspired, residual, and total lung volumes and D_{LCO} . Neon was used as the inert gas to measure residual volume. Neon and CO concentrations in the collected alveolar sample were analyzed using a Quintron thermoconductivity chromatograph. Two measurements were made each testing day and the mean of the two was the accepted value.



The control room of the PDP-12 computer. To the left is the equipment for the recording of respiratory function. In the center is the control console for recording the central necked response and spontaneous activity in the chamber. To the right is the PDP-12 Digital computer system. The control console includes tests such as the "clock" test.

Cognitive Testing:

A battery of cognitive tests was performed by the male subjects exposed for 3 and 7-1/2 hr. An alertness test lasting 1-1/2 hr was performed on Days 2 and 4 of each week. It began 2 hr after the start of the 7-1/2 hr exposure and 1 hr after start of the 3-hr exposure. No training was required for this test, therefore, it was also performed by the female subjects. On Days 1, 3, and 5 of each week, the remaining tests in the series were performed by the male subjects beginning at 3 and 2 hr after beginning exposure for the 7-1/2 and 3-hr groups, respectively. The subjects were trained to a performance plateau before these tests were used during exposures.

The subjects sat in comfortable chairs at individual carrels to perform the cognitive tests. The subjects were not permitted to talk or have access to watches, food, soft drinks, radios, etc. during the tests. All instructional commands were made from outside of the chamber via an intercom system. The tests are described below in the order in which they were performed.

Alertness Test: This test, called the "clock" test because the subject watches a black clock face from which all numerals and hands have been removed except the sweep second hand, was administered and graded by a PDP-12 computer. It presented a primary and secondary task. For the primary task, the subject pressed a hand-held micro-switch as rapidly as possible whenever he observed a "stop and start" of the sweep second hand. The clock stoppages were for 0.23 sec or 0.13 sec, occurring at random 30 times during the 90-min test. For the secondary task, the subject pressed the hand-held switch whenever a tone was heard through

the headphones he was wearing. These auditory signals were presented randomly for 1 sec, 3 to 6 times per test. At the completion of the test, the computer printed the results in table form for each subject. The table listed signal duration, time of occurrence, reaction time or miss for each signal, percent correct for the day, and the average reaction times for clock stoppages and for tones.

Ten- and Thirty-Second Time Estimation Test: Each male subject upon verbal signal "ready, begin," depressed a hand-held, silent, push-button micro-switch for an interval of time he estimated to be 10 sec. This was repeated 2 additional times, and then 3 30-sec estimates were made. The micro-switches were connected to a polygraph whose pen-deflection could be read to the closest 10 msec. This test took approximately 3 min to perform.

Marquette Time Estimation Test: This test consisted of a series of 9 tone stimuli followed by 9 light stimuli of approximately 1, 3 or 5 sec duration presented in a random sequence but always with 3 stimuli of each time interval. At the termination of each stimulus, the subject depressed the push button for that interval of time he estimated to be equal in length to the original auditory or light stimulus. A detailed description of the test and the instrumentation used to carry it out has been described by Stewart, et al⁽²³⁾. This test took approximately 7 min to perform.

Coordination Test: This test was the Flanagan Aptitude Classification Tests, 7A, Coordination, published by Science Research Associates, Inc., 259 East Erie Street, Chicago, Illinois. This test asked the subject to rapidly follow a spiral pathway with a pencil. The subject

was allowed 40 sec to complete each of 6 spirals. The first 2 were considered practice and the last 4 were scored and totaled. The total score depended upon the longest distance attained in each spiral minus the number of times the sides of the spiral pathway were touched with the pencil. This test took approximately 5 min to perform.

Arithmetic Test: This test, which measured the subject's ability to work with numbers, was divided into 2 parts. The first part, lasting 5 min, consisted of simple addition and subtraction problems while the second part, lasting 3 min, consisted of multiplication and division. The maximum score attainable if all answers were correct was 125; however, no subject completed the tests in the allotted time. In order to minimize memorization of answers, 4 permutations of problem order were used.

Inspection Test: This test was a measure of the subject's ability to spot the number "3" in rows of random numbers on an 8-1/2 in x 11 in page. The subject was asked to scan each row, beginning at the top of the page, and slash out with a red pencil each "3" encountered. The subject was given 2 min to strike out as many as possible. No subject ever finished the entire page. A subject's score was the total number of "3's" struck. Six differing pages with random numbers were utilized so that no subject received an identical number sheet on successive tests.

Subjective Responses:

Each subject was asked to note on an individualized form any subjective responses occurring during the exposure in the chamber or during the first 3 hr post-exposure. The form contained rows for noting headache, nausea, dizziness, abdominal pain, eye, nose, throat irritation, other,

PART I
MIXED ADD and SUBTRACT

41. $95 - 8 + 6 + 5 - 8 =$
42. $47 - 2 + 1 + 3 - 6 =$
43. $63 - 4 + 9 + 9 - 2 =$
44. $16 + 9 - 7 - 7 + 9 =$
45. $81 + 1 - 5 + 4 - 7 =$
46. $27 + 9 - 3 + 5 - 8 =$
47. $48 - 5 + 8 - 3 - 3 =$
48. $73 - 2 + 8 + 6 + 6 =$
49. $65 - 1 - 4 + 9 - 2 =$
50. $89 + 6 + 1 - 2 - 4 =$
51. $92 - 4 + 2 - 8 + 9 =$
52. $54 - 3 - 5 + 1 + 1 =$
53. $36 - 7 - 9 + 5 - 4 =$
54. $11 + 8 - 6 + 7 + 7 =$
55. $26 - 5 + 4 + 8 + 8 =$
56. $53 + 2 - 7 - 6 + 9 =$
57. $69 - 9 + 8 - 1 - 3 =$
58. $85 + 3 + 3 - 5 - 6 =$
59. $17 + 8 + 5 - 4 - 4 =$
60. $92 + 7 - 9 + 3 + 1 =$

STOP HERE, DO NOT GO ON.



40075424232161325826344796365903161348205
1453427990H1034897928008H9926094299R83R51
48729528347174912400086522298H1R67131H35074
416600H64160R981033415683474H3065585716637
6130930363H366451765628666308456748948709
4615032142H524904807849R672865252706361978
849676710740764445211030678374610374500151
785893444806669580738020545029065275522151
9907730465853101225084H8575772270736492551
021765320668298248816877648277623145087275
19576697216936180759583576492477714977499
10606071775404351154977015099846493929038
631758560075R16911035943724H84976147534510
04498028793758777940782753195963956697663
240202026H5273403363996504544246163418167
H7210023619240380361181263095611271867181
395324369648074688655760092392432664594302
00596040282224148872348456799517645467792
461447053355918943366163441266656820082021
153859152787515081238873107357977084504517
22893213570797538576592002231663711012655
26665962148897751581257018148772869422459
29127640426548569874882213836412013940585
595877502794740922137454619726028220177172
791958123317620355145616392144510711345036
147941775085202072401422201694668350669105
13807688852581231530750201622004399210740
H9615366575239544963653338154155639502012
37583490193840189846791021552844107453603
22757290530678434629307305161065600791738
06046423409714049514451760910191561702634
432748369283574754621451746611278276821445
141195699935370340200013005866961349405385
16832972209969610045231219073750016057707
25418224009186051584076778697240494635417
99272345062646963556895497296015060422283
5396555933612543423824092449111308H190639
55784587943947510822219957568H35052083313
47107486098689174405988342801441087102355
12571742187536149057522238559853777775671
2M062646200564470891241295292671086862704
9143H113276901901630718891742777335141664
9719717419155085H803823279364152727913918
73920555570917541841241300151198880127586
62363238393797439954811389521193149073661
0111563942867390928840512164321581720H425
801498313309002669213611823629283160043569
93198874586702883620780228918489462843746
90285991118893060993798J78824992895048726
43564538177358391629417115223286996268474

and odor, and columns for the "immediate," "1/2-hr," and hourly periods of time thereafter. The adjectives "mild, moderate, and strong" appeared on the sheet as cue words, and the phrase "only abnormalities recorded" was prominently typed at the bottom. Each Department physician's home telephone number appeared on the form and the subjects were encouraged to phone if they became ill while away from the laboratory.

RESULTS

Analysis of Exposure Chamber Atmosphere:

The daily time-weighted average (TWA) concentrations of 1,1,1-T vapor in the environmental chamber for each group of subjects are found in Table I. Actual TWA concentrations were within a few percent of those desired.

Medical Surveillance:

Pre- and post-exposure comprehensive medical examinations revealed that all subjects were in good health before and after the study. The attached forms (History - Appendix II, Physical Examination - Appendix III) were used and are retained in each subject's personal file. Blood clinical chemistries obtained before, during, and after the study revealed no unusual abnormalities. Included in the blood clinical chemistries obtained during the study were glucose, urea nitrogen (BUN), uric acid, total protein, albumin, total bilirubin, alkaline phosphatase, and SGOT. For the health examinations previous to any exposure and after the last exposure, calcium, inorganic phosphorous, cholesterol, SGPT, and protein

bound iodine (PBI) were added to the list. No female subjects became pregnant during the period of time they were in the study. All daily urinalysis tests were within normal color ranges (Combistix: glucose, blood, protein, pH).

Complete blood count studies included white blood cells (WBC), red blood cells (RBC), hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, differential count, and platelet concentration. All were within normal limits.

Breath Analysis:

1,1,1-T was readily detected in the expired breath of each of the subjects following exposure to the four vapor concentrations. These post-exposure breath data for male and female subjects are summarized in Table II. Examination of these breath data reveals that a predictable excretion pattern exists for each of the vapor concentrations studied. Furthermore, the rate of excretion of 1,1,1-T in the breath is seen to be a function of the duration of the exposure. Several of the breath decay curves obtained in this study are graphically presented in Figures 4-6.

A "family" of post-exposure breath decay curves useful in estimating the magnitude of vapor exposure can be constructed from the 1,1,1-T breath data. Such a "family" is presented in Figure 4. These are second degree polynomial curves which can be described by the empirical equation:

$$1/Y = B_0 + B_1X + B_2X^2$$

where: Y = breath vapor concentration

X = time after exposure

B_0, B_1, B_2 = arbitrary constants found by regression analysis

The constants for the "family" of empirical equations and the corresponding correlation coefficients are listed in Table III.

The concentration of 1,1,1-T in the breath after exposure is directly related to the time-weighted-average concentration during exposure, the duration of exposure being constant. The variation in breath concentration between male subjects identically exposed, while not great, was large enough to prevent segregation of subjects into one of the three exposure categories on the basis of a single breath sample collected more than 2 hr after exposure. The variation between subjects was due in part to genuine reproducible differences between individuals.

The length of time after exposure in which the 1,1,1-T could be detected in the breath was related to the magnitude of exposure. The solvent was still readily detectable 16 hr after exposure to 100 ppm for 7-1/2 hr. Breath analysis in samples collected 2-16 hr after exposure were highly reliable for estimating the time-weighted-average vapor concentration for a 7-1/2-hr exposure.

The duration of exposure to a given vapor concentration of 1,1,1-T was an important variable influencing the rate of excretion of the solvent in the breath. This is shown in Figure 5. In this example, serial breath sample analysis following exposure to 350 ppm would permit the construction of a decay curve which would indicate the probable duration of that exposure.

The influence of widely fluctuating 1,1,1-T vapor concentrations on the breath decay curves is illustrated in Figure 6. The overall breath decay curve very accurately reflects the time-weighted-average vapor concentration. A breath sample collected within a few minutes after exposure would reflect the most recent vapor concentration while a sample collected 1 hr after exposure would indicate the time-weighted average exposure.

The female subjects had breath decay curves very similar to the male curves during the first hours after exposure (Figure 6). The mean breath concentrations after exposure to 350 ppm were consistently lower than that for similarly exposed male subjects.

In contrast to methylene chloride and similar to tetrachloroethylene, there was a significant accumulation of 1,1,1-T in the body from day to day which did affect the breath decay curves (Figure 7; Table II). Therefore, the indicated correction factor for repetitive exposures need be considered when breath decay curves are used to estimate the magnitude of repetitive exposures.

The infrared scan of the 15-min post-exposure breath samples revealed no unusual absorptions except those expected in the 1,1,1-T region of the spectrum.

Table IV presents the glass tube storage data. These tubes seem to store the 1,1,1-T well although the mean solvent concentration is consistently lower than the true value. The actual concentration of the 1,1,1-T in the chamber atmosphere at the time of filling (zero time) was determined by sampling that air in a saran bag.

The larger standard deviation noted in the 1,1,1-T samples stored in glass tubes indicated probable leakage from these containers. Indeed, this was the case as 7.8% of the glass tube data were discarded when it was obvious that the glass tubes had leaked their contents.

Blood 1,1,1-T Concentrations:

1,1,1-T was detected in the venous blood of each subject following exposure to the solvent. The concentration of 1,1,1-T measured was directly related to the magnitude of the vapor exposure (vapor concentration and duration of exposure) and inversely related to the elapsed time following exposure. The blood 1,1,1-T data are presented in Tables V-VII.

Table V lists the daily blood 1,1,1-T concentrations for the male subjects. Exposures to 350 and 500 ppm resulted in a discernible cumulation of the solvent in the blood and measurable pre-exposure levels. This same build-up was also reflected in the breath decay curves.

Table VI presents the weekly blood 1,1,1-T average concentrations for the male subjects, and Table VII presents the blood 1,1,1-T concentrations for female subjects who were exposed to 350 ppm. The female blood levels are slightly lower than are the blood levels of the comparably exposed male subjects. These data correlate very well with the 1,1,1-T breath data obtained at the same times.

Urinary Metabolites:

It was not possible to measure accurately the trichloroethanol in the urine of the male subjects. This was probably due to loss of the

metabolite during the protracted period of storage before analysis. Trichloroethanol was measured in the urine of the female subjects. These data are presented in Table VIII, and a definite relationship between duration of exposure (1,1,1-T dose) and amount of trichloroethanol formed is apparent.

No significant amount of trichloroacetic acid was detected in the urine samples following exposure to 1,1,1-T.

Neurological Studies:

No significant neurological abnormalities occurred during the observation period. The modified Romberg test and the heel-to-toe test remained normal.

No alteration in the visual evoked response (VER) of either the male or female subjects was observed.

Figures 8-11 present the summary VER's for the male subjects exposed to five levels of 1,1,1-T for 7-1/2 hr per day for 5 days at each level. Each VER presented was taken on the afternoon of the fifth day of exposure at each exposure level and is representative of the VER's recorded that day. There was no significant change in the VER wave amplitude or configuration and the variation seen was similar to the variations seen on control days (Figures 12-15). There is a time lag in the appearance of all the VER's when compared with the precontrol VER. This is not a treatment effect but is due to mistakenly shortened interval between the beginning of the VER recording and the strobe flash on the precontrol day.

Figures 16-18 show that the female subjects exposed 5 days to 350 ppm also showed no change in wave configuration, timing or amplitude which was not within the normal range of variation (Figures 19-21).

There was no significant change in the spontaneous EEG of the male and female subjects exposed to 350 ppm or less. However, changes were observed in the EEG tracings of male subjects exposed to 500 ppm. Representative portions of the spontaneous EEG's for each of the 7-1/2 hr male subjects exposed to 350 and 500 ppm are presented in Figures 22-29. Increased amplitude of alpha activity can be seen in channel seven for all of the subjects, and in addition, in channels 3 and 4 in one subject (#150). This increased alpha amplitude was found only on the 5th and last day of exposure to 500 ppm for both the morning and afternoon recordings. The increased alpha activity was still apparent 3 days later during the post-control experiments.

Electrode preparation could cause a change in the EEG amplitude. However, to minimize the effect of the electrode moving or the electrode cream drying out for the VER, the electrode above theinion was placed in a small well marked and shaved area with collodium and the electrode cream was freshened prior to each recording. Therefore, any changes of the EEG in channel 7 is of slightly more credibility than the others since this care is taken to assure minimal artifact. The presence of increased alpha activity in channels 3, 4 and perhaps 6 in one subject would also negate any argument that this was an accidental change in preamplifier settings.

The female subjects showed no effect of 1,1,1-T on their EEG's. However, they were not exposed to the high concentration which produced the EEG changes in the males.

The EEG effect was noted on the last day of the high level exposure. This would not be an unexpected result. However, this was also the last full week for these subjects and it is possible that psychological factors could have caused the noted EEG changes. At this time, this data must be considered preliminary and an in-depth study is needed to determine the significance of the observation.

Pulmonary Function Studies:

The data presented in Table IX indicate that acute exposure to 1,1,1-T had no effect on lung volume (FVC) and expiratory flow rates (FEV, PEFR, and MMEF). Each of these variables was found to be highly reproducible within a testing session (SEM of trial - 1 vs trial - 2, mean difference less than 0.5% of actual values). Furthermore, there was no significant difference between data obtained on 0-ppm days and data obtained during exposure to 1,1,1-T (Table X). Functional integrity of pulmonary airways does not appear to be affected by a short series of repetitive exposures to this solvent.

There appeared to be a trend toward reduced D_{LCO} during exposure to 1,1,1-T which we interpret to be not significant. On 3 of the 4 days measurements were made during 1,1,1-T exposure, D_{LCO} was lower than on either the pre- or post-exposure days ($P < .05$). This observation must be considered inconclusive because of: 1) normal D_{LCO} during one exposure day, and 2) the small sample size. The within day variability of this measurement approximates our previous observations (SEM of trial-1 vs trial-2 = 3% of actual D_{LCO}).

Cognitive Testing:

There was no decrement observed in the performance of the cognitive tests. A malfunction in the alertness test equipment during the series of male exposures precluded its inclusion in the data analysis. The paired t values for comparison of control versus exposure for the 7-1/2 and 3 hr male subjects are presented in Tables XI and XII, respectively. From these it is apparent that exposure to 1,1,1-T at these concentrations exerted no detrimental effect on cognitive test performance. Any significant t values are spurious as there are t values at longer durations of exposure, or at higher concentrations of exposure, which are not significant. Table XIII presents the data analysis of the alertness test performed by the female subjects. No decrement in performance occurred.

Subjective Responses:

The odor of 1,1,1-T at a concentration of 350 ppm was reported to be moderate to strong by all of the subjects. After seven hours of exposure, the majority of subjects could no longer detect the odor of the solvent when breathing normally. All subjects reported that their ability to perceive the odor progressively diminished during the course of an exposure week. After one breath of uncontaminated air, each subject's ability to detect the solvent's odor was immediately restored.

None of the male subjects judged the odor of 1,1,1-T to be objectionable at the concentrations studied. In contrast all but one of the female subjects volunteered that the odor of 1,1,1-T at a concentration of 350 ppm was distinctly unpleasant.

There was a slight increase in the number of reported untoward subjective responses. These are tabulated in Table XIV.

COMMENTS

Previous studies reporting the effects of well-controlled exposures of humans to 1,1,1-T vapor have featured isolated exposures and with one exception⁽¹⁰⁾ have not simulated the repetitive exposure of the industrial setting. In this sense, this study was unique because it permitted close surveillance of subjects exposed daily for a period of several weeks. In this setting not only could the potential accumulation of 1,1,1-T in the body and its resultant effects be documented, but the individual's ability to adapt to a chemical stress studied.

This study did corroborate the findings of the only repetitive exposure study in the literature. No serious deleterious effects upon the health or performance of healthy adults was detected when they were repeatedly exposed to 500 ppm or less for 7-1/2 hr per day, 5 days per week. The health of the 20 subjects remained unimpaired during the inhalation studies. The blood chemistries, hematologies, urinalyses, electro-cardiograms, and pulmonary function all remained normal and did not vary significantly from pre-exposure values.

One of the two goals of this investigation was to develop a practical biologic standard based upon post-exposure breath analysis. To a major extent this was accomplished. Sufficiently good breath data was obtained to permit breath analysis to become a rapid means with which to estimate the magnitude of an industrial exposure. The only flaw in the system

was an imperfect breath collection device which resulted in the loss of about 8% of the samples collected.

The analysis of expired breath for 1,1,1-T in the post-exposure period provided an excellent diagnostic test of exposure. The detection of the solvent in the breath by infrared spectroscopy constituted an unequivocal diagnosis of exposure, while the use of gas chromatography provided a rapid and very sensitive method for 1,1,1-T detection.

The data reported in this paper indicate that the use of breath analysis provides an excellent screening test useful in estimating the time-weighted average 1,1,1-T exposure. Subjects identically exposed for five consecutive days had very similar breath decay curves, quite adequate for screening purposes. The 1,1,1-T breath decay data obtained during this series of experiments are in excellent agreement with those published in 1969⁽¹⁰⁾.

The concentration of 1,1,1-T in the breath in the early post-exposure period is a reflection of the 1,1,1-T vapor concentration to which the subject has been exposed most recently. If the vapor concentration has been steady and nonfluctuating, this sample will accurately reflect the time-weighted average vapor concentration. If, however, the 1,1,1-T vapor concentration has been fluctuating during exposure, a breath sample obtained in the first few hours following exposure may not accurately reflect the time-weighted average vapor exposure.

The ideal time for the collection of a 1,1,1-T breath sample which will most accurately reflect the time-weighted average vapor exposure is in the 12- to 16-hr period following exposure, at which time the solvent has reached a state of equilibrium within the body compartments. Thus,

for the majority of industrial operations, a breath sample obtained the morning following exposure would be the best for screening purposes.

Experience in this laboratory indicates that, should it be desirable to allow the subject to collect breath samples in glass tubes in the post-exposure period while at home, the breath samples should be collected in duplicate to reduce the troublesome problem of leakage. In addition, it is imperative that duplicate background samples be collected to eliminate the possibility of background contamination yielding a false analytical result.

Ideally, it would be desirable to construct an individualized breath decay curve for each workman following exposure to a known concentration of 1,1,1-T. This would provide a superior breath curve, further reducing the variation due to biological differences, sampling techniques, sex, body mass, and activity during and following exposure.

We are cognizant of some of the weaknesses inherent in the breath decay curves presented here. The number of subjects from whom breath data were obtained in each of the exposure settings is small, and if these breath decay data did not corroborate those reported previously⁽¹⁰⁾, one would hesitate to suggest that they could be immediately useful in industry for screening purposes. The usefulness of this method of exposure evaluation needs to be scrutinized in the industrial setting where the effect of other factors such as physical exertion with its influence on tidal volume, temperature, and the presence of other chemical compounds, can be evaluated.

The use of breath analysis for the purpose of estimating recent and time-weighted average exposure to 1,1,1-T is attractive because of the

simplicity, ease of collection, accuracy, and the low cost of the procedure. Breath analysis in the post-exposure period for the purpose of estimating the magnitude of exposure appears to be superior to the measurement of the urinary metabolites for the following reasons: First, one is measuring 1,1,1-T directly, not a metabolite which can be found in the urine of persons exposed to other compounds, such as trichloroethylene. Thus, breath analysis is a specific test. Second, workmen prefer to give a single breath sample than repeatedly collect their urine in a container over a work day or a 24-hr period.

As a routine screening test the authors would suggest that a breath sample for 1,1,1-T analysis be obtained at the plant entrance on the way into the work place. A value greater than the mean and upper range for 16 hr after exposure to the TLV for 7-1/2 hr would indicate the probability of an exposure in excess of the TLV. In such an instance the work place atmosphere could be checked by an industrial hygienist to determine the reason for the excessive exposure.

The blood 1,1,1-T data presented are good and had more data points been obtained, a biologic test of exposure based on blood analysis could be promulgated. Because the blood data points have a greater standard deviation and because workmen do not like venipunctures as well as breath sampling, the use of blood analysis as a routine screening test seems less attractive.

The subjective responses of the 20 subjects were somewhat surprising. The complaint of 9 of the 10 females that the odor of 1,1,1-T at 350 ppm was unpleasant indicates a sex difference in odor acceptance, should the 9 subjects prove representative of their sex. Of greater importance,

though, was the lack of sleepiness and fatigue which had been reported by the subjects in the first repetitive exposure study by Stewart, et al⁽¹⁰⁾. This would suggest that monotony and boredom may have been the responsible factors in the first study.

This study failed to corroborate the findings of Gamberale and Hultengren⁽¹²⁾ who reported that exposure to 1,1,1-T at 350 ppm for 30 min impaired reaction time, perceptual speed and manual dexterity and then suggested that the current TLV was too high. In our study, these cognitive tasks were not performed during the first 30 min but after several hours when the blood 1,1,1-T was higher and when the decrement in performance should have been more pronounced. While our cognitive studies were performed to rule out gross neurological impairment and were not intended to be the ultimate in sensitivity, it is reassuring that exposure to concentrations higher than studied by Gamberale and Hultengren did not impair reaction time, perceptual speed, or manual dexterity in our subjects. Our findings are in agreement with those reported by Salvini et al⁽¹¹⁾ who observed that exposure to 450 ppm for 4 hr failed to impair performance of a series of different psychophysiological tests.

The alteration in the spontaneous EEG observed on the last day of exposure to 500 ppm and the persistence of this alteration for several days into the post-exposure period is worrisome and merits additional study so that the full significance of the finding can be determined.

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STATEMENT OF VOLUNTARY CONSENT
FOR RESEARCH INVESTIGATION OF
HUMAN EXPOSURE TO:

1, 1, 1-TRICHLOROETHANE

I, _____, hereby agree to participate as a subject, in a program of research investigation under the direction and supervision of Dr. R. D. Stewart.

The general purpose of this research is to determine rates of uptake, excretion and metabolism of 1, 1, 1-Trichloroethane.

The studies have been described to me and the known risks involved in this experimental procedure have been explained to me. I understand that the most frequently described known risks are: none known at this level of
exposure.

I understand also that it is not possible to identify all potential risks in experimental procedures which involve controlled exposures to the chemical in a specially designed chamber.

I further understand that reasonable precautions and safeguards have been and will be taken to remove and reduce both the known and the potential but unknown risks and to provide for my safety and comfort.

I also understand that, while the program will be under the direction and supervision of Dr. R. D. Stewart, other professional persons who work with him may be designated to assist him or to act for him.

In view of those considerations, I hereby authorize Dr. R. D. Stewart and his representatives to proceed with the investigation on the understanding that I may terminate my service as a subject in this research at any time I so desire. I also authorize Dr. R. D. Stewart to use any type of data, pictures, films etc. for use in any scientific report or publication.

I am offering my service freely, in consideration of similar actions on the part of other subjects involved in like voluntary efforts to improve our society through research.

Witness _____
Investigator

Signed _____
Subject

Date _____

EARS	..LANI..			
NOSE	SMELL	OBST.	EPIS	DISCH.
C.R.	URI YR	SORE THROATS	HORSENESS	COUGH
	SPUTUM	HEMOP	NIGHT SWEATS	FEVER
	WHEEZE	PAIN		DOE
	EPEMA	OTHOP	PND	B.P
G.I.	MOUTH			
	APPETITE	DIET		DYSPHAGIA
	N & V	PAIN		
	STOOLS			
	JAUNDICE	MASS		
G.U.	FREQ.	HOC	PAIN	DYSURIA
	INCONTIN.		COLOR	
	ALB.	SUGAR	WBC	RBC
	V.D.			
M.S.	PREV. TRAUMA			
	NECK	BACK		VAR. VEIN
	JOINTS			LEG CRAMPS
NEURO	HEADACHE	TRAUMA		
	ATAXIA	PARALYSIS		
	ANESTH. PARE	TREMOR		
	FAINTING	CONVUL.		
	MEMORY	PERSONALITY		
SKIN	ERUPTION			
	ITCHING	COLOR CHANGE		
LYMPH-HEMAT.	BLEEDING DISORDER			
END.				
ALLERGY				
MENSES	ONSET	LAST	DURATION	FREQUENCY
	WEEKS AGO		PAIN	
	MENOPAUSE	SPOTTING		
	V.D.	VAGINAL DISCHARGE		
BREASTS				

NAME		48										
TEMP.	B.P.	P.	HT.	WT.	ST. W.							
APPEARANCE										POSTURE		
HAIR	COLOR	TEXTURE			DISTRIBUTION							
SCALP	CLEAN	ERUPTION			ALOPECIA							
SKULL	DEFORMITIES				TENDERNESS							
FACE	PALSIES			EXPRESSION				LIPS				
EARS	CERUMEN	TYM MEMB			WATCH HEARD			TOPHI				
NOSE	DISCHARGE			OBSTRUCTION				PERFORATION				
MOUTH	BREATH			ULCERS				AB. PIGMENTATION				
TEETH	R 8 7 6 5 4 3 2 1				1 2 3 4 5 6 7 8 L				X = CARIOUS			
	R 8 7 6 5 4 3 2 1				1 2 3 4 5 6 7 8 L				O = ABSENT			
GUMS	RETRACTION				PYORRHEA							
TONGUE	PROTRUDED MIDLINE			TREMOR				ATROPHY				
TONSILS	STATUS			ENLARGED			INJECTION			EXUDATE		
PHARYNX	GAG REFLEX			INJECTION.				EXUDATE				
EYES	COLOR		ARCUS SENILIS			PERRLA		NEOM		NYSTAGMUS		
	EXOPHTHAL		LID L * G			PTOSIS			PERIORBITAL EDEMA			
	VISION		NEAR		FAR		FIELDS					
	OPHTHAL		DISC		H GR.		A GR.		TONOMETER			
LARYNX	VOICE NORMAL			TRACHEA		MIDLINE		R		L TUG		
NECK	STIFFNESS		NODES		VEINS		CAROTID		THYROID		PALPABLE	
SPINE	TENDERNESS			RIGIDITY				AB. CURVATURE				
THORAX	SYMMETRICAL			CYA TENDERNESS				STERNAL TENDERNESS				
RESPIRA	RATE		REGULAR		DEPTH		SYMMETRICAL		FORCED			
LUNGS	COUGH			SPUTUM				PERCUSSION				
	RESONANT			BREATH SOUNDS				VESICULAR				
	RALES			TACTILE FREMITUS				VOICE SOUNDS				
	HEAVE			SHOCK				THRILL				
HEART	APEX IMPULSE PALPABLE IN _____ I.C.S. _____ CM.			TO L. OF M.C.L. FROM M.S.L.		B.C.D. EXTENDS _____ CM. TO L. OF M.S.L.						
	SOUNDS		A ₂ P ₂		M ₁ M ₂		RHYTHM		MURMUR			
BREASTS	SIZE NORMAL			TENDERNESS				MASSES				
ABDOMEN	SYMMETRICAL			DILATED VEINS			ASCITES					
	PALPABLE LIVER		SPLEEN		KIDNEY		MASSES					
	TENDERNESS		RIGIDITY		SOUNDS		HERNIA					
GENIT-ALIA	DISCHARGE		SKIN LESION			TESTES						
	PELVIC											
ARMS	RADIAL PULSE		TREMOR		CLUBBING		CYANOSIS		JOINTS			
LEGS	DORSALIS PEDIS			VARICOSITIES			EDEMA		ULCER			
	JOINTS											

TABLE I

1,1,1-TRICHLOROETHANE EXPOSURE SCHEDULE: MALE SUBJECTS

WEEK	DAY OF WEEK	DESIRED CONCENTRATION, PPM	ACTUAL TWA 1,1,1-T CONCENTRATIONS					
			7-1/2 Hours		3 Hours		1 Hour	
			PPM	+S.D.	PPM	+S.D.	PPM	+S.D.
1	4	0	0		0		0	
	5	0	0		0		0	
2	1	100	103.0	3.1	101.6	2.1	107.3	3.5
	2	100	102.3	2.7	103.3	2.6	104.7	2.2
	3	100	100.8	2.7	101.0	1.8	104.1	2.5
	4	100	100.8	3.8	100.7	4.5	101.7	4.6
	5	100	100.4	3.7	101.4	3.3	103.1	2.7
3	1	350	345.5	14.7	346.0	17.8	337.2	10.5
	2	350	348.7	19.6	349.8	11.6	325.7	37.7
	3	350	346.4	14.7	343.4	20.5	344.5	8.2
	4	350	344.4	10.6	344.0	13.3	341.7	8.0
	5	350	345.6	10.9	348.4	8.2	338.0	12.8
4	1		352.9	156.2	359.0	156.0	320.5	157.7
	2	350	345.3	146.2	359.6	132.7	361.4	146.5
	3	(wide	348.9	138.4	354.1	130.4	352.0	150.4
	4	fluctuation)	352.2	130.9	368.7	148.4	369.0	--
	5		359.2	133.4	364.7	135.3	358.1	134.1
5	1	500	508.6	14.8	510.3	15.0	514.9	6.8
	2	500	497.7	6.9	500.9	11.9	500.2	11.3
	3	500	504.7	13.0	508.3	14.7	493.0	10.0
	4	500	501.3	12.9	504.4	12.0	506.8	10.3
	5	500	503.1	10.7	500.0	10.3	506.2	8.4
6	1	0	0		0		0	

TABLE I (continued)

1,1,1-TRICHLOROETHANE EXPOSURE SCHEDULE: FEMALE SUBJECTS

WEEK	DAY OF WEEK	DESIRED CONCENTRATION, PPM	<u>ACTUAL TWA 1,1,1-T CONCENTRATIONS</u>					
			<u>7-1/2 Hours</u>		<u>3 Hours</u>		<u>1 Hour</u>	
			PPM	+S.D.	PPM	+S.D.	PPM	+S.D.
1	5	0	0		0		0	
2	1	350	353.6	10.9	354.5	8.0	345.5	19.2
	2	350	353.6	12.7	350.7	15.0	353.2	10.1
	3	350	350.0	8.0	348.6	6.0	348.7	6.4
	4	350	344.9	11.0	345.5	11.4	333.3	13.4
	5	350	349.8	7.3	349.9	5.9	350.2	10.8
3	1	0	0		0		0	

TABLE II

1,1,1-TRICHLOROETHANE BREATH CONCENTRATIONS OF SEDENTARY
MALES EXPOSED TO 500 PPM

Time	<u>Isolated 1 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 1 Hour Exposure</u>			
	N	Mean	Range	N	Mean	Range	Std. Dev.
- 2 min	3	245	242 - 252	8	249.5	216 - 305.7	30.69
1 min, post	2	143	132 - 154	7	148.2	129 - 176.6	17.96
15 min, post	3	66.3	50.1 - 75.2	7	62.14	41.1 - 79.7	14.4
30 min, post	2	54.4	49.6 - 59.1	7	47.29	34.3 - 56	7.0
1 hr, post	3	30.5	24.1 - 34.2	8	28.09	17.3 - 37.2	8.21
2 hrs, post	1	9.52	9.52 - 9.52	7	18.17	10.9 - 23.4	4.54
3 hrs, post	2	8.96	7.31 - 10.6	7	11.68	8.49 - 15.5	3.22
23 hrs, post	3	1.07	.77 - 1.39	7	1.47	.96 - 2.39	.05
71 hrs, post				4	2.5	1.21 - 3.66	1.25
	<u>Isolated 3 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 3 Hour Exposure</u>			
- 2 min	3	232	220 - 241	6	267.38	217 - 325.7	40.25
1 min, post	3	171	145 - 207	9	193.72	147 - 274.9	38.4
15 min, post	3	111	89.2 - 136	9	110.66	89.5 - 152	21.81
30 min, post	3	89.8	72.1 - 108	9	82.97	61.1 - 97.5	12.54
1 hr, post	3	63.5	59.3 - 69.1	9	60.39	48 - 75.1	9.29
2 hrs, post	3	35.6	34.3 - 37.9	8	38.43	30.5 - 43.7	3.96
3 hrs, post	3	27	25.9 - 27.9	8	25.48	19.2 - 32.6	4.21
20 hrs, post	3	3.42	2.34 - 5.34	9	4.68	2.57 - 6.52	1.74
68 hrs, post				2	2.84	2.49 - 3.19	.5
	<u>Isolated 7½ Hour Exposure</u>			<u>Final 3 Days of 5 Daily 7½ Hour Exposure</u>			
- 2 min	4	360	352 - 367	10	366.86	296 - 423.9	37.75
1 min, post	4	254	245 - 264	11	248.46	202.8 - 296.5	29.07
15 min, post	4	146	117 - 174	11	150.9	113 - 181	24.66
30 min, post	4	126	108 - 143	11	121.22	86 - 160	21.99
1 hr, post	4	81.6	69.8 - 93.5	10	91.72	78.3 - 108	8.76
2 hrs, post	3	52.1	45 - 63.5	7	70.67	53.8 - 81.2	9.21
3 hrs, post	3	48.3	37.3 - 54.2	7	55.51	46.1 - 77.3	11.29
16 hrs, post	3	8.38	6.19 - 10.6	10	14.81	12.4 - 18	1.95

TABLE II (Continued)

1, 1, 1-TRICHLOROETHANE BREATH CONCENTRATIONS OF SEDENTARY
MALES EXPOSED TO 350 PPM

<u>Time</u>	<u>Isolated 1 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 1 Hour Exposur</u>			
	<u>N</u>	<u>Mean</u>	<u>Range</u>	<u>N</u>	<u>Mean</u>	<u>Range</u>	<u>Std. Dev.</u>
- 2 min	3	150	144 - 157	9	169.4	159 - 193	14.5
1 min, post	3	76.4	48.6 - 108	9	84.52	44.2 - 118	30.2
15 min, post	2	40	32.3 - 47.6	8	48.76	35 - 60	10.24
30 min, post	3	25.9	23.5 - 30	9	32.99	19 - 40.2	7.49
1 hr, post	2	16.2	16 - 16.3	8	26.19	21 - 34.2	4.26
2 hrs, post	2	11.57	9.95 - 13.2	7	11.14	8.6 - 13.9	2.22
3 hrs, post	2	10.74	7.08 - 14.4	9	6.05	3.53 - 8.24	1.74
23 hrs, post	3	1.11	.75 - 1.63	9	.92	.35 - 1.49	.4
71 hrs, post				3	.78	.66 - .92	.13
	<u>Isolated 3 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 3 Hour Exposur</u>			
- 2 min	3	184	150 - 206	9	173.2	146 - 187	12.53
1 min, post	3	114	79.8 - 136	7	122.2	91 - 168	26.28
15 min, post	3	70.4	49.1 - 98.3	9	77.53	66.4 - 99.1	11.54
30 min, post	3	48.9	41.1 - 58.9	8	57.15	44.7 - 76	8.95
1 hr, post	3	28.9	24.1 - 34.5	9	42.58	33.6 - 54	7.63
2 hrs, post	3	25.5	20.8 - 32.1	6	27.7	24.5 - 34	3.82
3 hrs, post	3	18.5	18 - 19	8	16.14	9 - 21.4	4.28
20 hrs, post	3	3.12	2.46 - 3.60	9	2.86	1.43 - 4.38	1.04
68 hrs, post				3	1.27	1.25 - 1.30	.03
	<u>Isolated 7½ Hour Exposure</u>			<u>Final 3 Days of 5 Daily 7½ Hour Exposu</u>			
- 2 min	4	234	222 - 252	12	255.83	233 - 287	14.64
1 min, post	4	149	144 - 153	10	152.8	115 - 189	27.49
15 min, post	4	86.7	72.5 - 106	12	102.84	82.4 - 125	12.76
30 min, post	4	71	58.8 - 77	12	76.37	55.9 - 103	14.23
1 hr, post	4	48.1	40.1 - 62	12	66.53	55 - 82.8	9.34
2 hrs, post	4	38.1	28.9 - 48	10	41.32	33 - 49	5.4
3 hrs, post	4	37.4	32.2 - 40.5	7	35.79	33.3 - 42.1	3.08
16 hrs, post	4	7.07	6.62 - 7.73	10	9.12	7.07 - 10.9	1.46
64 hrs, post				3	2.16	1.45 - 2.82	.69

TABLE II (Continued)

1, 1, 1-TRICHLOROETHANE BREATH CONCENTRATIONS OF SEDENTARY
FEMALES EXPOSED TO 350 PPM

<u>Time</u>	<u>Isolated 1 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 1 Hour Exposur</u>			
	<u>N</u>	<u>Mean</u>	<u>Range</u>	<u>N</u>	<u>Mean</u>	<u>Range</u>	<u>Std. Dev.</u>
- 2 min	3	183	173 - 193	9	167.94	157 - 180	9.26
1 min, post	2	120	116 - 123	9	89.98	83.3 - 105	6.95
15 min, post	3	53.9	49.4 - 61.7	9	42.68	36.7 - 51	4.92
30 min, post	3	32.9	30.9 - 37	9	31.34	22.2 - 41.3	6.62
1 hr, post	3	22.2	21 - 24.7	9	19.08	14.7 - 23.8	3.22
2 hr, post	2	6.67	5.06 - 8.28	7	4.48	2.7 - 5.59	.94
3 hr, post	2	6.55	5.75 - 7.36	8	3.02	1.22 - 4.28	.99
23 hrs, post	2	.8	.57 - 1.03	4	.33	.2 - .49	.12
	<u>Isolated 3 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 3 Hour Exposur</u>			
- 2 min	2	199	173 - 226	8	211.13	176 - 235	23.2
1 min, post	3	151	146 - 154	8	141.13	124 - 152	12.04
15 min, post	3	89.3	86.4 - 92.6	8	77.55	70 - 92.6	8.08
30 min, post	3	65.4	61.7 - 70.4	8	63.31	55.6 - 73.8	6.01
1 hr, post	3	42.4	40.7 - 43.2	8	39.75	20.9 - 46.3	5.35
2 hrs, post	3	11.65	11.26 - 12.07	7	16.33	11.6 - 23.8	4.51
3 hrs, post	2	9.14	9.08 - 9.20	7	14.18	8.7 - 19.3	4.09
20 hrs, post	3	2.26	1.84 - 2.76	6	2.03	.68 - 3.43	1.18
68 hrs, post				2	1.6	1.02 - 2.18	.82
	<u>Isolated 7½ Hour Exposure</u>			<u>Final 3 Days of 5 Daily 7½ Hour Exposu</u>			
- 2 min	3	254	247 - 262	12	244.83	219 - 278	16.7
1 min, post	4	181	156 - 205	12	180.67	151 - 215	17.82
15 min, post	4	78.6	66.2 - 89.6	11	101.74	82.3 - 123	12.42
30 min, post	4	62.3	52 - 71.4	12	81.47	64.8 - 96.1	9.95
1 hr, post	4	57.5	49.4 - 63.6	12	63.08	46.3 - 75.3	8.34
2 hrs, post	4	17.1	15.5 - 18.5	10	23.23	11.8 - 33	7.12
3 hrs, post	4	14.05	12.2 - 16.3	11	18.36	12.4 - 28.3	5.41
16 hrs, post	4	6.93	4.83 - 8.74	12	6.09	3.74 - 10.3	2.05
64 hrs, post				4	3.53	1.98 - 5.53	1.49

TABLE II (Continued)

1, 1, 1-TRICHLOROETHANE BREATH CONCENTRATIONS OF SEDENTARY
MALES EXPOSED TO 350 FLUCTUATING PPM

Time	<u>Isolated 1 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 1 Hour Exposure</u>			
	N	Mean	Range	N	Mean	Range	Std. Dev.
- 2 min	3	138	135 - 142	7	171.29	142 - 187	15.64
1 min, post	3	82.1	68.5 - 92.9	6	106.77	77.6 - 122	16.73
15 min, post	2	42	41.5 - 42.5	6	50.68	36.6 - 59.8	.29
30 min, post	2	27.9	26.3 - 29.5	6	37.2	30 - 44	4.61
1 hr, post	3	17	13.4 - 22.3	8	23.93	16.3 - 29	4.11
2 hrs, post	3	9.38	6.51 - 12.5	7	13.01	8.66 - 19.4	4.13
3 hrs, post	2	7.22	3.84 - 10.6	7	7.41	4.12 - 12.9	3.37
23 hrs, post	3	1.06	.77 - 1.37	8	1.54	.94 - 2.28	.47
71 hrs, post				3	.8	.59 - 1.15	.31
	<u>Isolated 3 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 3 Hour Exposure</u>			
- 2 min	2	208	190 - 226	8	181.75	149 - 238	33.76
1 min, post	3	155	148 - 183	9	132.44	101 - 176	23.93
15 min, post	2	76.1	71.9 - 80.2	9	80.57	62.4 - 104	14.95
30 min, post	2	73.1	59.8 - 86.4	9	64.16	38 - 79	13.89
1 hr, post	3	43.7	39.6 - 49.8	8	45.84	39.6 - 55.3	5.24
2 hrs, post	2	27	22 - 31.3	8	29.44	24.5 - 35.3	4.36
3 hrs, post	3	21.9	20 - 23.7	9	21.47	17.3 - 24.6	2.67
20 hrs, post	3	3.87	3.41 - 4.1	9	4.06	2.33 - 6.03	1.22
68 hrs, post				3	2.11	1.23 - 2.87	.83
	<u>Isolated 7½ Hour Exposure</u>			<u>Final 3 Days of 5 Daily 7½ Hour Exposure</u>			
- 2 min	4	2.64	221 - 290	9	243.7	205 - 282	27.13
1 min, post	4	185	170 - 194	11	178	142 - 210	22.42
15 min, post	4	109	91 - 123	12	118.7	102 - 139	11.46
30 min, post	4	88.7	81.6 - 95.4	11	92.76	76 - 108	9.56
1 hr, post	4	69	62.7 - 78.8	12	74.11	57.7 - 86.6	8.14
2 hrs, post	3	48.5	39.8 - 54.2	8	53.11	41.9 - 66.4	8.20
3 hrs, post	3	37.2	30 - 46	7	41.89	37.2 - 58.5	6.45
16 hrs, post	4	8.02	6.83 - 8.99	11	10.98	7.79 - 16.3	2.75
64 hrs, post				3	3.09	3.2 - 3.7	.26

TABLE II (Continued)

1,1,1-TRICHLOROETHANE BREATH CONCENTRATIONS OF SEDENTARY
MALES EXPOSED TO 100 PPM

Time	<u>Isolated 1 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 1 Hour Exposure</u>			
	N	Mean	Range	N	Mean	Range	Std. Dev.
- 2 min	3	48.3	45.9 - 50.3	8	71.2	54.6 - 90.3	13.92
1 min, post	3	21.0	19.6 - 22.3	6	41.03	24.6 - 58.9	14.86
15 min, post	3	14.3	12.8 - 15.1	8	18.01	12 - 27.03	5.05
30 min, post	3	9.9	7.5 - 11.5	6	12.87	9.33 - 16	2.28
1 hr, post	3	6.38	5.61 - 7.68	8	7.91	5.12 - 11.1	2.2
2 hrs, post	2	2.96	2 - 3.92	8	3.34	1.51 - 5.07	1.38
3 hrs, post	3	2.1	1.8 - 2.46	7	2.11	.1 - 3.74	1.10
23 hrs, post	2	.32	.29 - .35	9	.33	.16 - .58	.13
71 hrs, post				2	.43		
	<u>Isolated 3 Hour Exposure</u>			<u>Final 3 Days of 5 Daily 3 Hour Exposure</u>			
- 2 min	3	50.5	45.1 - 56.1	9	56.08	48 - 64.5	6.7
1 min, post	3	33.9	30 - 37.9	9	40.21	33.2 - 47.6	4.62
15 min, post	2	18.6	18.4 - 18.7	9	23.57	19.5 - 32.3	4.24
30 min, post	3	17.1	11.3 - 23.6	7	17.71	16.3 - 19.5	1.15
1 hr, post	2	13.4	11.7 - 15.1	9	12.88	10.4 - 15.5	1.82
2 hrs, post	3	12.1	11 - 14	6	10.82	8.1 - 13.3	1.69
3 hrs, post	1	8.16		7	6.88	6.8 - 1	.80
20 hrs, post	2	1.08	.88 - 1.29	9	1.25	.76 - 1.62	.28
	<u>Isolated 7½ Hour Exposure</u>			<u>Final 3 Days of 5 Daily 7½ Hour Exposure</u>			
- 2 min	3	77.3	69.6 - 87.4	12	98.2	68.6 - 114	12.78
1 min, post	4	48.9	42 - 61.7	12	68.93	50.4 - 89.7	11.8
15 min, post	4	30.1	20.3 - 36	12	42	33.6 - 47.4	4.66
30 min, post	4	24.5	20.6 - 28	11	29.39	22 - 36	4.65
1 hr, post	4	12.5	11.2 - 19.1	12	20.05	14.4 - 26.7	3.28
2 hrs, post	4	15.2	13.1 - 16.3	5	19.66	5 - 23.5	3.28
3 hrs, post	3	11.3	9.25 - 15.4	5	15.68	10 - 19.9	4.20
16 hrs, post	4	3.09	2.76 - 3.32	10	4.37	2.84 - 6.8	1.43
64 hrs, post				4	.68	.57 - .81	.1

TABLE III

"BEST FIT" EMPIRICAL EQUATIONS FOR
1,1,1-TRICHLOROETHANE BREATH DECAY CURVES

$$1/Y = B_0 + B_1X + B_2X^2$$

EXPERIMENTAL CONDITION	$B_0 \times 10^{-2}$	$B_1 \times 10^{-3}$	$B_2 \times 10^{-6}$	r	S.E
MALES:					
100 PPM, 7-1/2 hrs, 1st day	3.136	.3533	-.051	.9925	.02
100 PPM, 7-1/2 hrs, 3-day av.	2.233	.2595	-.046	.9961	.01
350 PPM, 1 hr, 1st day	2.261	.4304	.1493	.9996	.01
350 PPM, 1 hr, 3-day av.	.342	.8299	-.3232	.9997	.01
350 PPM, 3 hrs, 1st day	1.119	.2574	.00	.9994	.00
350 PPM, 3 hrs, 3-day av.	.740	.2851	.00	.9997	.00
350 PPM, 7-1/2 hrs, 1st day	1.023	.1063	.0316	.9981	.00
350 PPM, 7-1/2 hrs, 3-day av.	.7960	.1224	-.0172	.9994	.00
350 PPM fluct., 7-1/2 hrs, 1st day	.6997	.1115	.0115	.9998	.00
350 PPM fluct., 7-1/2 hrs, 3-day av.	.6842	.1001	-.0129	.9997	.00
500 PPM, 7-1/2 hrs, 1st day	.5319	.0926	.0272	.9993	.00
500 PPM, 7-1/2 hrs, 3-day av.	.5325	.0754	-.0110	.9993	.00
FEMALES:					
350 PPM, 7-1/2 hrs, 1st day	.3097	.0439	-.3045	.9938	.01
350 PPM, 7-1/2 hrs, 3-day av.	.3584	.3136	-.1524	.9985	.00

Y = breath vapor concentration
X = time after exposure
r = correlation coefficient
S.E. = standard error

TABLE IV
STORAGE OF 1,1,1-TRICHLOROETHANE IN GLASS BREATH TUBES

Time in Hours Post - Filling	0	0	17	40	96	120	120
Container	Saran Bag	Glass tube stored in laboratory					Glass tube air mailed
Number	10 (aliquots)	10	4	4	4	5	8
Mean concentra- tion, ppm	112	94	103	105	92	94	90
+S.D.	0.8	11.8	2.4	7.9	4.8	7.7	9.7

TABLE V

1,1,1-TRICHLOROETHANE CONCENTRATION IN BLOOD

Parts Per Million

Group I: 4 Male Subjects.

Exposure Time: 7½ Hours

Date		Baseline	4 Hours	Pre-Exit	15' Post
Chamber Concentration: 100 ppm					
7-10-73	Mean	0.05	2.02	1.82	1.21
	± S. D.	0.10	0.18	0.96	0.29
7-12-73	Mean	0.036	1.72	1.99	1.61
	± S. D.	0.02	0.04	0.58	0.18
Chamber Concentration: 350 ppm					
7-17-73	Mean	0.17	5.94	6.13	4.88
	± S. D.	0.07	0.42	0.36	0.19
7-19-73	Mean	0.375	6.18	6.75	5.23
	± S. D.	0.06	0.24	0.13	0.17
Chamber Concentration: 350 ppm (Fluctuating)					
7-24-73	Mean	0.26	5.91	7.05	5.64
	± S. D.	0.06	0.19	0.15	0.41
7-26-73	Mean	0.56	5.45	5.74	4.97
	± S. D.	0.36	0.25	0.25	0.16
Chamber Concentration: 500 ppm					
7-31-73	Mean	0.28	6.87	5.83	5.87
	± S. D.	0.03	0.84	1.35	0.32
8-2-73	Mean	0.58	5.64	6.16	5.41
	± S. D.	0.13	0.24	0.23	0.24

TABLE V (Continued)

1,1,1-TRICHLOROETHANE CONCENTRATION IN BLOOD

Parts Per Million

Group II: 3 Male Subjects

Exposure Time: 3 Hours

Date		Baseline	Pre-Exit	15' Post
Chamber Concentration: 100 ppm				
7-10-73	Mean	0.05	1.78	1.24
	† S. D.	0.09	0.16	0.21
7-12-73	Mean	0	1.73	1.18
	† S. D.		0.10	0.11
Chamber Concentration: 350 ppm				
7-17-73	Mean	0.06	5.59	4.02
	† S. D.	0.02	0.45	0.33
7-19-73	Mean	0.12	5.45	4.20
	† S. D.	0.05	0.23	0.69
Chamber Concentration: 350 ppm, Fluctuating				
7-24-74	Mean	0.12	5.92	5.10
	† S. D.	0	0.31	1.11
7-26-74	Mean	0.46	5.09	4.01
	† S. D.	0.12	0.08	0.72
Chamber Concentration: 500 ppm				
7-31-73	Mean	0.18	6.94	5.24
	† S. D.	0.11	0.61	0.56
8-2-73	Mean	0.46	5.57	4.93
	† S. D.	0.08	0.37	0.09

TABLE V (Continued)

1,1,1-TRICHLOROETHANE CONCENTRATION IN BLOOD

Parts Per Million

Group III: 3 Male Subjects

Exposure Time: 1 Hour

Date		Baseline	Pre-Exit	15' Post
Chamber Concentration: 100 ppm				
7-10-73	Mean	0.16	1.15	0.585
	± S. D.	0.11	0.16	0.01
7-12-73	Mean	0.453	1.30	0.83
	± S. D.	0.79	0.36	0.13
Chamber Concentration: 350 ppm				
7-17-73	Mean	0.01	4.79	2.78
	± S. D.	0.005	0.25	0.17
7-19-73	Mean	0.033	5.00	3.00
	± S. D.	0.02	0.51	0.39
Chamber Concentration: 350 ppm, Fluctuating				
7-24-73	Mean	0.08	5.09	4.06
	± S. D.	0.05	0.08	0.24
7-26-74	Mean	0.16	4.58	2.94
	± S. D.	0.06	0.17	0.23
Chamber Concentration: 500 ppm				
7-31-73	Mean	0.22	5.59	4.00
	± S. D.	0.03	0.20	0.24
8-2-73	Mean	0.32	5.02	3.17
	± S. D.	0.15	0.06	0.29

TABLE VI

THE WEEKLY AVERAGES OF 1,1,1-TRICHLOROETHANE

CONCENTRATION IN BLOOD

Parts Per Million

Group I: 4 Male Subjects

Exposure Time: 7½ Hours

Chamber Concentration		Baseline	4 Hours	Pre-Exit	15' Post
100 ppm	Mean	0.045	1.87	1.92	1.41
	+ - S. D.	0.03	0.20	0.69	0.31
350 ppm	Mean	0.27	6.06	6.44	5.06
	+ - S. D.	0.14	0.17	0.44	0.25
350 ppm Fluctuating	Mean	0.41	5.68	6.40	5.31
	+ - S. D.	0.21	0.33	0.93	0.47
500 ppm	Mean	0.43	6.23	6.00	5.64
	+ - S. D.	0.21	0.87	0.23	0.33

TABLE VI (Continued)

THE WEEKLY AVERAGES OF 1,1,1-TRICHLOROETHANE

CONCENTRATION IN BLOOD

Parts Per Million

Group II: 3 Male Subjects

Exposure Time: 3 Hours

Chamber Concentration		Baseline	Pre-Exit	15' Post
100 ppm	Mean	0.025	1.76	1.21
	+ - S. D.	0.04	0.04	0.04
350 ppm	Mean	0.09	5.52	4.11
	+ - S. D.	0.04	0.10	0.13
350 ppm Fluctuating	Mean	0.29	5.51	4.56
	+ - S. D.	0.24	0.59	0.77
500 ppm	Mean	0.32	6.23	5.09
	+ - S. D.	0.20	0.97	0.22

TABLE VI (Continued)

THE WEEKLY AVERAGES OF 1, 1, 1-TRICHLOROETHANE

CONCENTRATION IN BLOOD

Parts Per Million

Group III: 3 Male Subjects

Exposure Time: 1 Hour

Chamber Concentration		Baseline	Pre-Exit	15' Post
100 ppm	Mean	0.32	1.24	0.73
	± S. D.	0.59	0.28	0.16
350 ppm	Mean	0.02	4.90	2.89
	± S. D.	0.016	0.15	0.16
350 ppm Fluctuating	Mean	0.05	4.84	3.50
	± S. D.	0.045	0.36	0.79
500 ppm	Mean	0.27	5.31	3.59
	± S. D.	0.07	0.40	0.59

TABLE VII

1,1,1-TRICHLOROETHANE IN BLOOD IN PPM

Group I: 4 Female Subjects

Exposure Time: 7½ Hours

Chamber Concentration: 350 ppm

Date of Collection of Samples: January 15, 1974

Subject Number	182	183	184	185	Mean ⁺ S. D.
Preexposure	0.125	0.275	0.150	0.100	0.163 ⁺ 0.078
4-Hours Exposure	4.0	4.6	5.2	4.2	4.50 ⁺ 0.53
7½ Hours Exposure	3.8	4.2	4.0	4.2	4.04 ⁺ 0.19
15 Min. Postexposure	3.4	No Sample	3.0	3.2	3.2 ⁺ 0.12

Date of Collection of Samples: January 17, 1974

Preexposure	0.175	0.150	0.125	0.130	0.145 ⁺ 0.02
4-Hours Exposure	4.3	4.4	4.1	4.4	4.3 ⁺ 0.14
7½ Hours Exposure	5.1	4.3	3.1	3.6	4.03 ⁺ 0.87
15 Min. Postexposure	2.8	2.8	3.3	3.1	3.00 ⁺ 0.24
54 Hours Post-exposure	0.05	0.05	0.05	0.05	0.05 ⁺ 0

TABLE VII (Continued)

1,1,1-TRICHLOROETHANE IN BLOOD IN PPM

Group II: 3 Female Subjects

Exposure Time: 3 Hours

Chamber Concentration: 350 ppm

Date of Collection of Samples: January 15, 1974

Subject Number	186	187	188	Mean [±] S. D.
Preexposure	0.05	< 0.05	0.05	0.05
3-Hour Exposure	3.2	3.2	3.1	3.17 [±] 0.06
15-Min. Post-exposure	2.0	2.2	2.2	2.13 [±] 0.12

Date of Collection of Samples: January 17, 1974

Preexposure	0.125	< 0.01	< 0.01	< 0.1
3-Hour Exposure	4.1	4.2	4.1	4.13 [±] 0.06
15-Min. Post-exposure	2.1	2.4	1.8	2.10 [±] 0.30
68½ Hours Post-exposure	< 0.05	< 0.05	< 0.05	< 0.05 [±] 0

TABLE VII (Continued)

1,1,1-TRICHLOROETHANE IN BLOOD IN PPM

Group III: 3 Females

Exposure Time: 1 Hour

Chamber Concentration: 350 ppm

Date of Collection of Samples: January 15, 1974

Subject Numbers	189	190	191	Mean \pm S. D.
Preexposure	0.05	0.075	0.05	0.06 \pm 0.01
1-Hour Exposure	3.8	3.8	3.8	3.8 \pm 0
15-Min. Post-exposure	2.6	2.6	2.4	2.53 \pm 0.12

Date of Collection of Samples: January 17, 1974

Preexposure	< 0.1	< 0.1	< 0.05	< 0.1
1-Hour Exposure	4.2	4.0	4.1	4.1 \pm 0.10
15-Min. Post-exposure	2.5	2.3	2.3	2.37 \pm 0.12
69 $\frac{1}{2}$ Hours Post-exposure	< 0.05	< 0.05	-	< 0.05

TABLE VIII

TRICHLOROETHANOL IN URINE IN MG/24 HOURS

AFTER SUBJECTS WERE EXPOSED TO 1,1,1-TRICHLOROETHANE

Group I: 4 Female Subjects

Exposure Time: 7½ Hours

Chamber Conc., ppm	Date Of Urine Collection	Subject Numbers				Mean + S. D.
		182	183	184	185	
350 ppm	1-14-74 to 1-15-74	21.00	14.00	(6.38)	15.49	16.83 [±] 3.69
350 ppm	1-15-74 to 1-16-74	23.45	12.15	15.30	22.75	18.41 [±] 5.57
350 ppm	1-16-74 to 1-17-74	11.20	18.20	15.60	27.63	18.16 [±] 6.94
350 ppm	1-17-74 to 1-18-74	15.95	22.00	14.63	29.90	20.62 [±] 6.97
350 ppm	1-18-74 to 1-19-74	14.00	14.38	(4.55)	25.20	17.86 [±] 3.67
0 ppm	1-21-74 to 1-22-74	2.75	3.50	2.50	5.30	3.51 [±] 1.27

TABLE VIII (Continued)

TRICHLOROETHANOL IN URINE IN MG/24 HOURS
AFTER SUBJECTS WERE EXPOSED TO 1,1,1-TRICHLOROETHANE

Group II: 3 Female Subjects

Exposure Time: 3 Hours

Chamber Conc., ppm	Date Of Urine Collection	Subject Numbers			
		186	187	188	Mean + S. D.
350 ppm	1-14-74 to 1-15-74	10.80	7.00	7.8	8.53 \pm 2.00
350 ppm	1-15-74 to 1-16-74	15.40	6.63	10.80	10.94 \pm 2.53
350 ppm	1-16-74 to 1-17-74	(6.30)	12.50	12.15	12.33 \pm 0.25
350 ppm	1-17-74 to 1-18-74	12.00	10.50	11.25	11.25 \pm 0.75
350 ppm	1-18-74 to 1-19-74	8.85	(0.180)	8.55	8.70 \pm 0.21
0 ppm	1-21-74 to 1-22-74	2.35	(1.05)	3.20	2.78 \pm 0.60

TABLE VIII (Continued)

TRICHLOROETHANOL IN URINE IN MG/24 HOURS

AFTER SUBJECTS WERE EXPOSED TO 1,1,1-TRICHLOROETHANE

Group III: 3 Female Subjects

Exposure Time: 1 Hour

Chamber Conc., ppm	Date Of Urine Collection	Subject Numbers			
		189	190	191	Mean \pm S. D.
350 ppm	1-14-74 to 1-15-74	0.9	0.9	1.8	1.20 \pm 0.52
350 ppm	1-15-74 to 1-16-74	0.95	(5.63)	No Sample	0.95
350 ppm	1-16-74 to 1-17-74	1.10	1.95	0.70	1.25 \pm 0.64
350 ppm	1-17-74 to 1-18-74	0.70	1.10	1.25	1.02 \pm 0.28
350 ppm	1-18-74 to 1-19-74	1.73	2.20	0.85	1.59 \pm 0.69
0 ppm	1-21-74 to 1-22-74	0.40	0.33	No Sample	0.37 \pm 0.05

TABLE XI
 PAIRED t VALUES FOR COMPARISON OF CONTROL VERSUS
 EXPOSURE TEST SCORES

(7-1/2 Hour Subjects)

Test	1,1,1 - Trichloroethane Concentration					
	100 PPM	350 PPM	350 PPM fluctuating	500 PPM	t	df
Marquette: E/S	-1.01	-1.68	1.11	0.77		3
Sound Stimulus 1E-S1	-0.78	-1.09	1.17	0.79		3
RXT	-5.09*	-0.94	-0.84	-2.45		3
M/S	-1.08	-0.50	-1.71	0.06		3
Light Stimulus 1E-S1	-0.74	1.06	0.47	-0.42		3
RXT	-1.18	-2.16	-1.22	-1.97		3
10 Second Estimation	-1.25	0.39	0.35	-0.92		3
30 Second Estimation	1.49	0.54	-0.17	-1.01		3
Arithmetic Test	-0.70	-1.57	-0.42	0.60		3
Coordination Test	-1.28	-1.04	-0.71	0.82		3
Inspection Test	-1.73	-13.89**	-3.02	-1.57		3

* Significant P < .05

** Significant P < .01

TABLE XII
 PAIRED t VALUES FOR COMPARISON OF CONTROL VERSUS
 EXPOSURE TEST SCORES

(3 Hour Subjects)

Test	1, 1, 1 - Trichloroethane Concentration					
	100 PPM	350 PPM	350 PPM fluctuating	350 PPM	500 PPM	500 PPM
	t	df	t	df	t	df
Marquette Test: E/S	0.32	2	0.16	2	-1.55	2
Sound Stimulus 1E-S1	-3.31	2	-0.40	2	-2.21	2
RxT	-3.99	2	-22.85**	2	-10.99**	2
E/S	-0.91	2	-0.94	2	-1.28	2
Light Stimulus 1E-S1	-0.02	2	-0.21	2	-0.58	2
RxT	-3.66	2	-1.91	2	-1.77	2
15 Second Estimation	-2.41	2	-0.79	2	-1.12	2
30 Second Estimation	-0.21	2	-1.01	2	-1.06	2
Arithmetic Test	-2.12	2	0.64	2	-3.61	2
Coordination Test	-0.58	2	-0.74	2	-7.94*	2
Inspection Test	1.37	2	0.165	2	0.21	2
					-6.79*	2
					-1.30	2
					0.05	2
					0.86	2
					-1.69	2
					-0.44	2

TABLE XIII

Alertness Test Results For 1, 1, 1-T Females

Paired-t Test
Group I (7½ Hour Subjects)

	Monday (1/14/74)		Wednesday (1/16/74)		Friday (1/18/74)	
	t	df	t	df	t	df
Percent Correct	-.727	2	-.555	2	-.115	2
Reaction Time	-.589	2	-1.491	2	-.531	2

Group II (3 Hour Subjects)

	Monday (1/14/74)		Wednesday (1/16/74)		Friday (1/18/74)	
	t	df	t	df	t	df
Percent Correct	-1.801	2	.701	2	.335	1
Reaction Time	-1.5	2	-.64	2	-5.00	1

Level of Significance

.05*

.025**

FIGURE 4

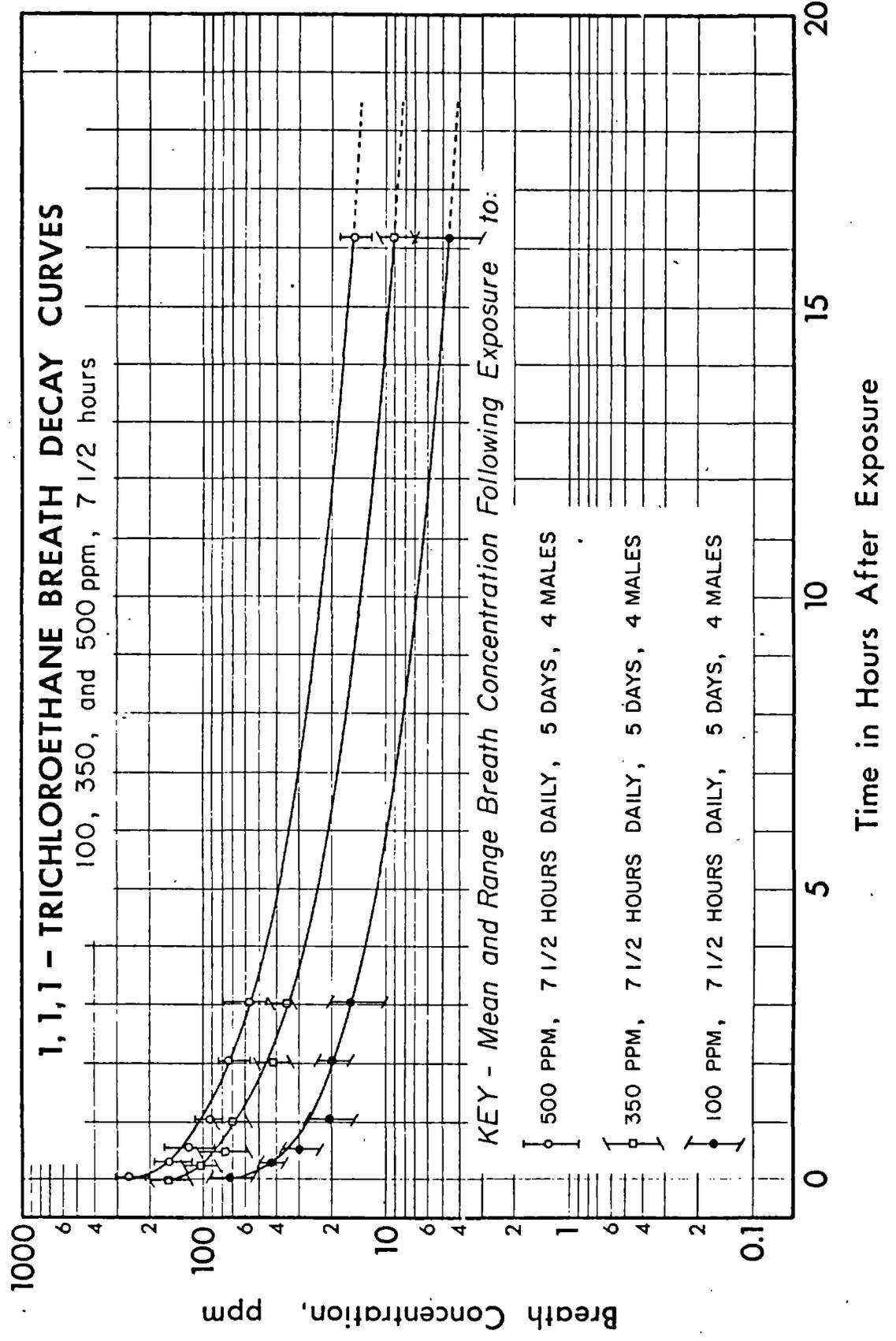


FIGURE 5

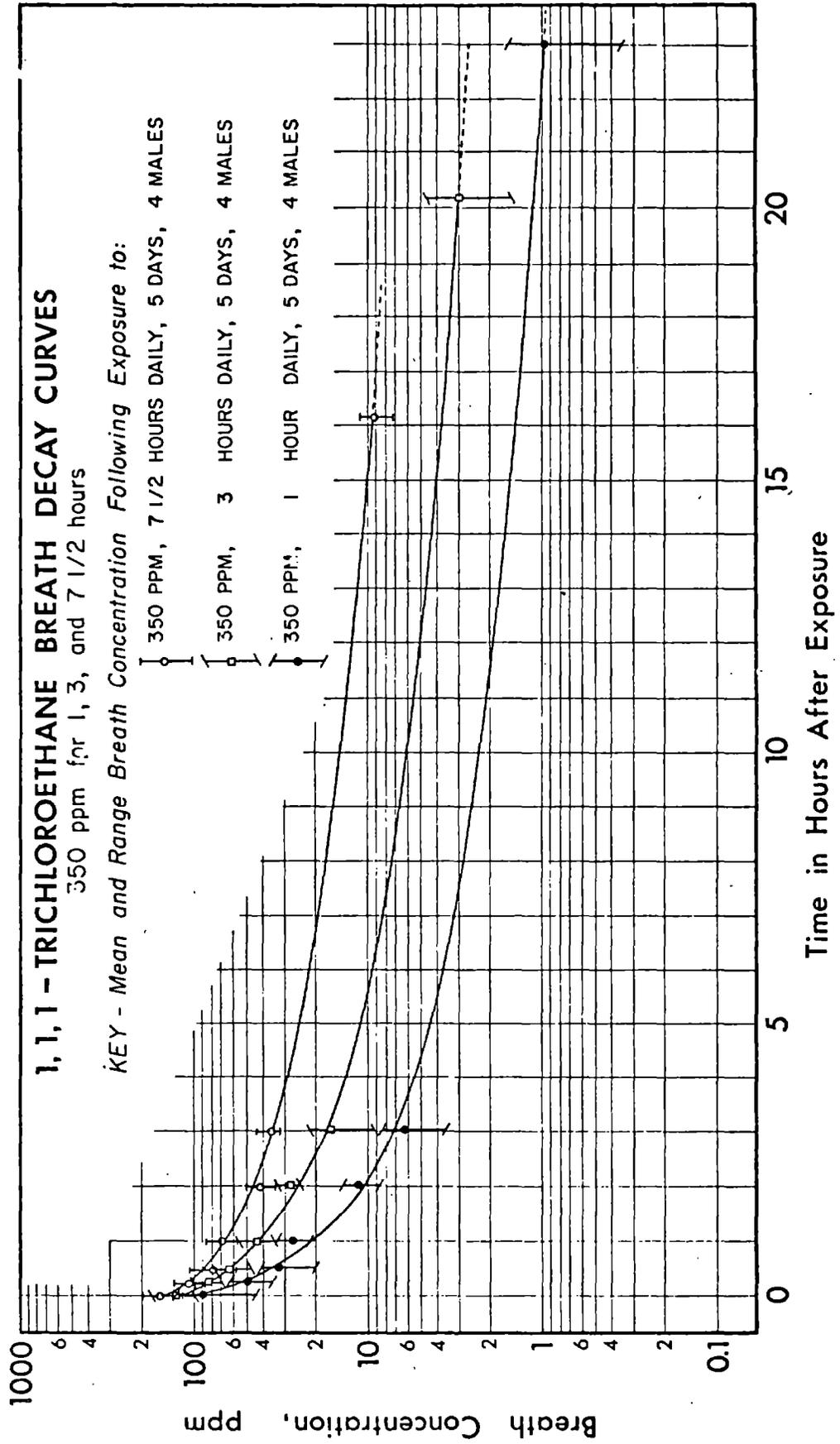


FIGURE 6

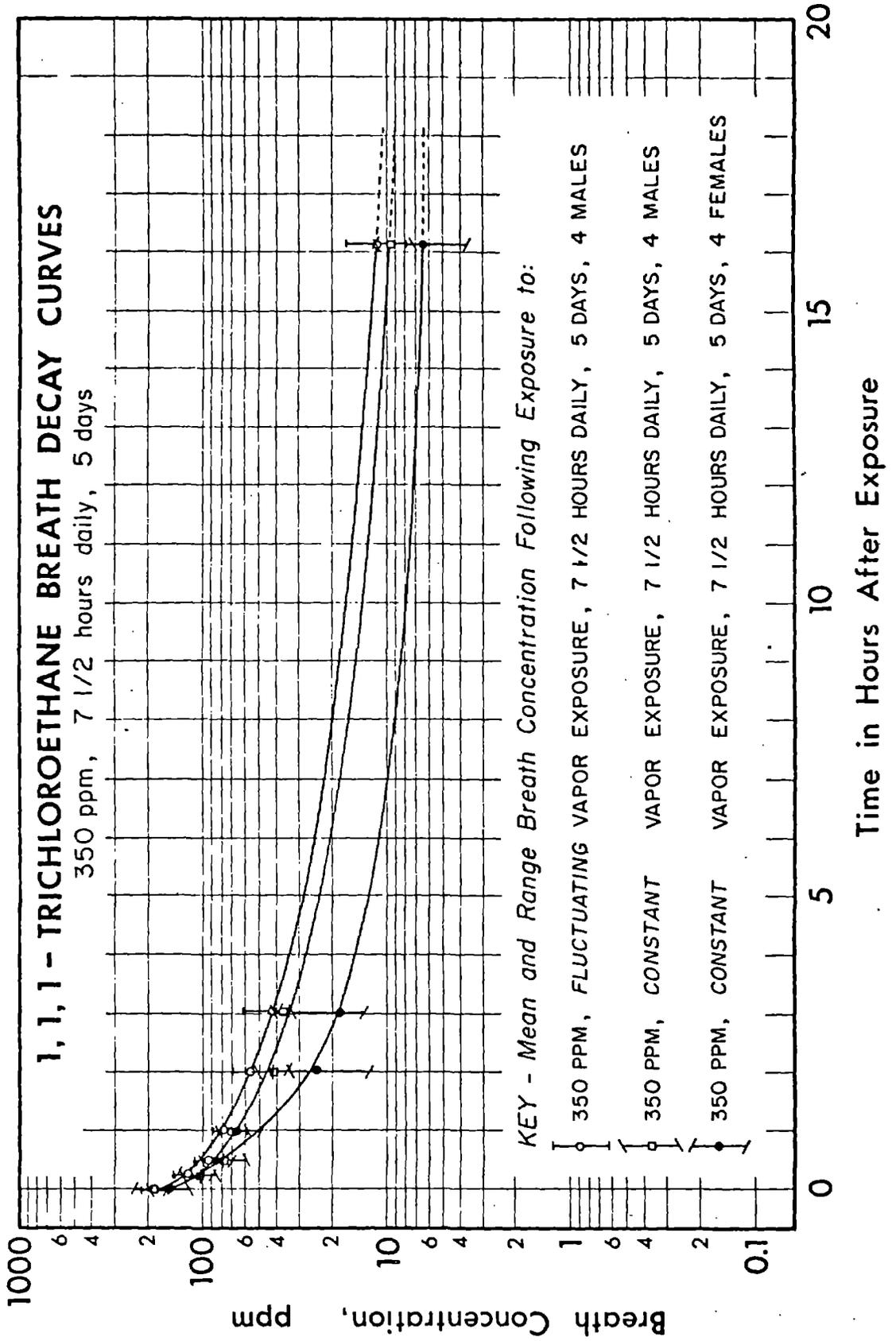


FIGURE 7

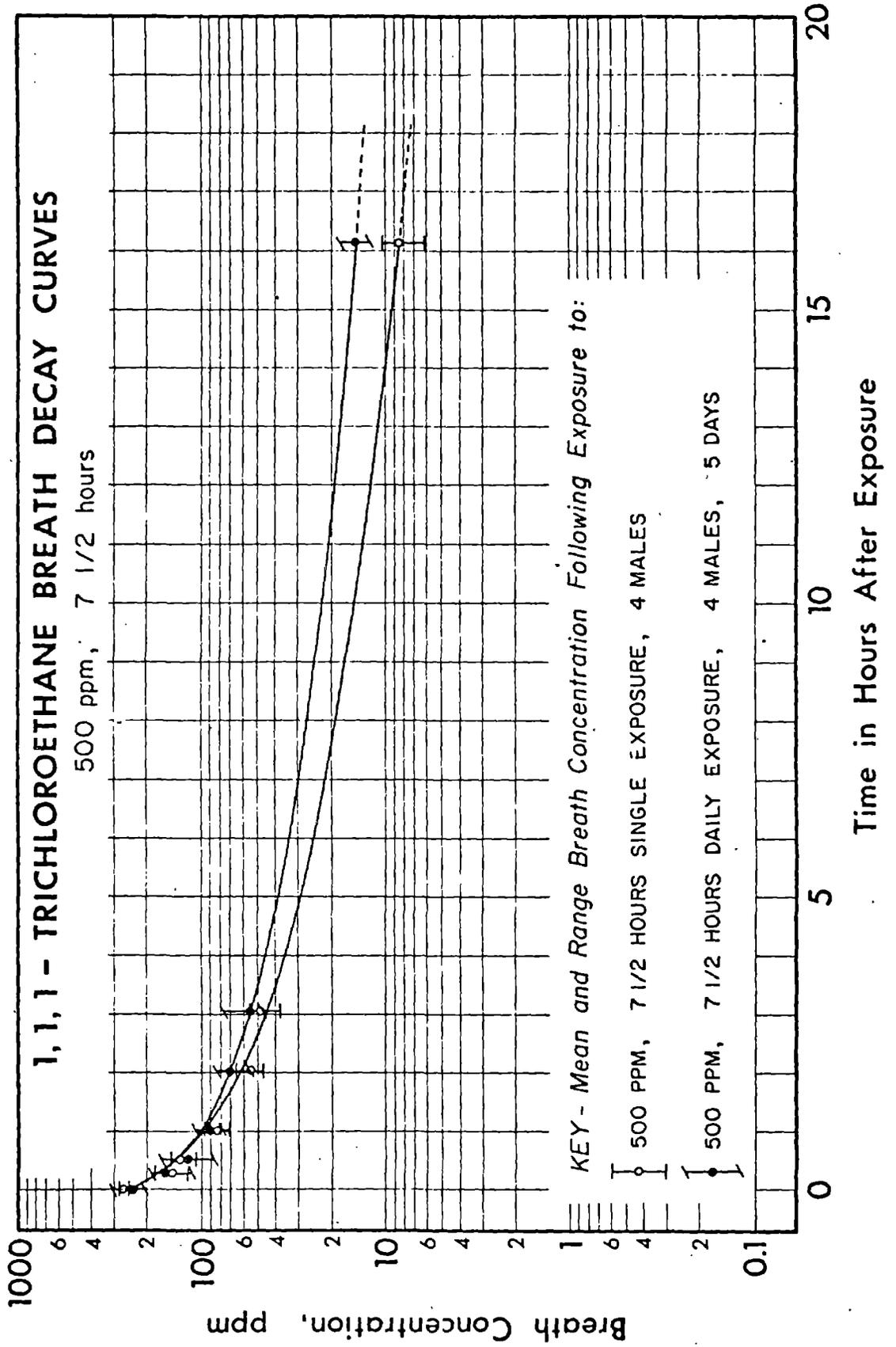


FIGURE 8

SUMMARY VER'S OF EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #150

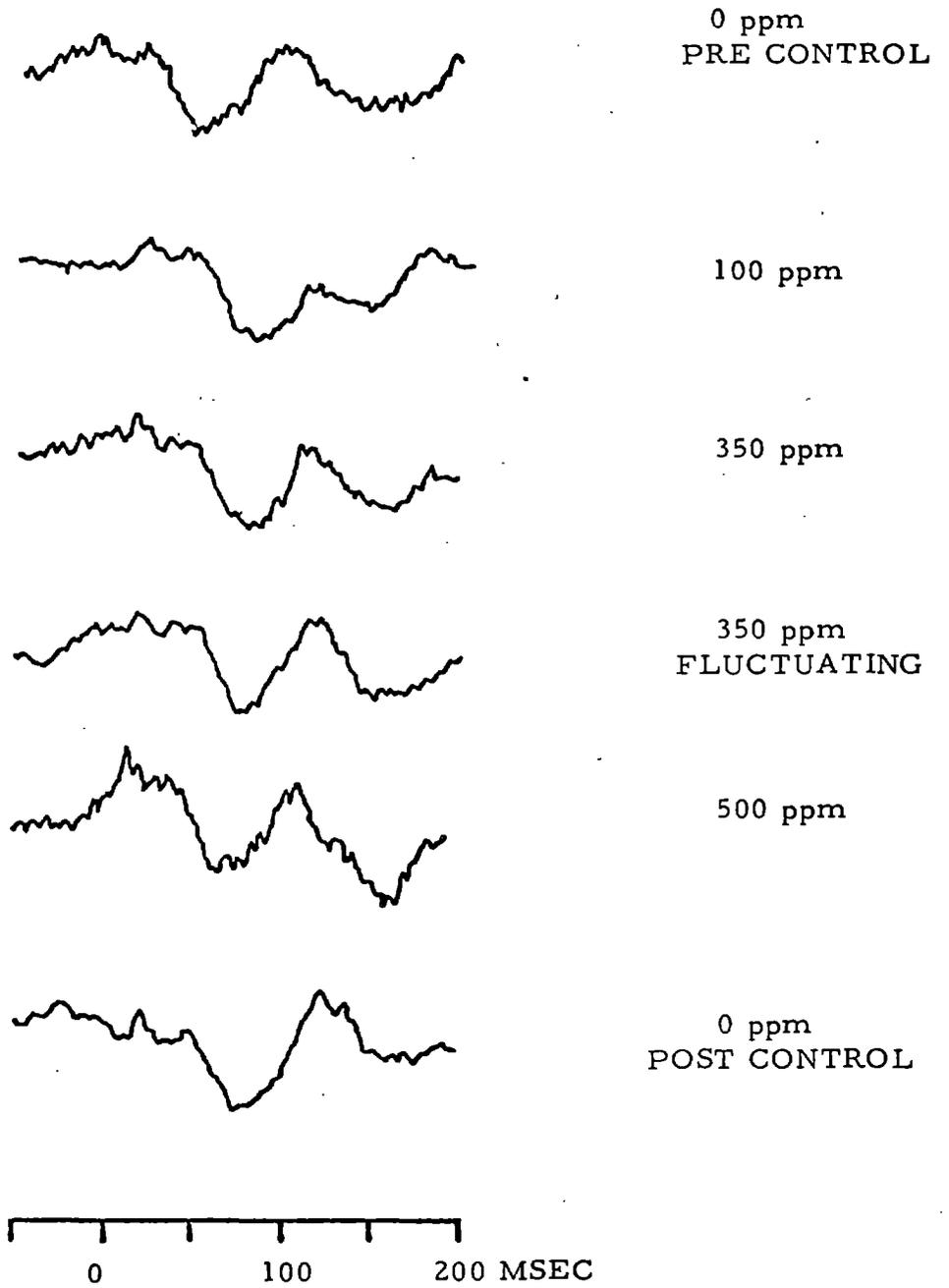


FIGURE 9

SUMMARY VER'S OF EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #151

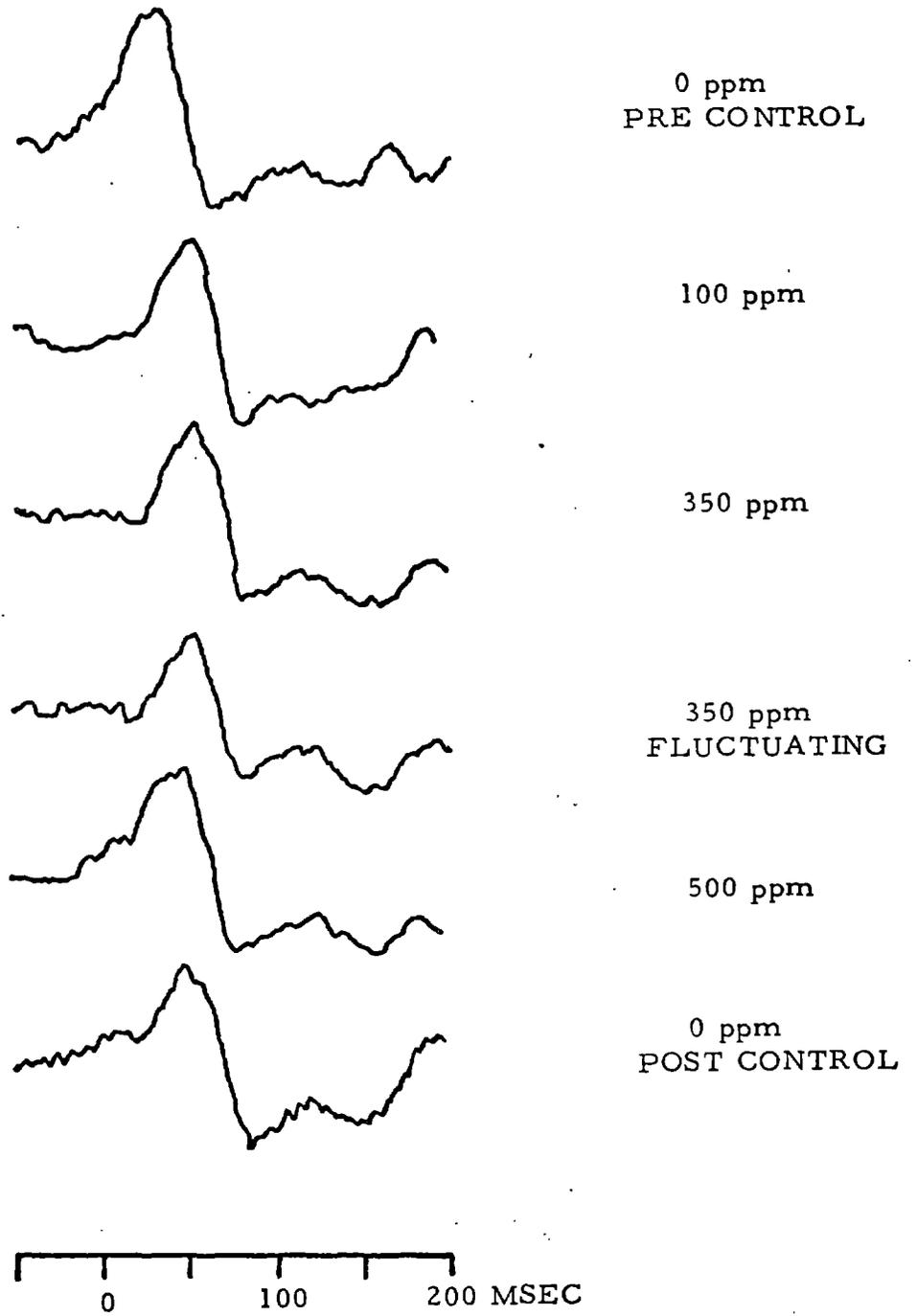


FIGURE 10

SUMMARY VER'S OF EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #153

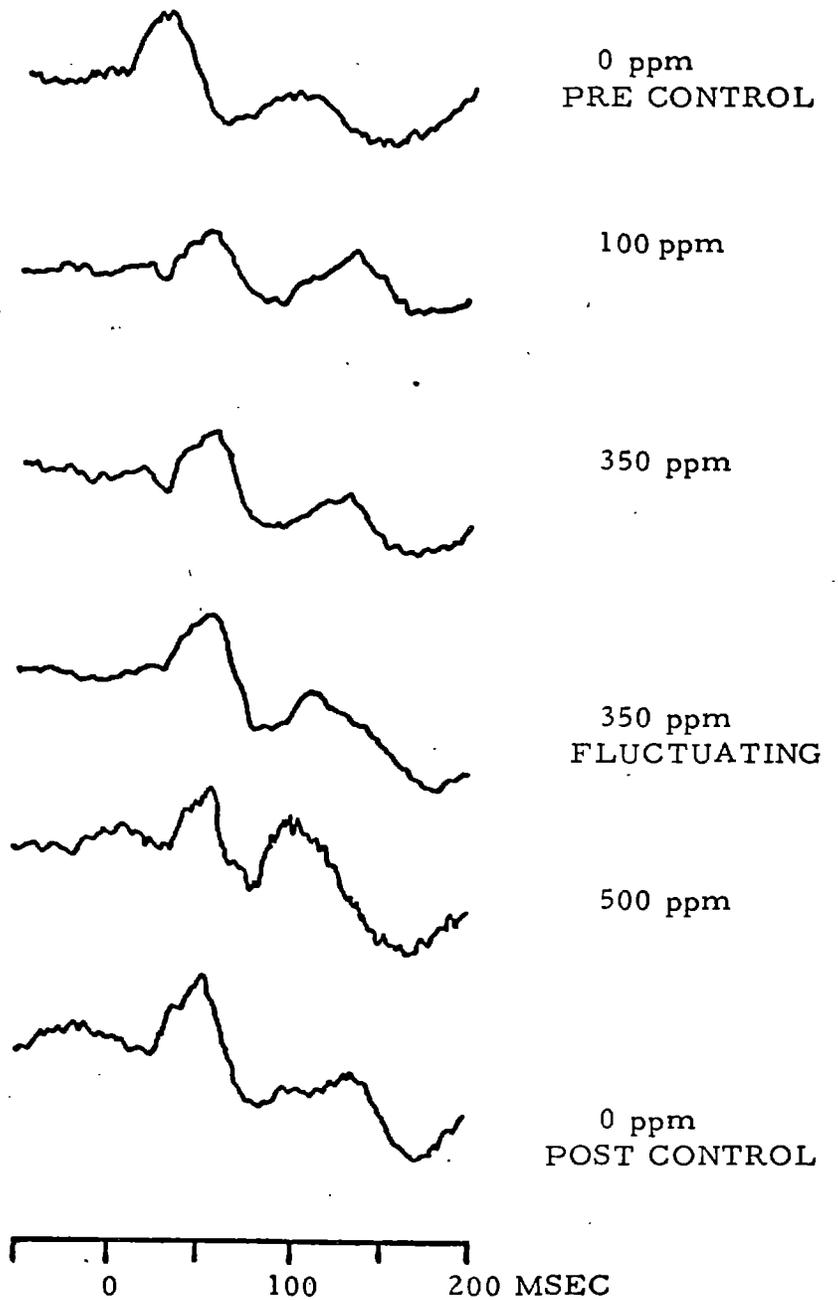


FIGURE 11

SUMMARY VER'S OF EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #155

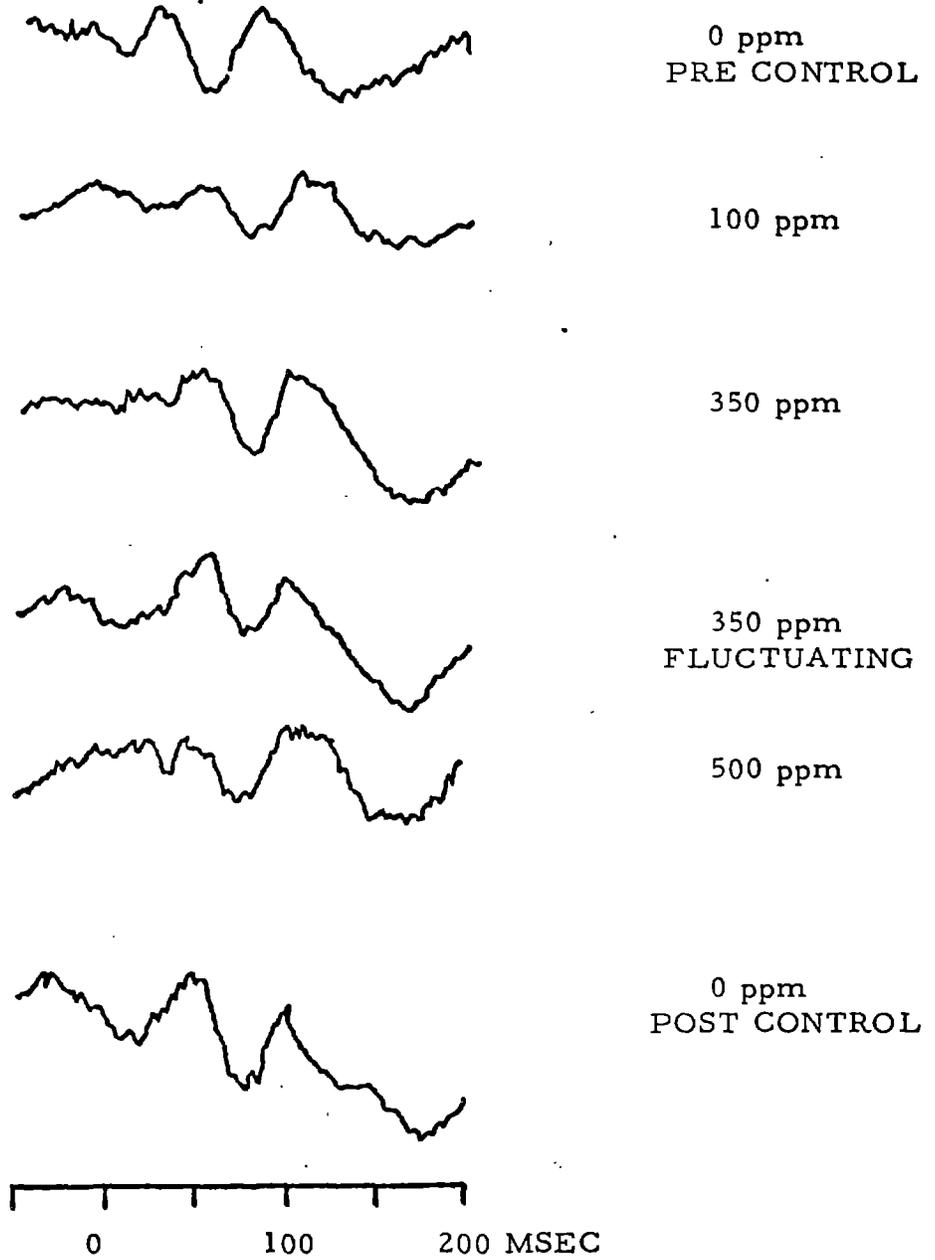


FIGURE 12

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #150

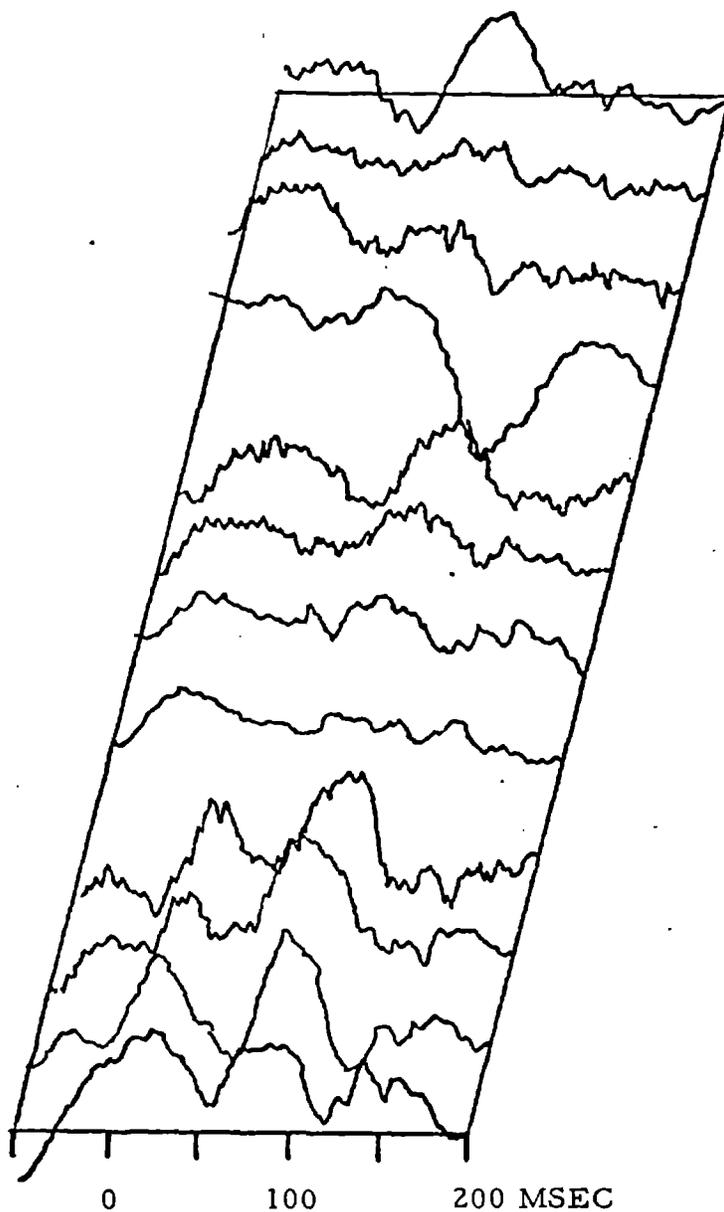


FIGURE 13

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #151

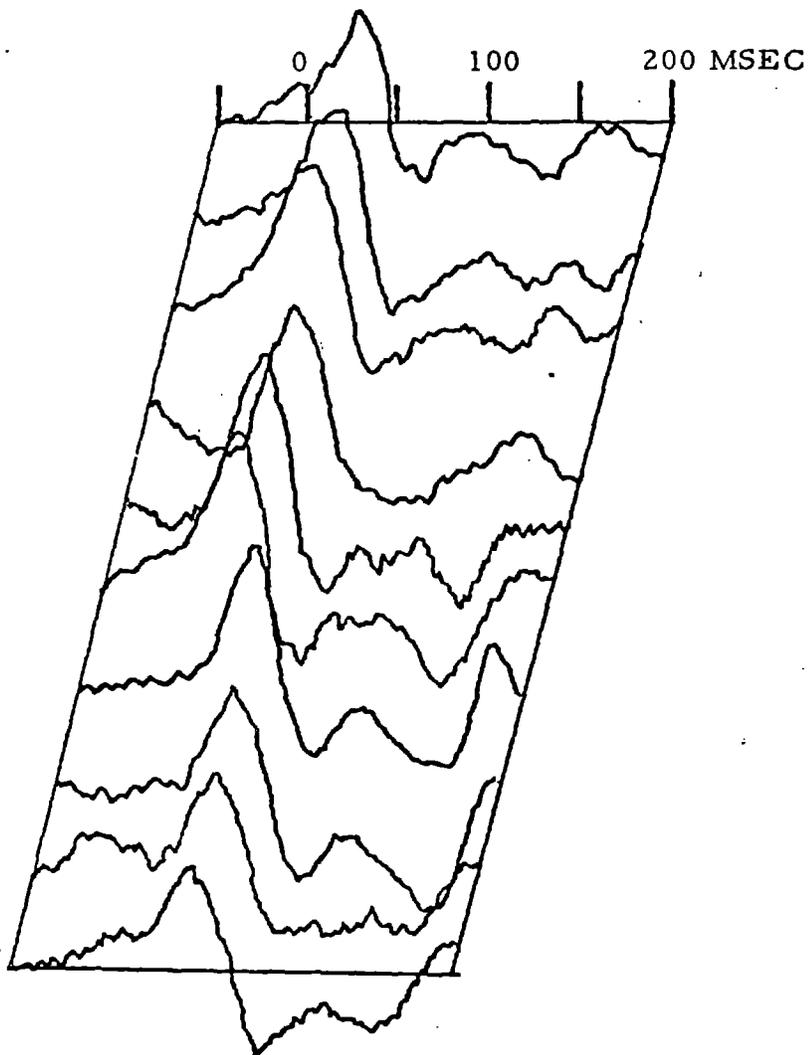


FIGURE 14

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #153

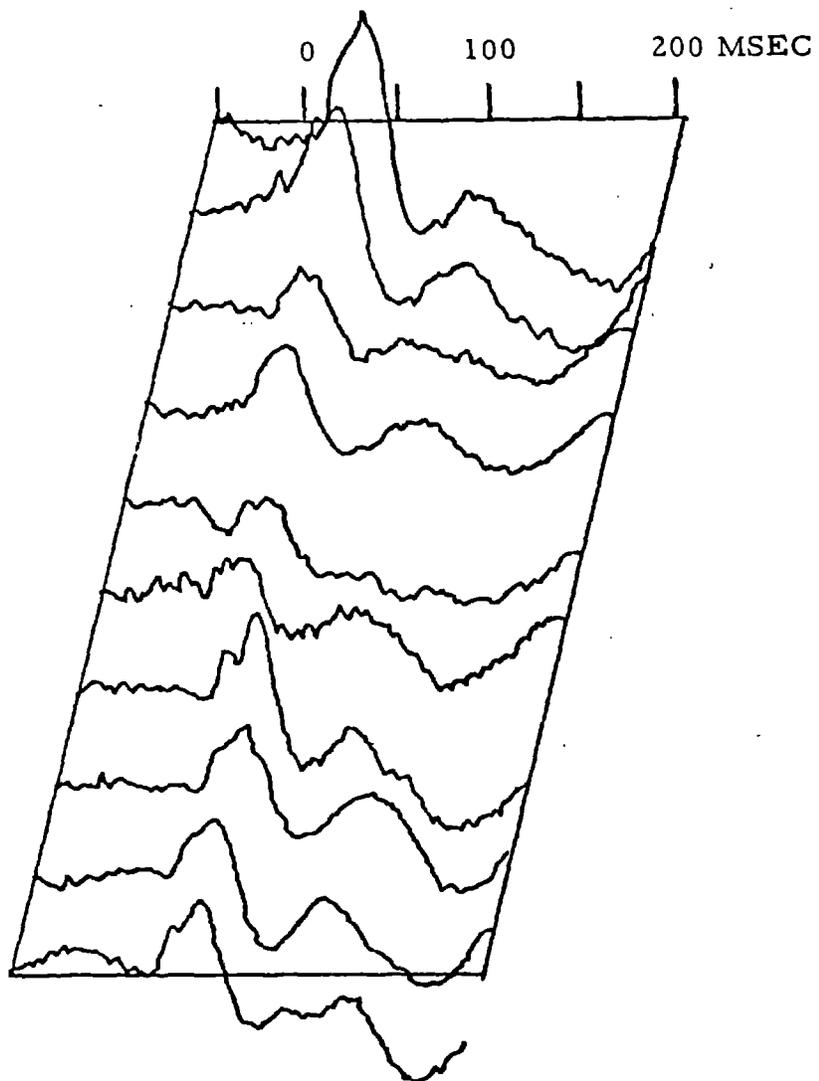


FIGURE 15

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #155

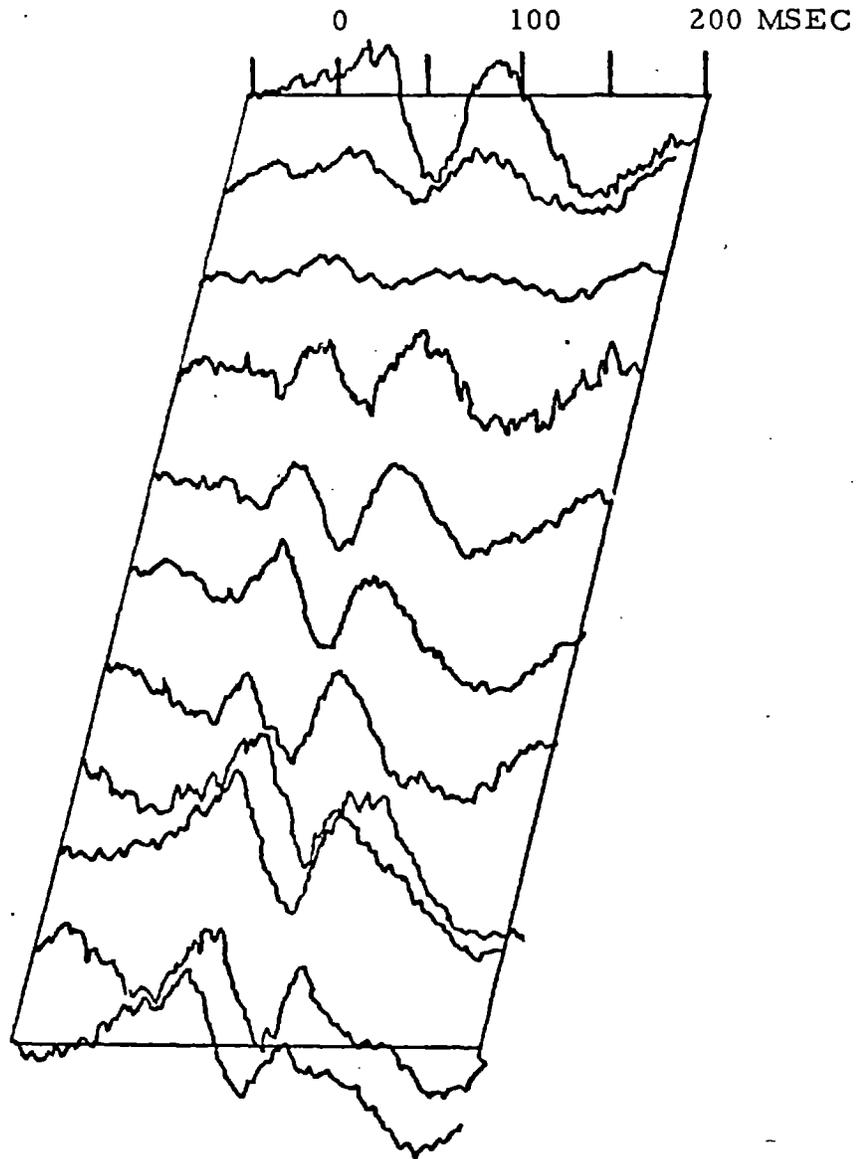


FIGURE 16
SUMMARY VER'S OF EXPOSURE TO 1, 1, 1 - TRICHLOROETHANE
SUBJECT # 182

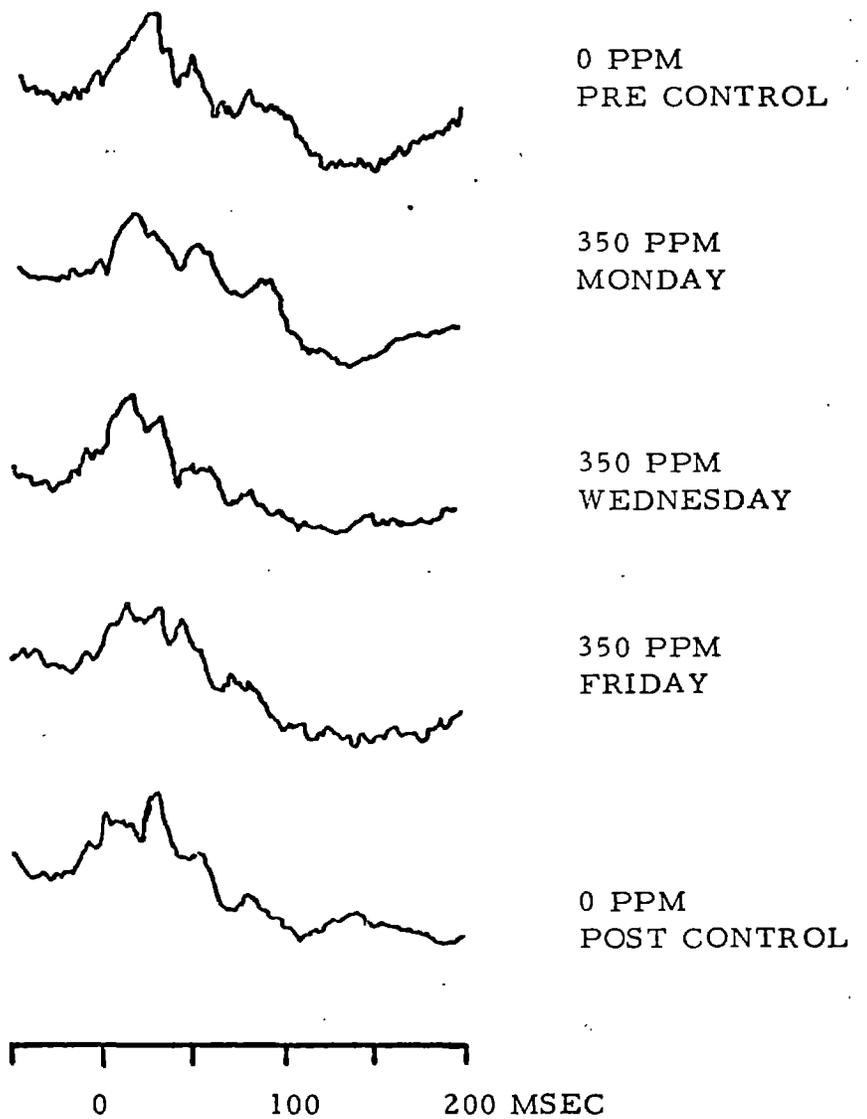


FIGURE 17

SUMMARY VER'S OF EXPOSURE TO 1, 1, 1 - TRICHLOROETHANE
SUBJECT # 184

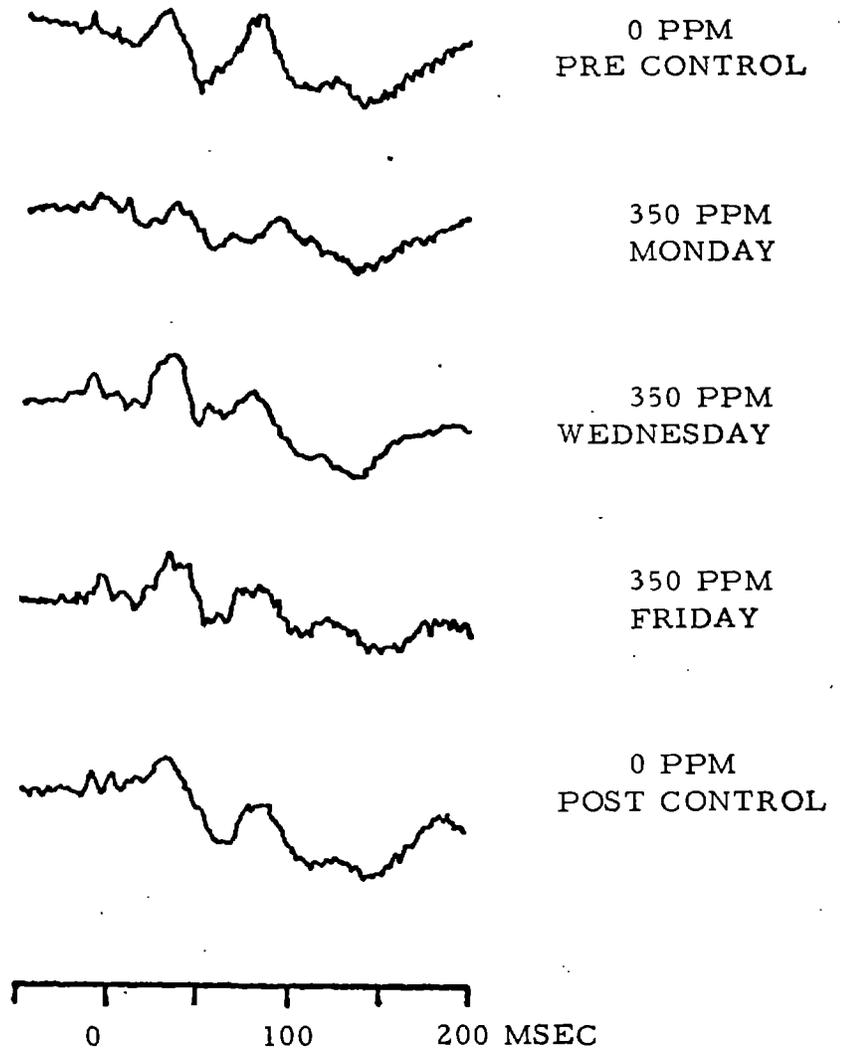


FIGURE 18

SUMMARY VER'S OF EXPOSURE TO 1, 1, 1 - TRICHLOROETHANE

SUBJECT # 185

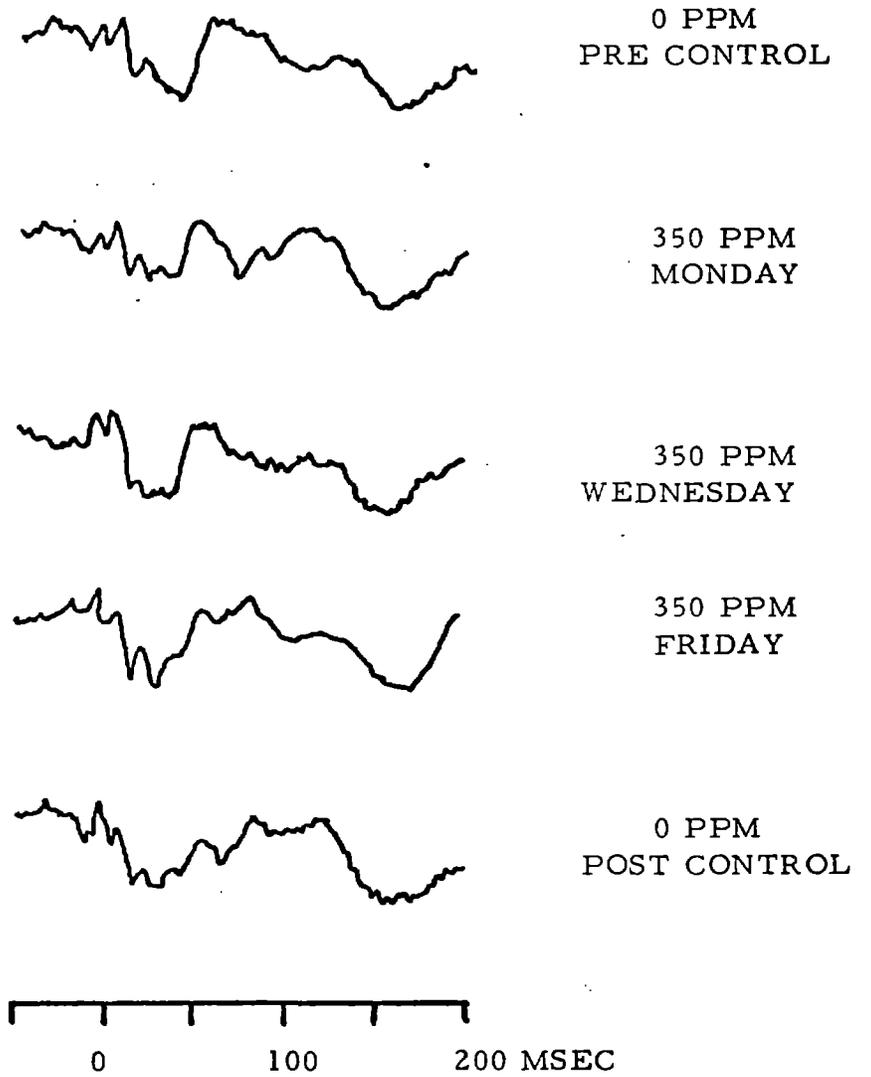


FIGURE 19

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #182

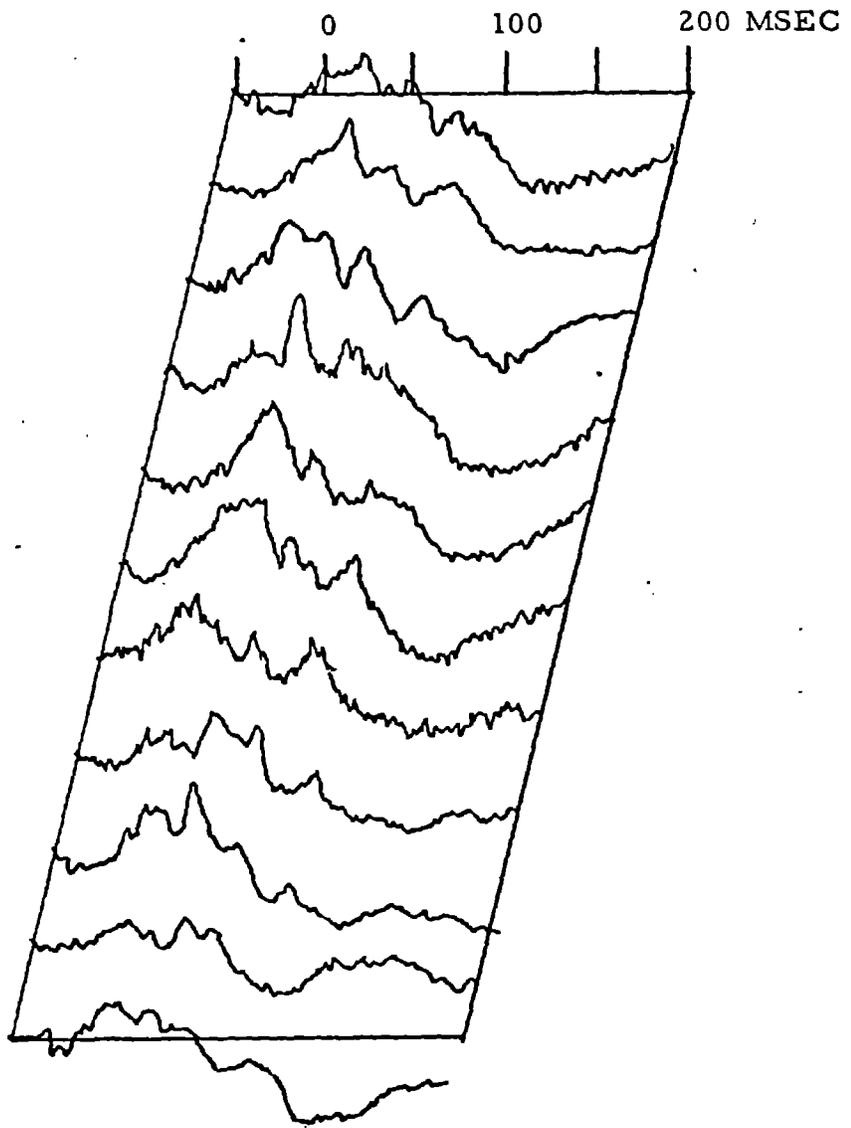


FIGURE 20

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #184

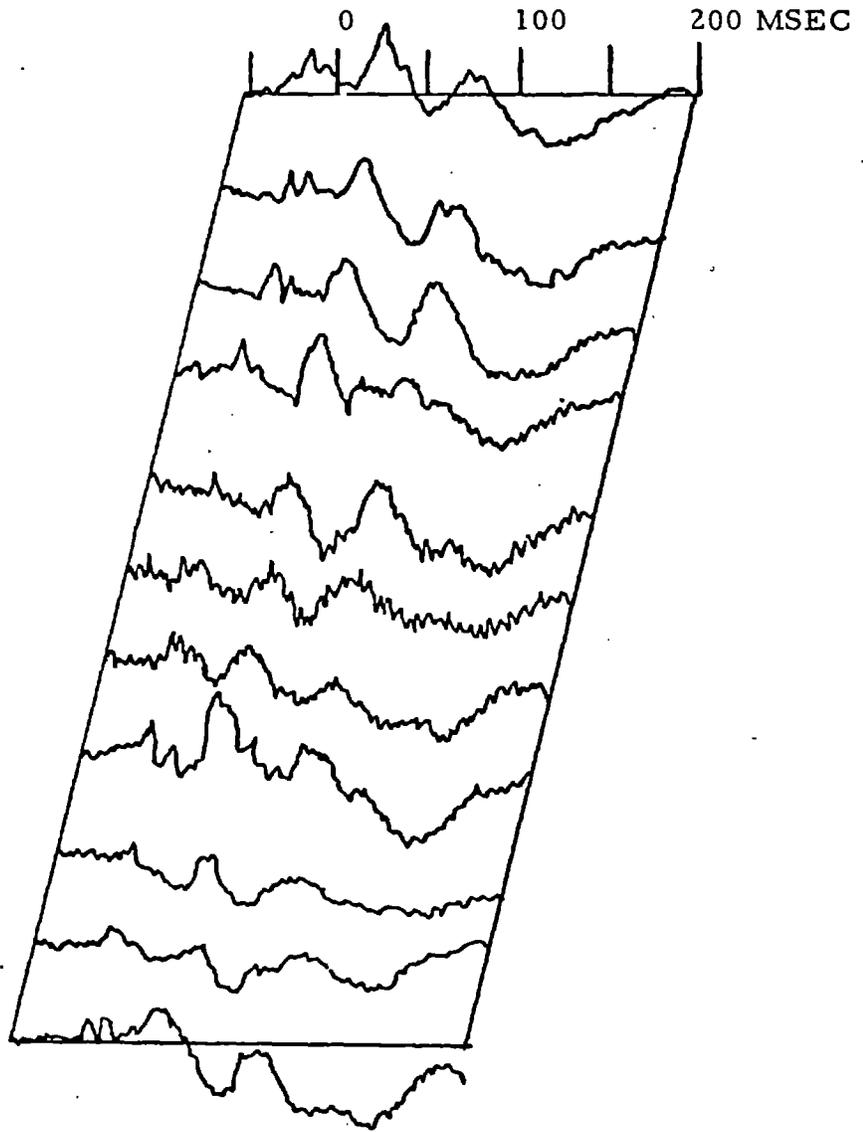
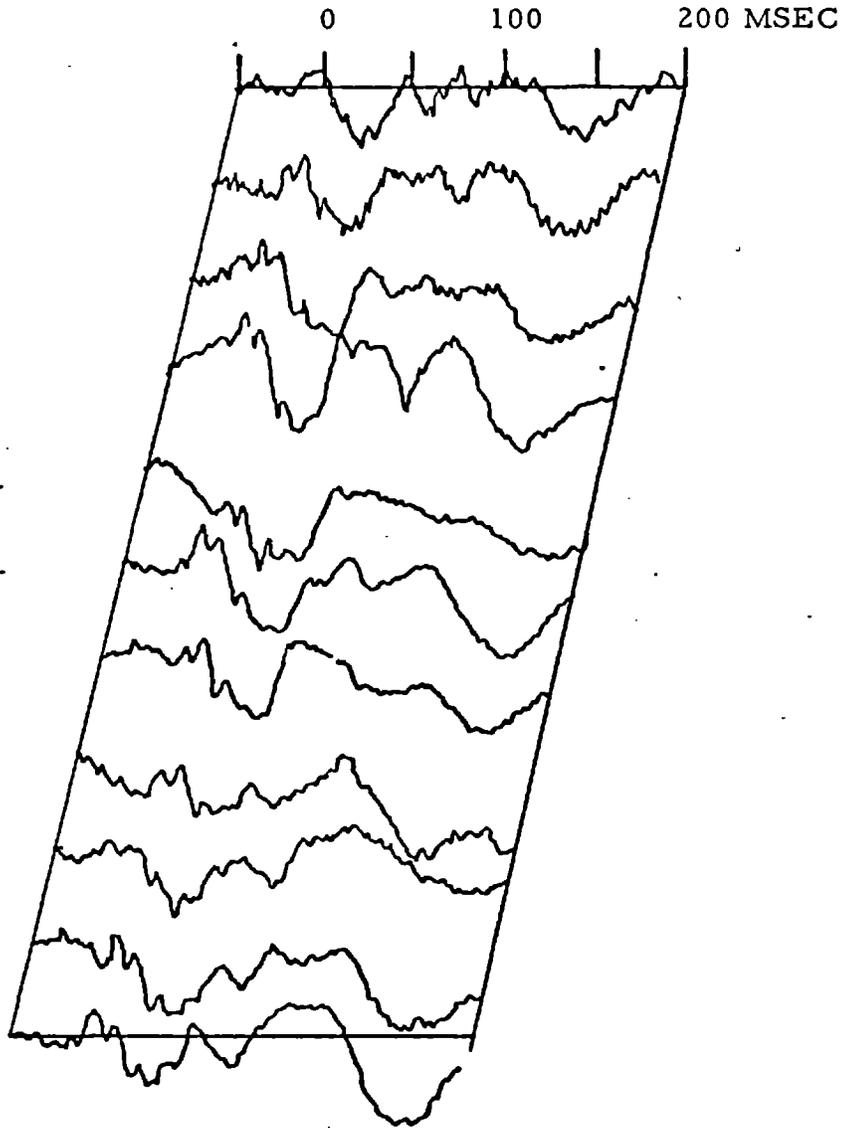


FIGURE 21

CONTROL VER'S FOR EXPOSURE TO 1,1,1-TRICHLOROETHANE
SUBJECT #185

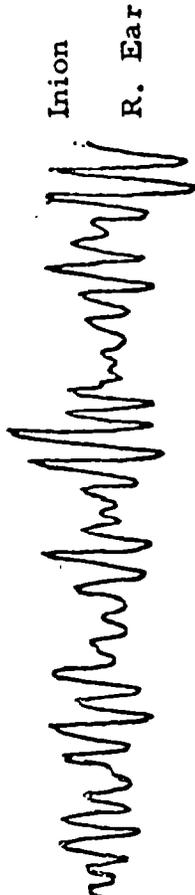
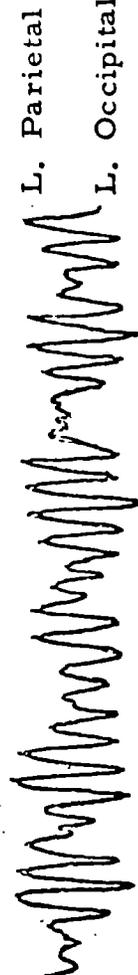


Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 150

0 PPM



500 PPM



R. Ear

50
50

FIGURE 23

Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 151

0 PPM



500 PPM



R. Frontal

R. Parietal



L. Frontal

L. Parietal



R. Parietal

R. Occipital

100 μV



L. Parietal

L. Occipital



R. Parietal

R. Temporal



L. Parietal

L. Temporal

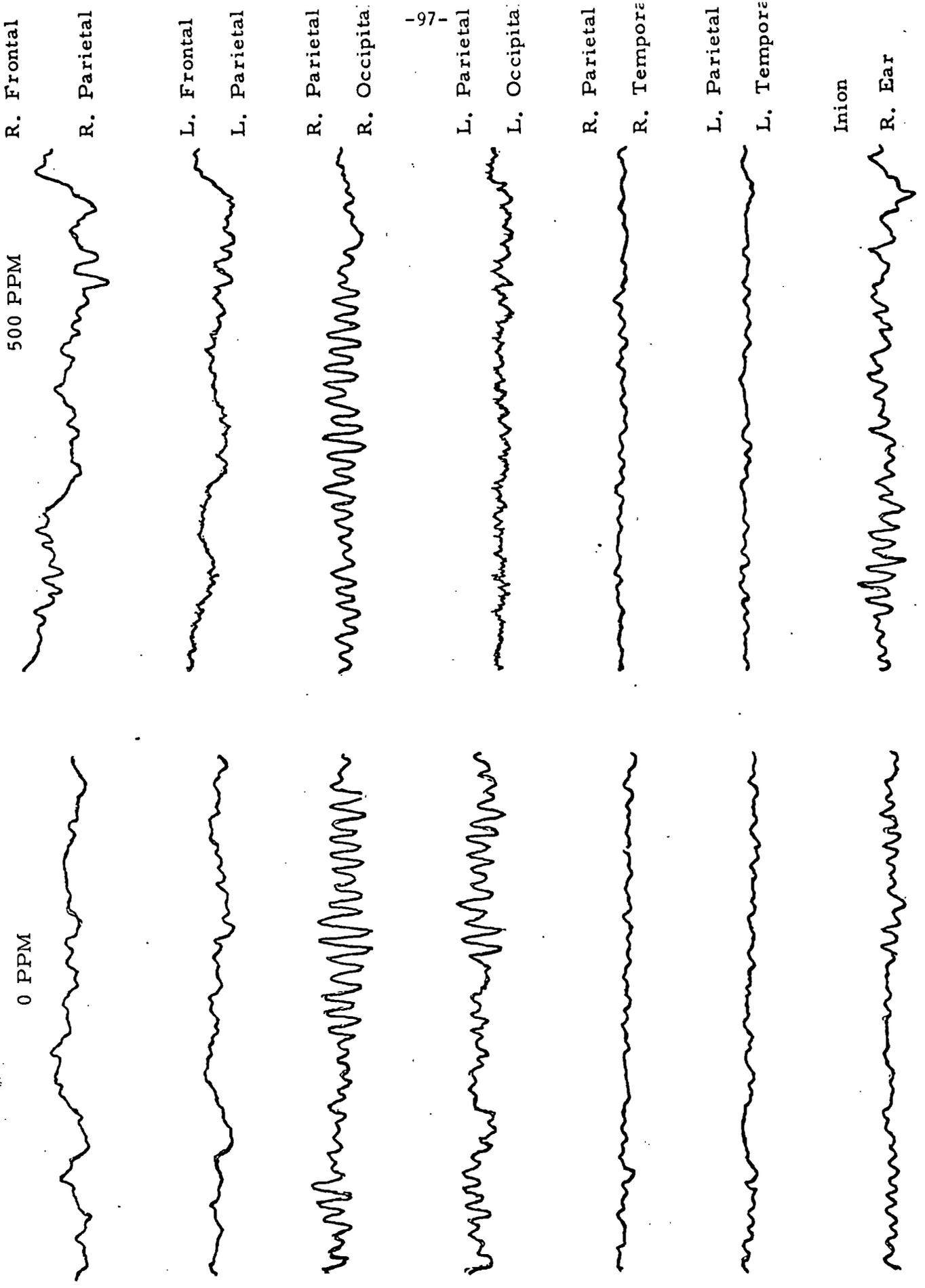


Inion

R. Ear

FIGURE 24

Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 153



Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 155

FIGURE 25

0 PPM



500 PPM



$\frac{1}{8}$
PPM



Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 183

350 PPM

R. Frontal
R. Parietal

0 PPM

L. Frontal
L. Parietal

R. Parietal
R. Occipital

100

L. Parietal
L. Occipital

R. Parietal
R. Temporal

L. Parietal
L. Temporal

Inion
R. Ear



Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 184

0 PPM

350 PPM

R. Frontal
R. Parietal

L. Frontal
L. Parietal

R. Parietal
R. Occipital

101
L. Parietal

L. Occipital

R. Parietal
R. Temporal

L. Parietal
L. Temporal

Inion

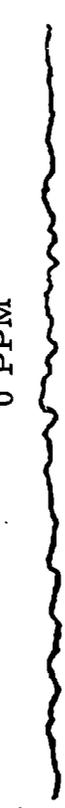


FIGURE 29

Spontaneous EEG Activity During Exposure to 1, 1, 1 - Trichloroethane
Subject # 185

350 PPM

R. Frontal



R. Parietal

L. Front



L. Parietal

R. Parietal



R. Occip

L. Parietal



L. Occip

R. Parietal



R. Temp

L. Parietal



L. Temp

0 PPM

Inio

