

PB82-172917



ACETONE:  
DEVELOPMENT OF A BIOLOGIC STANDARD  
FOR THE INDUSTRIAL WORKER  
BY BREATH ANALYSIS



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BIBLIOGRAPHIC DATA SHEET		1. Report No.	2. NA	3. Recipient's Accession No. PB02 072917	
4. Title and Subtitle Acetone: Development of a Biologic Standard for the Industrial Worker by Breath Analysis				5. Report Date June 1975	
7. Author(s) Anonymous				6. NA 067046	
9. Performing Organization Name and Address The Medical College of Wisconsin Department of Environmental Medicine Milwaukee, Wisconsin				8. Performing Organization Rept. No. NA	
12. Sponsoring Organization Name and Address NIOSH 4676 Columbia Parkway Cincinnati, Ohio 45226				10. Project/Task/Work Unit No. NA	
				11. Contract/Grant No. 099-72-0084	
15. Supplementary Notes				13. Type of Report & Period Covered contract	
				14. NA	
16. Abstracts In order to determine physiological responses and develop a practical biological test to indicate the magnitude of industrial exposure to acetone (67641), 20 healthy adults of both sexes were exposed to known concentrations of acetone vapor in a controlled environment chamber. Exposures consisted of both steady, nonfluctuating vapor concentrations and widely fluctuating vapor concentrations. Male subjects were exposed to acetone vapor concentrations of 0, 200, 1000, and 1250ppm for periods of 3 or 7.5 hr. Blood samples were taken. Various neurological and physiological tests were performed. Highly reproducible breath decay curves were obtained. Minimal variations in range of acetone in breath in identically exposed groups indicated breath analysis to be a rapid method for detection of the magnitude of recent acetone exposure and provides a biologic threshold-limit. Repetitive exposure to the current threshold-limit-value (TLV) of 1000ppm produced no serious health responses in healthy subjects. Changes observed in the visual evoked response of males given 1250ppm and the possible effect of 1000ppm on the menstrual cycle indicate that the current TLV may not afford a					
17. Key Words and Document Analysis - 17a. Descriptive substantial safety margin.					
17. Key Words NIOSH-Publication, NIOSH-Contract, Contract No. HSM 99-72-84, Organic-solvents, Testing Breathing, Organic-vapors, Vision-tests, Visual-performance, Reproduction-system-disorder, Biological-sampling, Urinalysis, Blood-sampling, Blood-tests, Sensory-processes					
17b. Identifiers/Open-Ended Terms					
17c. COSATI Field/Group					
18. Availability Statement Available to the public				19. Security Class (This Report) UNCLASSIFIED	
				20. Security Class (This Page) UNCLASSIFIED	
				21. No. of Pages 73	
				22. Price	

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INDUSTRIAL WORKER BY BREATH ANALYSIS

By

R. D. 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.

W. H. Keeler, M.D.

A. J. Lebrun, M.D.

P. E. Newton, M.S.

R. J. Soto, M.S.

Report No.: NIOSH-MCOW-ENVM-A-75-5

June, 1975

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.

This investigation was supported by Contract No. HSM 99-72-84 from The National Institute of Occupational Safety and Health.

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## ACETONE

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## SYNOPSIS - ABSTRACT

Twenty adults of both sexes were exposed repetitively to acetone vapor concentrations of 0, 200, 1000, and 1250 ppm for periods of 1, 3, and 7-1/2 hr 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, including the Threshold Limit Value of 1000 ppm for four consecutive days.

A series of acetone post-exposure breath decay curves was obtained. These curves were highly reproducible and the narrow range of acetone in the breath at a specific time in the early post-exposure period of persons identically exposed indicated that breath analysis could be used as a rapid method with which to estimate the magnitude of recent acetone exposure. Post-exposure breath analysis proved to be a practical screening method with which to determine the body burden of acetone and so provides a Biologic Threshold Limit measurement for workmen.

Repetitive vapor exposure to the current TLV of 1000 ppm produced no serious subjective or objective health responses in the healthy subjects. The changes observed in the VER's of the male subjects exposed to 1250 ppm and the possible effect of 1000 ppm exposure on the menstrual cycle indicate that the current TLV may not afford a substantial safety margin.



## INTRODUCTION

Acetone is used extensively in American industry and in the chemical laboratory. In 1974, 2.06 billion pounds of this solvent were produced in the United States<sup>(1)</sup>. To protect the American worker from harmful exposures, a Threshold Limit Value of 1000 ppm for an 8-hr work day has been established<sup>(2)</sup>. This TLV has been responsible in part for the excellent industrial health record this solvent has enjoyed.

Studies investigating the absorption, tissue distribution, and elimination of acetone following vapor exposures at or above the Threshold Limit Value have been reported<sup>(3-5)</sup>. The first investigation to explore the possibility of using the elimination and distribution data as a biologic monitoring method was performed by DiVincenzo, Yanno, and Astill<sup>(6)</sup>. However, their study was extremely limited. They used only four subjects who were exposed for 2 or 4 hr to concentrations of 100 or 500 ppm.

In the series of experiments to be reported, 20 adults of both sexes were exposed repetitively to acetone vapor concentrations of 0, 200, 1000, and 1250 ppm for varying periods for the purpose of expanding our existing human data base. The goals were to: 1) observe the physiologic response of man to exposure to acetone vapor and 2) develop a practical biologic test useful for estimating the magnitude of exposure to acetone.

## EXPERIMENTAL

Healthy adults of both sexes were exposed to known concentrations of acetone 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 acetone.

### Exposure Schedule:

The vapor exposure sequence is presented in Table I. The sequence was initiated with male subjects who were exposed to acetone vapor concentrations of 0, 200, 1000, and 1250 ppm for periods of 3 or 7-1/2 hr. The female subjects were exposed to 0 and 1000 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 exposure during Week 6 when the wide fluctuation experiment was performed. Figure 2 illustrates the male subject exposure sequence for the 6-week period. The female subject exposure sequence occurred subsequent to the exposure of male subjects and duplicated Week 3 for males.

The widely fluctuating concentrations of acetone vapor during Week 6 of exposure of male subjects was attained by varying the concentration of acetone in the chamber from 750 to 1000 to 1250 ppm during equal periods of time. The sequence of the up and down concentrations was designed so that the last hour of exposure for all subjects was to a vapor concentration of 1000 ppm acetone.

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 hr spent at the laboratory, plus overtime, with a 3-hr 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 ages ranged from 22 to 27 years, height from 168 to 180 cm, and their weight from 50.5 to 74.0 kg. None was obese. Four of these subjects were assigned to Group I (7-1/2 hr exposure), 4 to Group II (3 hr exposure), and 2 to Group III (1 hr exposure). Unfortunately, both Group III subjects dropped out of the study during the 0-ppm exposures, and one Group II subject dropped out on Day 1 of Week 3. His exposures to acetone were limited to 3 days at 200 ppm. One Group I subject transferred to Group II for the last week of exposure to 100 ppm, fluctuating.

The ages of the 10 participating females ranged from 18 to 25 years, their height from 152 to 172 cm, and their weight from 43.3 to 82.3 kg. One Group III subject was obese. The division of subjects into groups was identical to that for the study with male subjects.

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 acetone 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 was adjoined by a 3 x 5 x 8 ft toilet facility and a 7 x 7-1/2 x 8 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 had its independent air handling system and all outside doors were self-sealing when closed. Air flow through the complex was approximately 1500 cu ft per min 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 acetone 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 acetone into the flask.

#### Analysis of Exposure Chamber Atmosphere:

Each 5-gal (14.9 kg) container of acetone (Aldrich Chemical, certified at least 99% acetone) used to contaminate the chamber atmosphere



was individually analyzed by gas chromatography before use. No impurities at levels greater than a few ppm were found.

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 acetone was injected into the bag using a microliter syringe. Necessary amounts of acetone 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 2.25-m path-length and the absorption band at 8.25  $\mu\text{m}$  with a 2-mm slit 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 write on a CRT 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 940 GC was equipped with a column packed with Poropak Q operated at 155° C. Nitrogen was used as the carrier gas to a hydrogen flame detector operated at 280° 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. After each exposure ended, a calibration curve for the GC values was established with the computer using regression analysis on the standards that had been analyzed during the day. With that equation, peak-height values read manually were transformed into concentrations which were then used to calculate time-weighted averages and standard deviations for exposure increments to compare 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, complete panel of clinical chemistries (23 values plus 2 calculated), 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, subjective signs or symptoms, and urinalysis (Labstix<sup>®</sup>, Ames and Acetest<sup>®</sup>, Ames). The urinalysis was repeated on a urine sample voided 30-60 min post-exposure. 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 upon exit from the chamber, and at the following times after exiting the chamber (post-exposure): 15 and 30 min; 1, 2, and 3 hr. These samples were each collected in 5-l saran bags. The pre-exposure sample from the following morning represented the 16-, 21-, or 23-hr post-exposure sample for Group I, II, or III, respectively. Alveolar breath samples were obtained by expelling a breath which had been held for at least 20 sec into the saran bag and stoppering the bag securely. Sampling of the breath in the bag was accomplished by puncturing with a syringe needle. All samples, except the 2- and 3-hr post-exposure samples, were analyzed the same day as they were obtained. The 2- and 3-hr post-exposure samples were collected by the subjects while at home, and they were analyzed the following day upon return to the laboratory.

A Varian Aerograph Model 900 gas chromatograph (GC) equipped with a hydrogen flame ionization detector was used to determine acetone in the breath samples. The GC was fitted with a stainless steel column 3.5 ft x 1/3 in, packed with 25% Apiezon L on Chromosorb W, 45/60 mesh. The column was preconditioned at 210° C overnight prior to use. The operating conditions of the GC were as follows: carrier gas (nitrogen) flow rate of 30/ml per min; column temperature of 90° C; injection port, 190° C; and detector, 260° C. Both hydrogen and air flow were kept at the optimum. The sample size was usually 1 ml. Standards at four 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 acetone in the unknowns was obtained by direct comparison of peak heights to the standards. Because the breath bags always contained a small amount of water precipitated from the breath, acetone standards were prepared with 1 ml of water added to the standard bags. The minimal amount of acetone detectable from breath by this method was 0.05 ppm with an accuracy of  $\pm 0.1$  ppm.

#### Blood Sampling and Acetone Analysis in Blood:

Blood samples were withdrawn from an antecubital vein of each subject on Days 2 and 5 of each acetone exposure week. The blood samples were obtained pre-exposure, immediately pre-exit from the chamber, 30 min, and 60 min post-exposure, all in Vacutainer<sup>®</sup> tubes with edetic acid anticoagulant. Analysis of acetone was carried out on 2 ml

of serum from each blood sample, introduced into a 4-ml glass vial containing 1 ml aqueous solution of 5 mg% n-propyl alcohol as internal standard. The mixture was mixed thoroughly prior to analysis. One  $\mu$ l of the mixture was injected directly into the gas chromatograph. Samples were analyzed within 24-hr.

A Varian Aerograph Model 2700 Moduline<sup>®</sup> gas chromatograph (GC) equipped with a hydrogen flame ionization detector was used to determine acetone levels in the serum. The GC was fitted with a stainless steel column 6 ft x 1/8 in, packed with Porapak Q, 45/60 mesh. The column was preconditioned at 210° C overnight prior to its use. Throughout the analysis for acetone in the serum, the column was baked at 200° C when it was not in use. The operating conditions of the GC were: carrier gas (nitrogen) flow rate of 30/ml per min; column temperature, 120° C; injection port, 235 C; and detector, 250° C. A calibration curve (peak height ratio of acetone to n-propyl alcohol vs concentration) was prepared daily. Samples were injected in duplicate and the concentration of acetone in serum was obtained directly from the calibration curve. The detectable limit of acetone by this method was 0.05 mg% while the accuracy was  $\pm 0.1$  mg%.

#### Analysis of Acetone in Urine Samples:

As noted under the section on medical surveillance, urinalysis samples were obtained prior to and 30-60 minutes after each exposure to acetone vapor. These samples were tested for acetone by two "spot test" methods using Labstix<sup>®</sup> and Acetest<sup>®</sup> reagents. Both of these tests indicate ketones by a color change.

Urine samples were analyzed for acetone by gas chromatography on Day 5 of each exposure week and occasionally on Day 1 of each week. The methodology used was identical to that used for determining the acetone level in serum with the exception that 2 ml of urine were used instead of serum, and the aqueous n-propyl alcohol internal standard solution was 2-1/2 mg% in concentration rather than 5 mg%.

#### 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<sup>(7)</sup> from this laboratory. Gold-plated silver disk electrodes were oriented on the scalp according to the 10-20 International Electrode System<sup>(8)</sup>. 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  $\mu$ 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<sup>(9)</sup>. 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)<sup>(10-12)</sup>. 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.

#### Cardio-Pulmonary Function Studies:

Measurements designed to evaluate functional integrity of pulmonary airways, alveolar-capillary gas exchange, and regulation of pulmonary ventilation and heart rate were made on male Group I subjects between the 5th and 7th hours of exposure on Day 4 of each acetone exposure week. Baseline measurements were obtained during Weeks 1 and 5. Male Group II subjects were studied on a more limited basis between the 2nd and 3rd hr of exposure on identical days.

Group II: Minute ventilation, expiratory flow rates and vital capacity were measured on Group II subjects 1) during 0 ppm acetone concentration before and near the completion of the study and 2) on the 4th day of exposure at each acetone concentration > 0 ppm (200 ppm, 1000 ppm steady, 1250 ppm, 1000 ppm fluctuating). In addition, minute ventilation was also measured on the 2nd day of each exposure week.

For measurement of minute ventilation, the subjects were in a seated position. The expired port of the breathing valve was connected via corrugated tubing (1" I.D.) to a 13-l spirometer (W.E. Collins). After approximately 1 min breathing on the valve, ventilation was collected for 3-4 min, and the average minute volume over this time was tabulated.

A forced maximum expiratory maneuver was performed by the subjects while seated erect, and breathing through a mouthpiece connected with wide-bore tubing to a Fleisch 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<sub>1</sub>), peak expiratory flow rate (PEFR), and flow rate at 50% of FVC (MMEF). The expiratory maneuver was performed at least 3 times each day, with the data from the 2 "best" maneuvers being saved on magnetic tape. The mean of the 2 values was taken as indicative of the function for each specific condition.

Group I: Three maximum and partial forced expiratory maneuvers were performed by each Group I subject on the days noted in the preceding section. The components of the system employed in these forced expiratory maneuvers were: a) in series a mouthpiece, a flexible tube, a heated Fleisch No. 3 Pneumotachograph, and a water spirometer, and b) the essentials of a computer system for analysis, i.e. PDP-12 mini-computer, oscilloscope, teletype, etc. Initially, under control conditions, each subject's vital capacity (VC) and functional residual capacity (FRC) were determined on the water spirometer. For the actual maneuver, the subject in sequence: a) breathed quietly on the system for 3 or 4 breaths, b) inspired to his 70% VC mark on the spirometer (based on FRC), c) expired maximally, d) inspired maximally, and finally, e) expired maximally. Step-by-step software analysis of the acquired flow-time data included: a) integration to determine volumes, b) generation of flow-volume curves, and c) calculation and print out of such variables as total expiratory volumes (VC), volume expired in one second (FEV<sub>1</sub>), and flow rates at 40% and 25% of vital capacity for both the maximum and partial expiration. It is important to note that in our

system, because expired flow rate was dependent on lung volume, necessary adjustments were made so that all flow rate determinations were at the same absolute lung volume.

Metabolic, pulmonary, cardiac, and hematologic parameters were measured on Group I subjects at rest and during two levels of dynamic muscular exercise. The exercise was performed on a bicycle ergometer for 11 consecutive minutes, 6 minutes at 350 KPM followed by 5 minutes at 750 KPM. In addition, minute ventilation was also measured at rest on the second day of each exposure week (same method as for Group II).

The essential components of the expired gas collection and measurement system were a breathing valve, corrugated tubing, a Parkinson-Cowan gas meter, a 150-l Douglas bag, and a Hewlett-Packard recorder. Minute ventilation was quantitated using the gas meter and recorder. Expired gas was collected in the Douglas bag for 1 min at rest and 1 min at each exercise intensity (between 4.5 and 5.5, and 9.5 and 10.5 min of exercise). Fifty ml of this mixed expired air was stored in a glass syringe and subsequently analyzed for  $[CO_2]$  and  $[O_2]$  using a Quintron gas chromatograph. Ventilation and  $[CO_2]$  and  $[O_2]$  were used to calculate metabolic rate and respiratory quotient.

For sampling of blood, a 21-gauge needle was placed in a superficial dorsal hand vein<sup>(13)</sup>. The needle was attached to a tubing stopcock arrangement which during non-sampling periods was filled with heparinized saline. For 5 min prior to sampling, the entire hand was heated to approximately 42° C. This procedure sufficiently "arterialized" the venous blood so that  $P_{CO_2}$  and pH were virtually identical to arterial<sup>(13)</sup>. Three to 5 ml of blood were sampled over the 1-min period of

expired air collection. The blood was analyzed within 15 min for  $P_{CO_2}$  and pH with the Radiometer electrode arrangement.

Alveolar-capillary gas exchange was assessed by the single breath carbon monoxide diffusion technique<sup>(14)</sup> ( $D_LCO$ ). Measurements were made twice on each subject at rest and after 5.5 and 10.5 min of exercise. The previously described computerized system was used to calculate inspired, residual, and total lung volume 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 chromatograph.

Heart rate was measured using the Biotel 170 ECG patient telemetry system developed by Spacelabs, Inc. (Chatworth, California). Heart rate was measured during the 30-sec interval preceding initiation of the exercise and over the final 30-sec interval of each exercise period (350 and 750 KPM).

#### Cognitive Testing:

A battery of cognitive tests were performed in a group situation by the male Group I and II subjects on days 1, 3, and 5 of each week. The testing was carried out 3 and 2 hr after the start of 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 to acetone.

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

testing. All instructional commands were made from outside of the chamber via an intercom system. The tests, in order of performance, are described below.

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" x 11" 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, 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. The home telephone numbers of each of the Department physicians 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 acetone vapor in the environmental chamber for each group of subjects are found in Table I. Also listed are the number of subjects participating in each group. 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, SGOT, calcium, inorganic phosphorous, cholesterol, SGPT, creatinine, thymol turbidity, direct bilirubin, LDH, amylase, beta lipids, total lipid, sodium, potassium, chloride and gamma-glutamyl transpeptidase. No female subjects became pregnant during the period of time they were in the study. All daily urinalysis tests were within normal color ranges with the exception of tests for blood in urines of menstruating females and ketones at high exposure levels.

Complete blood count studies remained within normal limits and included a measurement of white blood cells (WBC) with differential count, red blood cells (RBC), platelets, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration.

Breath Analysis:

Acetone was readily detected in the expired breath of each of the subjects following exposure to the three 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 acetone 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 5-7.

A "family" of post-exposure breath decay curves useful in estimating the magnitude of vapor exposure can be constructed from the acetone breath data. Such a "family" is presented in Figure 5. 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 concentration of acetone 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 exposed to 1000 ppm from those exposed to 1250 ppm on the basis of a single breath sample. The variation between subjects was due in part to genuine reproducible differences between individuals.

The length of time after exposure in which the acetone could be detected in the breath was related to the magnitude of exposure. The

solvent was still readily detectable 16 hr after exposure to 1000 or 1250 ppm for 7-1/2 hr (Figure 5). Breath analysis of samples collected 1-16 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 acetone was an important variable influencing the rate of excretion of the solvent in the breath. This is shown in Figure 6. Serial breath sample analyses following exposure to 1000 ppm would permit the construction of a decay curve which would indicate the probable duration of that exposure.

The influence of widely fluctuating acetone vapor concentrations on the breath decay curves is illustrated in Figure 7. The overall breath decay curve very accurately reflects the time-weighted average vapor concentration and does not differ from the decay curve obtained following exposure to a non-fluctuating 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 (Figure 7).

In contrast to methylene chloride and similar to trichloroethylene, there was a slight but significant accumulation of acetone in the body following exposure to 1000 ppm. This small amount did not affect the breath decay curves (Table II). Therefore, no correction factor for repetitive exposures need be considered when breath decay curves are used to estimate the magnitude of repetitive exposures as would be the case with solvents like tetrachloroethylene.



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

Approximately 6% of the breath sample acetone determinations were excluded from the data due either to breath container leakage or incorrect time of breath collection. The loss of acetone from the breath collection containers was not determined as this had been recently reported<sup>(15)</sup>.

#### Blood Acetone Concentrations:

Acetone was measured in the venous blood of each subject following exposure to the solvent. The concentration of acetone 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 acetone data are presented in Table III. These data correlate very well with the acetone breath data obtained at the same times.

#### Urine Acetone Concentrations:

Acetone was measured in urine samples collected 30 to 60 min post-exposure after the third or fourth consecutive day of exposure to a given vapor concentration. The acetone concentration approximated that measured in the blood at the same time (Table IV).

#### Neurological Studies:

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

Visual Evoked Response: No alteration in the visual evoked response (VER) of either the male or female subjects was observed during exposure to acetone 200 or 1000 ppm. Male subjects exposed to 1250 ppm showed an increase in total VER amplitude.

Wave Form and Latency: The overall VER configuration remained stable throughout the acetone study for the male and female subjects. This is demonstrated in Figures 8-11 where representative VER's for each exposure condition are plotted. These figures clearly show consistent wave form and latency in the VER's.

Amplitude: The method of analysis was that of Forster et al<sup>(16)</sup> where the summed amplitudes of each wave are used to quantify and analyze the VER. This method possesses the advantage of having a single number (total VER amplitude) to represent the overall VER.

Male Subjects: Table V illustrates the mean total VER amplitudes of three afternoon VER's (n=3). The control VER's are the mean of three 0 ppm exposure days prior to the first acetone exposure (n=9). The control values (n=9) therefore are a "statistically good" representation of the mean of control conditions since three 0 ppm days were employed. A paired-t test for each subject was used to check for statistical significances. The t-test consisted of comparing the mean of three control (total summed amplitudes) with the mean of one total amplitude for the first, second, and third VER of the afternoon (Table VI).

#169 - There is no statistically significant change in the total VER amplitude (Table V).

#229 - This subject has a remarkably stable amplitude (low t-values) at 0 ppm conditions during the exposure schedule. After the fourth day of exposure at 1250 ppm of acetone, this subject had a statistically significant increase in total amplitude. This subject also demonstrated increases at 1250 ppm (second day) and 1000 ppm although not significant. On the second day of 1000 ppm fluctuating, there was a significant decrease in amplitude (Table V).

#230 - This subject demonstrated statistically significant amplitude increases during exposure to 1250 ppm of acetone. However, during the 0 ppm days throughout the exposure the amplitude remained slightly above control conditions (Table V).

#231 - This subject had a statistically significant increase on the fourth day of exposure at 1000 ppm. Although not significant he had increased amplitudes at 1250 ppm also (Table V).

Female Subjects: The same analysis method as for males was used for females. Table VII summarizes the findings. Although subject #237 showed a significant decrease in amplitude, the other subjects did not. From the available data there appears to be no overall effect of 1000 ppm acetone on the VER of the female subjects tested.

Spontaneous EEG: The spontaneous EEG was unaltered by acetone for the male subjects (#169, 229, 230, 231) at concentrations of 200, 1000 fluctuating, and

1250 ppm, and also for the female subjects (#237, 238, 239, 240) at a level of 1000 ppm for four days.

Figure 12 is a representative EEG for male subject #229 comparing the control EEG to that at the highest concentration of 1250 ppm. Figure 13 shows control vs 1000 ppm for female subject #238. Both of these figures demonstrate constant frequency, amplitude, and overall wave configuration between control and exposure.

#### Electrocardiograms:

No change from the control EKG tracings was observed in the standard 12-lead EKG's or in Lead-II monitored continuously during exposure by telemetry. There was a trend toward a greater increase in heart rate during exercise when exposure to acetone was occurring. However, this was not statistically significant.

#### Pulmonary Function Studies:

The functional integrity of the pulmonary airways as monitored by the pulmonary function tests did not appear to be affected by the short series of repetitive exposures to acetone. The spirometric data for those subjects exposed for 3 hr each day are listed in Table VIII. No trends or consistent changes were noted.

The spirometric data for those subjects exposed for 7-1/2 hr each day are listed in Tables IX and X. In addition to those tests performed on the 3-hr subjects, the Zuskin-Bouhuys partial-flow volume measurement was made<sup>(17)</sup>. Figure 14 shows the partial flow volume curves for male subject #231 during exposure to acetone 1250 ppm contrasted with 0 ppm exposure.

Metabolic rate, pulmonary diffusion, cardiac and blood gas data for the 7-1/2-hr subjects at rest and during exercise are presented in Tables XI and XII. No abnormalities were observed.

#### Cognitive Testing:

Exposure to acetone vapor did not result in cognitive test performance decrements.

Test performances under control and exposure conditions are presented in Figures 15-20. The mean  $\pm$  1 S.D. is plotted for each day and a linear regression line with 75% confidence limits is drawn through the 0 ppm data. After adjusting for the trend through the 0 ppm data, t-tests were performed to determine if the exposure data were significantly different from the regression line. The results of these t-tests are presented in Table XIII. The only significant differences occurred on the arithmetic test for the 3-hr exposed group. At 200 ppm the test was performed significantly better and at 1250 ppm the test was performed significantly poorer. Since during a subsequent exposure to 1250 ppm the performance was not significantly different, and the 7-1/2-hr exposed group showed no significant effects, the significance is attributed to random chance and a small sample size (n=2).

#### Subjective Responses:

During the three control days, two subjects recorded slight eye irritation, one subject recorded throat irritation and one developed a headache while in the chamber.

During exposure to 200 ppm all male subjects reported the odor to be moderate to strong. After three hours of exposure, the majority of the subjects could no longer detect the odor when breathing normally. After one breath of uncontaminated air, each subject's ability to detect the solvent's odor was immediately restored. Two subjects reported eye irritation on one day, two reported transient dizziness, one had a headache after 3 hr of exposure, and two complained of tiredness.

During the first week of exposure to 1000 ppm the odor was reported as stronger than during the previous week and was present throughout the entire exposure period. There were three complaints of eye and throat irritation and three complaints of tiredness.

During the week of exposure to 1250 ppm, odor intensity and the number of eye and throat irritation complaints remained the same.

During the final week of exposure to 1000 ppm, the odor was reported as being mild to moderate and noticeable throughout the entire exposure period. There were no complaints of eye or throat irritation or tiredness.

#### Other Observations of Importance:

Three of the four 7-1/2-hr female subjects volunteered that they had begun a prematurely early menstrual period after four days of exposure to 1000 ppm. The periods were all one week or more early and occurred in women who maintained they had very regular menstrual cycles. Two subjects were taking a birth control pill while the third was not using a contraceptive drug or device.

The senior investigator noted the sudden onset of vertigo after 40 min of exposure to 1000 ppm. The episode featured a transient rotary

nystagmus triggered by turning the head. Three hr after the exposure the vertigo subsided. A diagnosis of Bárány's paroxysmal vertigo had been made on this 48-yr-old physician after a similar but very protracted episode in 1960. Two other episodes had occurred since 1960, and each was associated with an exposure to high concentrations of a ketone. Exposure in the past 12 months to methylene chloride 1000 ppm, perchloroethylene 100 ppm, trichloroethylene 200 ppm, and 1,1,1-trichloroethane 500 ppm had not triggered the vertigo.

Following exposure to acetone 1000 or 1250 ppm, the majority of subjects had trace amounts of ketone present in their 30 min post-exposure urine as determined by the Ames Acetest<sup>®</sup> tablet. The male subjects exposed to 200 ppm all had negative Acetest tablet tests.

#### COMMENTS

Previous studies reporting the effects of well-controlled exposures of humans to acetone vapor have featured isolated exposures to low concentrations for short periods of time. None had simulated the repetitive exposure characteristic of the industrial setting. In this study subjects were repetitively exposed to the TLV in a setting where not only close surveillance of subjects was possible, but where the individual's ability to adapt to a chemical stress could be studied.

No serious deleterious effects upon the health or performance of healthy adults was detected when they were repeatedly exposed to 1000 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, electrocardiograms, and pulmonary function tests 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 major weakness in the system was an imperfect breath collection device which resulted in the loss of about 6% of the samples collected.

The analysis of expired breath for acetone 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 acetone 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 acetone exposure. Subjects identically exposed for 4 consecutive days had very similar breath decay curves, quite adequate for screening purposes.

The concentration of acetone in the breath in the early post-exposure period is a reflection of the acetone 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 acetone 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 acetone breath sample which will most accurately reflect the time-weighted average vapor exposure is in the 1- 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 1 hr after exposure would offer a screening test adequately sensitive to detect a vapor exposure in excess of the TLV.

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 acetone. 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<sup>(6)</sup>, 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 acetone 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 acetone in the blood or urine for the following reasons: First, the amount of acetone in the breath is directly related to the amount in the blood, and hence, the measurement is quantitative. The concentration of acetone in the urine is not as reliable a measurement of body burden since urine volume greatly influences concentration. Second, workmen prefer to give a single breath sample than be subjected to the discomfort of a venipuncture.

As a routine screening test the authors would suggest that a breath sample for acetone analysis be obtained at the plant entrance either on the way from or on the way into the work place. A breath acetone concentration greater than the mean and upper range for the specific post-exposure time interval on the 7-1/2 hr 1000 ppm curve 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 acetone data presented are good and had more data points been obtained, a biologic test of exposure based on blood analysis could

be promulgated. Because workmen do not accept routine venipunctures as well as breath sampling, the use of blood analysis as a routine screening test seems less attractive.

The early onset of menstrual period in three of the four female subjects exposed to 1000 ppm for 7-1/2 hr is worrisome and merits additional study to determine whether acetone, like styrene has the potential to influence this important biologic process. Diabetics in poor control and with elevated acetone levels often are troubled with irregular, abnormal menstrual periods. They have a higher incidence of spontaneous abortion than non-diabetics, the reason for which has not been established. However, the ingestion of acetone or isopropanol, which is metabolized to acetone, has been used as a method to induce abortion in the first trimester.

The probably induction of Bárány's paroxysmal vertigo is interesting in that this organic solvent may have the potential to adversely influence the natural history of neurological disorders. This merits special attention in the future.

This study failed to corroborate the findings of Suzuki<sup>(18)</sup> who reported that exposure to acetone 250-750 ppm for 6 hr resulted in EEG abnormalities and then suggested that the current TLV was too high. In our study, the spontaneous EEG remained normal. Suzuki monitored the concentration of acetone in his chamber only once an hour and so raises the question as to the precise magnitude of his exposures.

Our findings are in good agreement with those reported by DiVincenzo et al<sup>(6)</sup> regarding the amount of acetone in blood, breath and urine following human exposure to acetone. Our studies extend and expand his

observations, and we concur with his conclusion that the use of a biologic test of exposure is much to be desired.

The increase in total VER amplitude following exposure to 1250 ppm suggests that depression or synchronization of cerebral cortical activity had occurred. This finding, if corroborated, implies that the current TLV may not possess much of a safety margin.

#### ACKNOWLEDGEMENTS

All personnel in the Department including K. Callahan, L. Ebert, S. Kamke, L. Pearson, Dr. J.E. Peterson, D. Shekoski, K. Suschil, P. Stadler and T. Stewart, provided technical expertise in carrying out the study and/or aided in preparing this report. Their assistance is gratefully acknowledged. The expertise of Michael Hosko, Ph.D., Department of Pharmacology, and Gregory Harrington, M.D., Department of Neurology, in reviewing and interpreting the electroencephalograms is also gratefully acknowledged.

## REFERENCES

1. U.S. Chemical Industry Production. C & E News, June 2, 1975.
2. Threshold Limit Values of Airborne Contaminants. American Conference of Governmental Industrial Hygienists, 1971.
3. Patty, F.A.: Industrial Hygiene and Toxicology, Vol. 2, 3rd ed., p. 1729, Interscience Publishers, New York, 1963.
4. Browning, E.: Toxicity and Metabolism of Industrial Solvents, p. 413, Elsevier Publishing Company, New York, 1965.
5. Raleigh, R.L., and McGee, W.A.: Effects of Short, High Concentration Exposures to Acetone as Determined by Observation in the Work Area. J. Occup. Med. 14:607, 1972.
6. DiVincenzo, G.D., Yanno, F.J., and Astill, B.D.: Exposure of Man and Dog to Low Concentrations of Acetone Vapor. Am. Ind. Hyg. Assoc. J. 34:330-336, 1973.
7. Hosko, M.J.: The Effect of Carbon Monoxide on the Visual Evoked Response in Man. Arch. Environ. Health 21:174-180, 1970.
8. Jasper, H.H.: The 10-20 Electrode Systems of the International Federation. EEG Clin. Neurophysiol. 10:371-375, 1958.
9. Bergamasco, B.: Excitability Cycle of the Visual Cortex in Normal Subjects During Psychosensory Rest and Cardiovascular Activation. Brain Res. 2:51-60, 1966.
10. Gastaut, H., Regis, H.: Visually Evoked Potentials Recorded Transcranially in Man, in Procter, L.D., Adey, W.R. (eds.): Symposium on the Analysis of CNS and CU Data Using Computer Methods, publication SP-72, National Aeronautics and Space Administration, Washington, D.C., 1964.

11. Perry, N.W., Childers, D.G.: The Human Visual Evoked Response.  
C.C. Thomas, Springfield, Ill., 1969.
12. Ciganek, L.: A Comparative Study of Visual, Auditory, and Comato-  
sensory EEG Responses in Man. Exp. Brain Res. 4:118-125, 1967.
13. Forster, H.V., Dempsey, J.A., Thomson, J., Vidruk, E., do Pico,  
G.A.: Estimation of Arterial  $P_{O_2}$ ,  $P_{CO_2}$ , pH, and Lactate from  
Arterialized Venous Blood. J. Appl. Physiol. 32:134-137, 1972.
14. Forster, R.E.: Diffusion of Gases. Handbook of Physiology, Sec. 3,  
Vol. 1. American Physiological Society, Washington, D.C., 1964,  
pp. 839-872.
15. Stewart, R.D.: The Use of Breath Analysis in Clinical Toxicology.  
Essays in Toxicology, W. Hayes Ed., Vol. V, Chapter 5, Acad. Press,  
1974.
16. Forster, H.V., Soto, R.J., Dempsey, J.A., Hosko, M.J.: The Effect  
of Sojourn at 4300M on the Electroencephalogram and the Visual Evoked  
Response. J. Appl. Physiol. To be published.
17. Zuskin, E., Mitchell, C.H., and Bouhuys, A.: Interaction Between  
Effects of Beta Blockade and Cigarette Smoke on Airways. J. Appl.  
Physiol. 36:449-452, 1974.
18. Suzuki, H.: An Experimental Study on Physiological Functions of the  
Autonomic Nervous System of Man Exposed to Acetone Gas. Jap. J. Ind.  
Health. 15:147-164, 1973 (Japanese).

STATEMENT OF VOLUNTARY CONSENT

FOR RESEARCH INVESTIGATION OF

36

HUMAN EXPOSURE TO:

ACETONE

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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 acetone.

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

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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 \_\_\_\_\_

## HISTORY



37

PART I

NAME

DATE



37a

NAME			DATE
GENERAL HEALTH			WT
ILLNESSES	OP	HOSP.	INJ
S.F.			
R.F.			
D. MELL			
T.B.C.			
TYPHOID			
MALARIA			
NER. BK.			
GOUT			
MEDICATION			

RELIG.	ED.	IMMUNIZATIONS
VOCAT.		SMALLPOX
		TETANUS
		DIPHT.
MARITAL		POLIO
		INFLU.
		TYPH.
HABITS	SLEEP	COFFEE
		CIG.
		ALCOL.
WK. HRS./WK.		MEAS.

Q	#/H	D. MELL	CA
F		LARGE INFANTS	ASTHMA
		STILLBORN	MAY FEVER
		TBC	EPILEPSY
		B.P.	NER. BK.
		HEART	INSANITY
MM		COR. THROM	GOUT
MF		ANGINA	KIDNEY
FM		STROKE	
FF		BLEED. TEND.	

# PHYSICAL EXAMINATION

## APPENDIX III

X = NOT EXAMINED    - = NO, NEGATIVE  
✓ = NORMAL; YES    0 = ABSENT

NAME										DATE																																																												
TEMP.					B.P.					P.					HT.					WT.					ST. WT.																																													
APPEARANCE															POSTURE																																																							
HAIR	COLOR					TEXTURE					DISTRIBUTION																																																											
SCALP	CLEAN					ERUPTION					ALOPECIA																																																											
SKULL	DEFORMITIES										TENDERNESS																																																											
FACE	PALSIES					EXPRESSION					LIPS																																																											
EARS	CERUMEN					TYM MEMB					WATCH HEARD					TOPHI																																																						
											R					L																																																						
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																																																											
											CLEAN					ADEQUATE CHEWING SURFACE																																																						
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																																																						
						R					L					R					L																																																	
	OPHTHAL					DISC					H GR.					A GR.					TONOMETER																																																	
																R					L																																																	
LARYNX	VOICE NORMAL										TRACHEA										MIDLINE										TUG																																							
NECK	STIFFNESS					NODES					VEINS					CAROTID					PALPABLE																																																	
																					THYROID																																																	
SPINE	TENDERNESS										RIGIDITY										AB. CURVATURE																																																	
THORAX	SYMMETRICAL										CVA TENDERNESS										STERNAL TENDERNESS																																																	
RESPIRA	RATE					REGULAR					DEPTH					SYMMETRICAL					FORCED																																																	
LUNGS	COUGH										SPUTUM										PERCUSSION																																																	
	RESONANT										BREATH SOUNDS										VESICULAR																																																	
	RALES										TACTILE FREMITUS										VOICE SOUNDS																																																	
HEART	HEAVE										SHOCK										THRILL																																																	
	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.										I.C.S.									
	SOUNDS										A <sub>2</sub> P <sub>2</sub>										M <sub>1</sub> M <sub>2</sub>										RHYTHM										MURMUR																													
BREASTS	SIZE NORMAL										TENDERNESS										MASSES																																																	
ABDOMEN	SYMMETRICAL										DILATED VEINS										ASCITES																																																	
	PALPABLE LIVER										SPLEEN										KIDNEY										MASSES																																							
	TENDERNESS										RIGIDITY										SOUNDS										HERNIA																																							
GENIT. ALIA	DISCHARGE										SYN LESION										TESTES																																																	
	PELVIC																																																																					
ARMS	RADIAL PULSE					TREMOR					CLUBBING					CYANOSIS					JOINTS																																																	
LEGS	DORSALIS PEDIS										VARICOSITIES										EDEMA										ULCER																																							
	JOINTS																																																																					

MODES	CERVICAL	ARTILARY	INGUINAL	ENLARGED
	IDENT. MARKS			TEXTURE
KIM	COLOR	JAUNDICE	ERUPTION	AB. PIGMENTATION
ECTAL	HEMORRHOIDS	MASSSES	TENDERNESS	COLOR FECES
ROSTATE	ENLARGED	TENDER	MASS	
EURO- OLOGICAL				

CRANIAL NERVES			MUSCLES		
R		L	A. ATROPHY	F. FASCICULATION	
			STRENGTH		L
	SMELL			TEMPORAL CR V	
	VISION			MASSETER V	
	FIELD			FOREHEAD VII	
	FUNDUS			OPHIC. OC. VII	
	OCULAR MOVEMENTS			MOUTH VII	
	PTOSIS			SOFT PALATE X	
	NYSTAGMUS			PHARYNX X	
	PUPILS SIZE - SHAPE			STERNOMASTOID XI	
	PUPILS REFLEXES			TONGUE XII	
	HEARING			NECK FLEX. C 1-4	
	TASTE			NECK EXT. C1-T1	

FOLLOWING			MUSCLES		
R	REFLEXES (ENCIRCLE REINFORCED)	L	STRENGTH		L
	CORNEAL CR.			PECTORALIS MAJ. S-T1	
	SUCKING			DELTOID C 5-6	
	PHARYNX CR. IX, X			BICEPS BRACH. 3-6	
	JAW CR. V			TRICEPS 6-7-8	
	BICEPS C5-6			WRIST EXT. 6-7-8	
	BRACHIORADIALIS C5-6			WRIST FLEX. 6-7-8 T1	
	TRICEPS C6-7-8			DIGITS EXT. 6-7-8	
	HOFFMANN			DIGITS FLEX. 7-8 T1	
	EPIGASTRIC T6-9			THENAR 8-1	
	MID. ABD. T9-11			HYPOTHENAR 8-1	
	HYPOGASTRIC T11-L1			INTEROSSEI 8-1	
	CREMASTERIC L1-2			BACK	
	QUADRICEPS L2-3-4			ABDOMEN T6-L1	
	GASTROC. SOLEUS L5-S1-2			ILIOPSOAS L1-2-3-4	
	CLONUS (ANKLE)			ADDUCTORS, THIGH 2-3-4	
	HAMSTR. INT. L4-5 S1-2			ABDUCTORS, THIGH 4-5 S1	
	HAMSTR. EXT. L5-S1-2			GLUTEUS MAX. 5-12	
	ANAL S3-4			QUADRICEPS 2-3-4	
	BULBOCAY S3-4			HAMSTRINGS 4-5 1-2	
	BABIN'SKI			TIBIALIS ANT. 4-5 1	

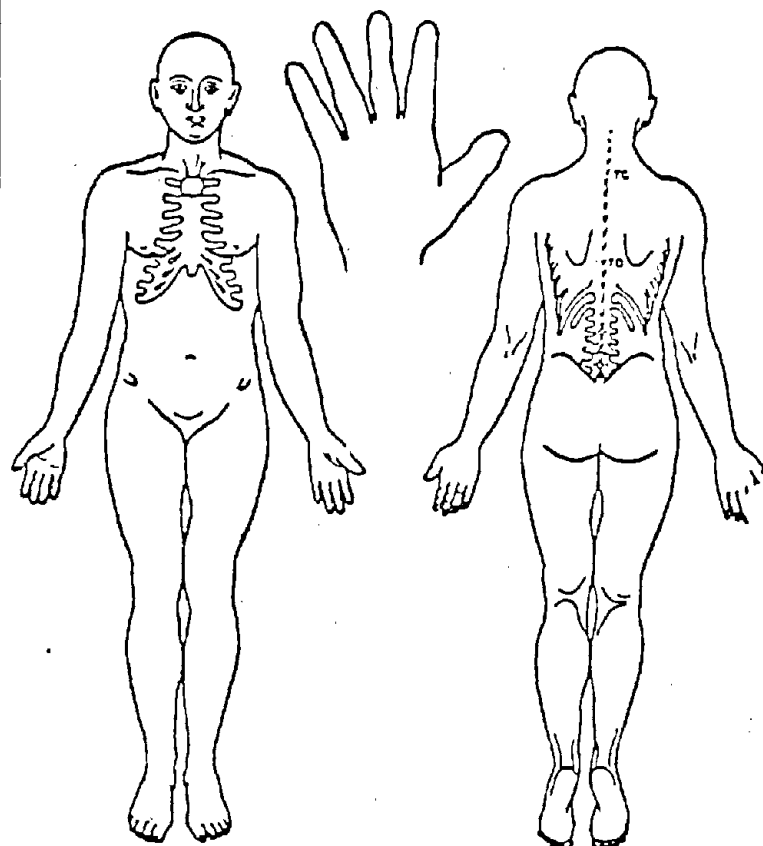
UMBERG
ACIES - POSTURE
PEECH
ENDEDNESS RT. LT.
ENTAL STATUS
PEMOR
ATION
GAIT
ON TOES
ON HEELS
HOPPING
APM SWING
RAIGHT AWAY
TURNS
ANDEN
SCRIPTION

ALT. MOT. RATE (A.M.R.)		
R		L
	HANDS (PRO. SUP.)	
	FINGERS	
	FEET	
	TONGUE	
COORDINATION		
R		L
	NOSE-FINGER-NOSE	
	KNEE PAT. (PRO. SUP.)	
	TOE-FINGER	
	FINGER-NOSE	
	HEEL-KNEE	

(UNDERLINE IF NORMAL - OTHERWISE ENCIRCLE AND CHART)

TOUCH  
PAIN  
TEMPERATURE  
DEEP PAIN  
VIBRATION

JOINT SENSE  
STEREOGNOSIS  
TRACED FIGURES  
TWO POINT



TOUCH - ARABIC, PAIN - ARABIC IN CIRCLE, TEMP. - ROMAN

LGR BACK SYNDROMES		
R		L
	S.L.R.	
	LOC. PAIN	
	FABERE	
	KERNIG	
	SPASM	
	CHIN-CHEST	
	LIST	
	SCOLIOSIS	
	LOPOOSIS	
RECTAL (SACROM. SPHINCTER)		
	STIFF NECK	
	CRANIUM	
	BRUIT	

EYES	VISION		PAIN		GLASSES	
EARS	HEARING		DISCHARGE		TINNITUS	
NOSE	SMELL		OBST.		EPIS	
C.R.	URI TR		SORE THROATS		HOARSENESS	
	SPUTUM		HEMOP		NIGHT SWEATS	
	WHEEZE		PAIN		DOE	
	EPEMA		OTHOPE		PND	
					B.P.	
G.I.	MOUTH					
	APPETITE			DIET		DYSPHAGIA
	H & V			PAIN		
	STOOLS					
	JAUNOICE			MASS		
G.U.	FREQ.		HOC		PAIN	
	INCONTIN.				COLOR	
	ALB.		SUGAR		WBC	
	V.D.				RBC	
M.S.	PREV. TRAUMA					
	NECK		BACK			VAR. VEIN
	JOINTS				LEG CRAMPS	
NEURO	HEADACHE			TRAUMA		
	ATAXIA			PARALYSIS		
	ANESTH-PARE			TREMOR		
	FANTING			CONVUL.		
	MEMORY			PERSONALITY		
SKIN	ERUPTION					
	ITCHING			CDLOR CHANGE		
LYMPH-HEMAT.	BLEEDING DISORDER					
END.						
ALLERGY						
MENSES	ONSET		LAST		FREQUENCY	
			WEEKS AGO		PAIN	
	MENOPAUSE			SPOTTING		
	V.D.			VAGINAL DISCHARGE		
BREASTS						

TABLE I

## ACETONE EXPOSURE SCHEDULE: MALE SUBJECTS

WEEK	DAY OF WEEK	DESIRED CONC. PPM	ACTUAL TIME-WEIGHTED AVERAGE VAPOR CONCENTRATION, PPM					
			Group I, 7-1/2 Hr			Group II, 3 Hr		
			No. of Subj.	Mean	±S.D.	No. of Subj.	Mean	±S.D.
1	1	0	4	0		4	0	
	2	0	4	0		4	0	
	3	0	4	0		4	0	
	5	0	4	0		3	0	
2	1	0	4	0		4	0	
	2	200	4	202	4	4	201	3
	3	200	4	200	3	4	200	3
	4	200	4	192	17	4	201	2
	5	200	4	201	4	4	200	4
3	1	0	4	0		3	0	
	2	1000	4	1006	48	2	998	56
	3	1000	4	1014	39	2	1028	45
	4	1000	4	1024	15	2	1020	16
	5	1000	4	1013	20	2	1011	24
4	1	0	4	0		3	0	
	2	1250	4	1249	41	3	1253	33
	3	1250	4	1252	19	2	1253	17
	4	1250	4	1233	74	2	1224	74
	5	1250	4	1232	54	1	1234	53
5	1	0	3	0		2	0	
	2	0	2	0		2	0	
6	1	0	3	0		3	0	
	2	1000 f*	3	1011	196	3	973	166
	3	1000 f	3	1010	210	2	1009	214
	4	1000 f	3	1026	193	3	1088	192
	5	0	3	0		2	0	

\* Concentration fluctuating from 750 to 1250 ppm.

TABLE I (Continued)

## ACETONE EXPOSURE SCHEDULE: FEMALE SUBJECTS

WEEK	DAY OF WEEK	DESIRED CONC. PPM	ACTUAL TIME-WEIGHTED AVERAGE VAPOR CONCENTRATION, PPM					
			<u>Group I, 7-1/2 Hr</u>			<u>Group II, 3 Hr</u>		
			No. of Subj.	Mean	S.D.	No. of Subj.	Mean	S.D.
1	1	0	4	0		4	0	
	2	1000	4	1005	17	4	1003	21
	3	1000	4	1000	17	4	1001	13
	4	1000	3	1002	14	3	1006	15
	5	1000	3	1002	15	3	103	13
<hr/>								
2	1	0	4	0		4	0	
<hr/>								
<u>Group III, 1 Hr</u>								
1	1	0	2	0				
	2	1000	2	1001	10			
	3	1000	2	1005	16			
	4	1000	2	1002	11			
	5	1000	2	1001	11			
<hr/>								
2	1	0	1	0				

TABLE II  
DAILY ACETONE BREATH CONCENTRATION OF  
SEDENTARY MALES

Exposure Time: 7 1/2 Hours - Chamber Concentration: 200 ppm

GROUP I

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subject</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	23.225	20.4-25.7	2.872	4
15 " "	14.75	13.5-16.0	1.041	4
30 " "	13.5	12.5-14.5	0.816	4
1 hour "	12.73	11.9-14.5	1.212	4
2 " "	10.33	8.5-12.0	1.756	3
3 " "	8.9	6.5-11.0	2.265	3
15.5 " "	3.375	2.5-4.0	0.75	4
<u>Day 3:</u> 1 min., post exit	24.875	23.5-26.0	1.109	4
15 " "	15.00	11.0-18.5	3.082	4
30 " "	14.5	12.5-17.5	2.449	4
1 hour "	11.875	9.5-15.5	2.562	4
2 " "	10.25	7.5-14.0	2.901	4
3 " "	8.5	7.0-13.5	3.391	4
15.5 " "	4.125	3.0-5.5	1.109	4
<u>Day 4:</u> 1 min., post exit	37.5	33.5-41.5	3.291	4
15 " "	23.875	21.0-27.5	2.955	4
30 " "	22.125	18.0-27.0	3.75	4
1 hour "	19.625	17.5-23.0	2.394	4
2 " "	13.875	9.0-18.0	3.838	4
3 " "	14.25	11.0-17.5	3.227	4
15.5 " "	5.0	4.0-7.5	1.683	4
<u>Day 5:</u> 1 min., post exit	32.25	25.0-37.0	5.123	4
15 " "	18.25	16.5-21.0	1.936	4
30 " "	18.875	14.5-25.0	4.571	4
1 hour "	16.00	11.5-19.0	3.342	4
2 " "	12.375	9.0-14.0	2.358	4
3 " "	9.6	7.4-12.5	2.13	4
15.5 " "	4.325	3.3-6.0	1.164	4

TABLE II (Continued)

DAILY ACETONE BREATH CONCENTRATION OF

SEDENTARY MALES

Exposure Time: 3 Hours - Chamber Concentration: 200 ppm

GROUP II

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>Standard Deviation</u>	<u>Number of Subject:</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	16.25	15.2-17.5	1.035	4
15 " "	7.4	6.6-8.2	0.673	4
30 " "	6.85	6.3-8.2	0.911	4
1 hour "	6.4	4.9-7.6	1.236	4
2 " "	4.65	4.1-5.5	0.597	4
3 " "	4.275	3.0-5.3	1.069	4
20 " "	3.125	2.0-4.0	0.854	4
<u>Day 3:</u> 1 min., post exit				
15 " "	17.125	16.0-18.5	1.109	4
30 " "	7.5	6.0-8.5	1.08	4
1 hour "	5.667	5.5-6.0	0.237	3
2 " "	5.25	4.5-5.5	0.5	4
3 " "	5.5	5.0-6.0	0.707	2
20 " "	4.5	4.0-5.0	0.707	2
	3.875	3.0-5.0	0.854	4
<u>Day 4:</u> 1 min., post exit				
15 " "	23.25	21.0-26.5	2.217	4
30 " "	10.25	7.0-12.5	2.398	4
1 hour "	9.25	5.5-11.5	2.723	4
2 " "	8.25	5.0-11.0	2.5	4
3 " "	6.25	3.5-8.5	2.398	4
20 " "	5.125	3.5-8.0	2.016	4
	4.625	3.0-8.0	2.287	4
<u>Day 5:</u> 1 min., post exit				
15 " "	27.125	22.5-38.5	7.609	4
30 " "	12.625	10.0-19.0	4.308	4
1 hour "	10.625	8.5-15.0	3.065	4
2 " "	9.875	7.5-15.0	3.473	4
3 " "	9.225	7.4-10.5	1.367	4
20 " "	10.0	7.5-14.5	3.317	4
	4.825	3.3-6.8	1.147	4



TABLE II (Continued)

## WEEKLY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Chamber Concentrations: 200 ppm

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>Standard + -Deviation</u>	<u>Number of Subjects</u>
<u>GROUP I</u>				
1 min., post exit	29.462	20.4-41.5	6.678	16
5 " "	17.969	11.0-27.5	4.365	16
0 " "	17.25	12.5-27.0	4.597	16
1 hour "	15.056	9.5-23.0	3.865	16
2 " "	11.8	7.5-18.0	3.011	15
3 " "	10.407	6.0-17.5	3.512	15
5.5 " "	4.206	2.5-7.5	1.247	16
<u>GROUP II</u>				
1 min., post exit	20.937	15.5-38.5	5.866	16
15 " "	9.444	7.0-19.0	3.191	16
30 " "	8.260	5.5-15.0	2.771	15
1 hour "	7.444	4.5-15.0	2.709	16
2 " "	6.536	3.5-10.5	2.321	14
3 " "	6.186	3.0-14.5	3.188	14
20 " "	4.112	2.0-8.0	1.443	16

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Exposure Time: 7 1/2 Hours - Chamber Concentration: 1000 ppm

## GROUP I

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subject</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	146.25	134.0-155.0	8.958	4
15 " "	95.0	85.0-105.0	9.129	4
30 " "	92.0	85.0-105.0	9.202	4
1 hour "	77.75	67.0-91.0	9.979	4
2 " "	70.25	54.0-86.0	13.124	4
3 " "	63.0	53.0-72.0	10.424	4
15.5 " "	37.5	35.0-42.0	3.317	4
<u>Day 3:</u> 1 min., post exit	160.0	145.0-170.0	13.229	3
15 " "	116.0	103.0-126.0	11.79	3
30 " "	110.0	92.0-121.0	15.948	3
1 hour "	101.667	97.0-108.0	5.686	3
2 " "	90.667	71.0-103.0	17.214	3
3 " "	74.333	55.0-94.0	19.502	3
15.5 " "	18.333	15.0-22.0	3.512	3
<u>Day 4:</u> 1 min., post exit	175.5	140.0-192.0	23.896	4
15 " "	94.25	79.0-104.0	11.758	4
30 " "	90.25	72.0-101.0	13.525	4
1 hour "	85.25	65.0-100.0	14.728	4
2 " "	86.25	59.0-100.0	19.328	4
3 " "	73.25	54.0-88.0	14.268	4
15.5 " "	16.75	5.0-32.0	12.230	4
<u>Day 5:</u> 1 min., post exit	142.75	102.0-190.0	37.322	4
15 " "	88.25	63.0-115.0	22.111	4
30 " "	81.5	61.0-105.0	18.699	4
1 hour "	75.0	53.0-93.0	17.739	4
2 " "	40.5	26.5-55.5	12.537	4
3 " "	40.0	25.0-58.0	14.737	4
15.5 " "	8.0	4.0-12.5	3.937	4

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Exposure Time: 3 Hours - Chamber Concentration: 1000 ppm

## GROUP II

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subject</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	87.0	80.0-94.0	9.899	2
15 " "	38.75	29.0-48.5	13.789	2
30 " "	36.0	27.0-45.0	12.728	2
1 hour "	34.5	25.0-44.0	13.435	2
2 " "	30.5	24.0-37.0	9.192	2
3 " "	28.0	19.0-37.0	12.728	2
20 " "	-	-	-	-
<u>Day 3:</u> 1 min., post exit	73.0	72.0-74.0	1.414	2
15 " "	30.5	27.0-34.0	4.95	2
30 " "	30.0	26.0-34.0	5.657	2
1 hour "	27.5	22.0-33.0	7.778	2
2 " "	19.0	15.0-23.0	5.657	2
3 " "	16.5	10.0-23.0	9.192	2
20 " "	5.0	5.0	0	2
<u>Day 4:</u> 1 min., post exit	97.0	94.0-100.0	4.243	2
15 " "	43.5	35.0-52.0	12.021	2
30 " "	41.0	32.0-50.0	12.728	2
1 hour "	41.0	32.0-50.0	12.728	2
2 " "	31.0	31.0	0	1
3 " "	25.0	25.0	0	1
20 " "	6.15	4.0-8.3	3.041	2
<u>Day 5:</u> 1 min., post exit	105.0	95.0-115.0	14.142	2
15 " "	45.0	37.0-53.0	11.314	2
30 " "	37.5	34.0-41.0	4.95	2
1 hour "	33.5	32.0-35.0	2.121	2
2 " "	17.0	17.0	0	1
3 " "	17.25	17.0-17.5	0.354	2
20 " "	5.0	4.5-5.5	0.707	2

TABLE II (Continued)

## WEEKLY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Chamber Concentrations: 1000 ppm

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>GROUP I</u>				
1 min., post exit	155.867	102.0-192.0	25.524	15
15 " "	96.533	63.0-126.0	17.033	15
30 " "	92.4	61.0-121.0	16.518	15
1 hour "	83.8	53.0-108.0	15.539	15
2 " "	70.667	26.5-103.0	6.367	15
3 " "	61.867	25.0-94.0	19.367	15
15.5 " "	23.7	5.0-42.0	12.561	10
<u>GROUP II</u>				
1 min., post exit	90.5	72.0-115.0	14.442	8
15 " "	39.437	27.0-53.0	10.301	8
30 " "	36.125	26.0-50.0	8.509	8
1 hour "	34.125	22.0-50.0	9.188	8
2 " "	24.5	15.0-37.0	8.337	6
3 " "	21.214	10.0-37.0	8.455	7
20 " "	7.912	4.5-18.0	5.036	8

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Exposure Time: 7 1/2 Hours - Chamber Concentration 1250 ppm

## GROUP I

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	177.0	137.0-214.0	34.244	4
15 " "	125.75	94.0-140.0	21.793	4
30 " "	122.25	94.0-140.0	21.203	4
1 hour "	119.5	92.0-140.0	21.61	4
2 " "	99.0	72.0-119.0	21.087	4
3 " "	87.5	72.0-105.0	15.588	4
15.5 " "	40.5	32.0-47.0	7.681	4
<u>Day 3:</u> 1 min., post exit	213.0	190.0-246.0	26.571	4
15 " "	126.5	105.0-148.0	20.728	4
30 " "	117.0	98.0-137.0	21.401	4
1 hour "	111.5	93.0-133.0	21.5	4
2 " "	106.0	77.0-130.0	26.851	3
3 " "	88.75	63.0-119.0	25.513	4
15.5 " "	36.75	23.0-57.0	14.385	4
<u>Day 4:</u> 1 min., post exit	214.5	157.0-263.0	43.707	4
15 " "	139.5	122.0-176.0	24.96	4
30 " "	117.75	99.0-149.0	22.111	4
1 hour "	114.25	94.0-149.0	24.636	4
2 " "	92.0	89.0-98.0	5.196	3
3 " "	88.25	67.0-116.0	20.37	4
15.5 " "	33.25	18.0-59.0	17.97	4
<u>Day 5:</u> 1 min., post exit	141.0	102.0-165.0	30.299	4
15 " "	86.5	69.0-113.0	19.553	4
30 " "	83.0	64.0-110.0	20.992	4
1 hour "	80.25	64.0-102.0	17.289	4
2 " "	66.75	53.0-86.0	14.431	4
3 " "	60.5	47.0-75.0	12.793	4
15.5 " "	7.1	4.6-10.0	2.905	4

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Exposure Time: 3 Hours - Chamber Concentration: 1250 ppm

## GROUP II

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subject</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	127.0	109.0-144.0	17.521	3
15 " "	42.667	22.0-59.0	13.877	3
30 " "	41.333	20.0-57.0	19.140	3
1 hour "	38.333	16.0-56.0	20.404	3
2 " "	32.5	27.0-38.0	7.778	2
3 " "	24.667	17.0-36.0	10.017	3
20 " "	7.0	4.0-10.0	3.00	3
<u>Day 3:</u> 1 min., post exit	130.5	93.0-168.0	53.033	2
15 " "	45.0	40.0-50.0	7.071	2
30 " "	45.5	37.0-54.0	12.021	2
1 hour "	42.0	34.0-50.0	11.314	2
2 " "	27.0	27.0	0	2
3 " "	22.5	20.0-25.0	3.536	2
20 " "	6.5	5.0-8.0	2.12	2
<u>Day 4:</u> 1 min., post exit	146.0	109.0-183.0	52.326	2
15 " "	52.5	41.0-64.0	16.263	2
30 " "	51.0	40.0-62.0	15.556	2
1 hour "	50.5	39.0-62.0	16.263	2
2 " "	30.0	30.0	0	1
3 " "	27.0	27.0	0	1
20 " "	9.5	4.0-15.0	7.778	2
<u>Day 5:</u> 1 min., post exit	109.5	91.0-128.0	26.163	2
15 " "	44.5	40.0-49.0	6.364	2
30 " "	42.5	38.0-47.0	6.364	2
1 hour "	39.5	34.0-45.0	7.778	2
2 " "	34.0	34.0	0	1
3 " "	26.0	26.0	0	1
20 " "	4.6	4.6	0	1

TABLE II (Continued)

## WEEKLY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Chamber Concentrations: 1250 ppm

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>GROUP I</u>				
1 min., post exit	186.375	102.0-263.0	43.748	16
15 " "	119.562	69.0-176.0	28.329	16
30 " "	110.0	64.0-149.0	25.118	16
1 hour "	106.375	64.0-149.0	24.870	16
2 " "	89.786	53.0-130.0	22.737	14
3 " "	81.25	53.0-119.0	21.161	16
15.5 " "	29.4	4.6-59.0	17.415	16
<u>GROUP II</u>				
1 min., post exit	128.11	91.0-183.0	32.010	9
15 " "	45.778	22.0-64.0	12.204	9
30 " "	44.667	20.0-62.0	12.669	9
1 hour "	42.111	16.0-62.0	13.615	9
2 " "	30.5	27.0-38.0	4.593	6
3 " "	24.571	17.0-36.0	6.188	7
20 " "	7.2	4.0-15.0	3.807	8

TABLE II (Continued)

DAILY ACETONE BREATH CONCENTRATION OF  
SEDENTARY MALES

Exposure Time: 7 1/2 Hours - Chamber Concentration: Fluc. 750-1250 ppm

GROUP I

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	140.667	97.0-166.0	37.978	3
15 " "	84.333	72.0-101.0	14.978	3
30 " "	78.333	65.0-92.0	13.503	3
1 hour "	71.0	52.0-91.0	19.519	3
2 " "	62.667	45.0-90.0	24.007	3
3 " "	54.0	41.0-76.0	19.157	3
15.5 " "	27.0	18.0-40.0	11.533	3
<u>Day 3:</u> 1 min., post exit	174.333	133.0-205.0	37.166	3
15 " "	81.0	65.0-99.0	17.088	3
30 " "	77.333	62.0-94.0	16.042	3
1 hour "	74.0	58.0-91.0	16.523	3
2 " "	67.0	57.0-85.0	15.620	3
3 " "	56.0	44.0-69.0	12.530	3
15.5 " "	9.667	7.0-14.0	3.786	3
<u>Day 4:</u> 1 min., post exit	95.333	78.0-110.0	16.166	3
15 " "	58.333	48.0-72.0	12.342	3
30 " "	48.333	47.0-51.0	2.31	3
1 hour "	49.333	41.0-64.0	12.741	3
2 " "	43.0	25.0-63.0	19.079	3
3 " "	37.0	19.0-51.0	16.371	3
15.5 " "	2.833	2.5-3.0	0.289	3



TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Exposure Time: 3 Hours - Chamber Concentration: Fluc. 750-1250 ppm

## GROUP II

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>Day 1: Zero Concentration Day</u>				
<u>Day 2:</u> 1 min., post exit	96.667	80.0-120.0	20.817	3
15 " "	44.667	40.0-51.0	5.686	3
30 " "	39.0	31.0-50.0	9.849	3
1 hour "	40.5	35.0-46.0	7.778	2
2 " "	31.0	30.0-32.0	1.414	2
3 " "	28.0	28.0	0.	2
20 " "	6.5	5.0-8.0	2.121	2
<u>Day 3:</u> 1 min., post exit	100.0	85.0-115.0	21.213	2
15 " "	42.0	36.0-48.0	8.485	2
30 " "	39.5	34.0-45.0	7.778	2
1 hour "	44.0	43.0-45.0	1.414	2
2 " "	21.5	17.0-26.0	6.364	2
3 " "	19.0	14.0-24.0	7.071	2
20 " "	4.667	3.0-6.0	1.528	3
<u>Day 4:</u> 1 min., post exit	92.0	75.0-115.0	20.664	3
15 " "	33.333	28.0-39.0	5.508	3
30 " "	31.333	26.0-37.0	5.508	3
1 hour "	30.667	25.0-37.0	6.028	3
2 " "	21.5	19.0-24.0	3.536	2
3 " "	19.5	18.0-21.0	2.121	2
20 " "	3.0	3.0	0	2

TABLE II (Continued)

## WEEKLY ACETONE BREATH CONCENTRATION OF

## SEDENTARY MALES

Chamber Concentrations: Fluct. 750-1250 ppm

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>GROUP I</u>				
1 min., post exit	136.778	78.0-205.0	44.158	9
15 " "	74.556	48.0-101.0	17.812	9
30 " "	68.0	47.0-94.0	18.138	9
1 hour "	64.778	41.0-91.0	18.438	9
2 " "	57.556	25.0-90.0	20.464	9
3 " "	49.0	19.0-76.0	16.726	9
15.5 " "	13.167	2.5-40.0	12.379	9
<u>GROUP II</u>				
1 min., post exit	95.75	75.0-120.0	17.934	8
15 " "	39.75	28.0-51.0	7.592	8
30 " "	36.25	26.0-50.0	7.851	8
1 hour "	36.0	25.0-46.0	7.572	7
2 " "	24.667	17.0-32.0	5.922	6
3 " "	22.167	14.0-28.0	5.601	6
20 " "	4.714	3.0-8.0	1.890	7

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY FEMALES

Exposure Time: 7 1/2 Hours - Chamber Concentration: 1000 ppm

## GROUP I

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	185.5	148-216	32.879	4
15 " "	123.25	93-157	31.095	4
30 " "	118.0	90-150	28.249	4
1 hour "	96.5	70-120	22.708	4
2 " "	83.75	64-102	18.154	4
3 " "	73.625	43-94	24.019	4
15.5 " "	29.75	16-36	9.465	4
<u>Day 3:</u> 1 min., post exit	180.0	150-207	23.509	4
15 " "	115.25	90-155	28.406	4
30 " "	111.75	89-152	28.064	4
1 hour "	81.5	39-131	38.484	4
2 " "	68.333	55-81	13.013	4
3 " "	56.5	26-75	21.641	4
15.5 " "	36.25	23-49.5	18.738	2
<u>Day 4:</u> 1 min., post exit	166.333	161-175	7.572	3
15 " "	101.333	95-110	7.768	3
30 " "	99.333	97-103	3.215	3
1 hour "	95.0	88-103	7.55	3
2 " "	73.0	63-87	12.49	3
3 " "	69.333	60-74	8.083	3
15.5 " "	3.333	3-4	0.577	3
<u>Day 5:</u> 1 min., post exit	167.00	145-181	19.287	3
15 " "	99.667	88-116	14.572	3
30 " "	98.333	88-117	16.197	3
1 hour "	74.333	66.5-87	11.072	3
2 " "	65.0	58.5-78	11.258	3
3 " "	60.0	57.5-62.5	3.536	2
15.5 " "	2.333	1-3.5	1.258	2

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY FEMALES

Exposure Time: 3 Hours - Chamber Concentration: 1000 ppm

## GROUP II

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>Day 1: Zero Concentration Day</u>				
<u>Day 2:</u> 1 min., post exit	90.25	70.0-108.0	16.215	4
15 " "	41.5	27.0-48.5	9.958	4
30 " "	39.25	27.0-46.0	8.995	4
1 hour "	35.375	27.0-43.0	6.7	4
2 " "	31.75	27.0-34.0	3.304	4
3 " "	26.75	22.0-31.0	4.924	4
20 " "	6.25	5.0-8.0	1.258	4
<u>Day 3:</u> 1 min., post exit	117.0	101.0-131.0	16.248	4
15 " "	43.25	40.0-47.0	3.304	4
30 " "	41.25	39.0-44.0	2.63	4
1 hour "	38.0	35.0-41.0	2.582	4
2 " "	27.0	25.0-28.0	1.732	3
3 " "	20.0	13.0-27.0	9.899	2
20 " "	5.0	5.0	0	3
<u>Day 4:</u> 1 min., post exit	98.0	87.0-110.0	11.533	3
15 " "	42.0	40.0-44.0	2.0	3
30 " "	39.667	38.0-41.0	1.528	3
1 hour "	36.333	35.0-38.0	1.528	3
2 " "	32.00	29.0-38.0	5.196	3
3 " "	23.333	20.0-27.0	3.512	3
20 " "	4.0	4.0	0	
<u>Day 5:</u> 1 min., post exit	110.333	101.0-116.0	8.145	3
15 " "	44.667	44.0-46.0	1.155	3
30 " "	40.0	38.0-42.0	2.0	3
1 hour "	39.0	37.0-40.0	1.732	3
2 " "	25.167	22.5-27.5	2.517	3
3 " "	20.167	19.0-21.5	1.258	3
20 " "	1.667	1.0-3.0	1.555	3

TABLE II (Continued)

## DAILY ACETONE BREATH CONCENTRATION OF

## SEDENTARY FEMALES

Exposure Time: 1 Hours - Chamber Concentration: 1000 ppm

## GROUP III

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>+Standard -Deviation</u>	<u>Number of Subjects</u>
<u>Day 1:</u> Zero Concentration Day				
<u>Day 2:</u> 1 min., post exit	75.5	75.0-76.0	0.707	2
15 " "	21.75	20.0-23.5	2.475	2
30 " "	20.0	19.0-21.0	1.414	2
1 hour "	18.5	18.0-19.0	0.707	2
2 " "	14.15	8.3-20.0	8.273	2
3 " "	10.95	6.9-15.0	5.728	2
22 " "	5.5	5.0- 6.0	0.707	2
<u>Day 3:</u> 1 min., post exit	74.0	68.0-80.0	8.485	2
15 " "	27.0	26.0-28.0	1.414	2
30 " "	23.0	21.0-25.0	2.828	2
1 hour "	22.5	22.0-23.0	0.707	2
2 " "	16.0	10.0-22.0	8.485	2
3 " "	15.0	14.0-16.0	1.414	2
22 " "	2.5	2.0- 3.0	0.707	2
<u>Day 4:</u> 1 min., post exit	72.0	67.0-77.0	7.071	2
15 " "	23.5	22.0-25.0	2.121	2
30 " "	20.5	20.0-21.0	0.707	2
1 hour "	19.5	19.0-20.0	0.707	2
2 " "	15.5	13.0-18.0	3.536	2
3 " "	12.5	11.0-14.0	2.121	2
22 " "	4.25	3.0-5.5	1.768	2
<u>Day 5:</u> 1 min., post exit	68.0	64.0-72.0	5.657	2
15 " "	22.0	22.0	0	2
30 " "	16.5	12.0-21.0	6.364	2
1 hour "	12.0	8.0-16.0	5.657	2
2 " "	9.5	9.0-10.0	0.707	2
3 " "	7.75	6.5-9.0	1.768	2
22 " "	1.0	1.0	0	2

TABLE II (Continued)

## WEEKLY ACETONE BREATH CONCENTRATION OF

## SEDENTARY FEMALES

Chamber Concentrations: 1000 ppm

<u>Time</u>	<u>Mean (in ppm)</u>	<u>Range (in ppm)</u>	<u>Standard + Deviation</u>	<u>Number of Subjects</u>
<u>GROUP I</u> - 7 1/2 Hr. Exposure				
1 min., post exit	175.857	145.0-216.0	22.715	14
15 " "	111.214	88.0-157.0	23.541	14
30 " "	108.0	88.0-152.0	21.951	14
1 hour "	87.143	39.0-131.0	24.026	14
2 " "	73.385	55.0-102.0	14.75	13
3 " "	65.269	26.0-94.0	18.191	13
15.5 " "	32.5	16.0-49.5	10.728	7
<u>GROUP II</u> - 3 Hr. Exposure				
1 min., post exit	103.857	70.0-131.0	16.733	14
15 " "	42.786	27.0-48.5	5.269	14
30 " "	40.071	27.0-46.0	4.682	14
1 hour "	37.107	27.0-43.0	3.854	14
2 " "	29.192	25.0-38.0	4.265	13
3 " "	23.125	13.0-27.0	5.197	12
20 " "	4.385	1.0-8.0	1.938	13
<u>GROUP III</u> - 1 Hr. Exposure				
1 min., post exit	72.375	64.0-80.0	5.579	8
15 " "	23.562	20.0-28.0	2.611	8
30 " "	20.0	12.0-25.0	3.665	8
1 hour "	18.125	8.0-23.0	4.643	8
2 " "	13.787	8.3-22.0	5.427	8
3 " "	11.550	6.5-15.0	3.735	8
22 " "	3.313	1.0-6.0	1.981	8

TABLE III

ACETONE IN BLOOD OF SUBJECTS EXPOSED  
TO SEVERAL CONCENTRATIONS OF ITS VAPOR

Exposure for 7-1/2 Hr daily <sup>b)</sup>	Blood Acetone Concentration <sup>(a)</sup> in mg%			
	(n)	<u>Males</u>	(n)	<u>Females</u>
0 ppm	4	1.29 ± 0.24 (1.11 - 1.61)	4	2.86 ± 1.00 (1.83 - 4.17)
	4	0.73 ± 0.14 (0.55 - 0.90)		
	3	0.91 ± 0.13 (0.82 - 1.00)		
200 ppm	4	1.96 ± 0.56 (1.56 - 2.78)		
1000 ppm	4	6.93 ± 1.75 (5.25 - 9.25)	3	9.77 ± 1.72 (8.77 - 11.75)
	3	9.02 ± 1.01 (8.82 - 10.11)		
1250 ppm	4	6.95 ± 0.97 (6.17 - 8.26)		
Exposure for 3 Hr daily <sup>b)</sup>				
0 ppm	2	1.23 ± 0.18 (1.10 - 1.35)	4	3.58 ± 0.17 (3.33 - 3.71)
	3	0.96 ± 0.20 (0.82 - 1.18)		
	2	1.32 ± 0.04 (1.29 - 1.35)		
200 ppm	4	2.18 ± 0.27 (2.04 - 2.59)		
1000 ppm	2	2.87 ± 0.28 (2.67 - 3.07)	3	7.27 ± 0.49 (6.71 - 7.64)
	2	4.91 ± 0.71 (4.41 - 5.41)		
1250 ppm	3	3.72 ± 1.56 (1.95 - 4.87)		

(a) Mean values, ±1 S.D., and range.

(b) Zero ppm values represent pre-exposure blood samples obtained at least 3 days after the last exposure to acetone. All other values represent samples obtained 30 min postexposure.

TABLE III (Continued)

## ACETONE CONCENTRATIONS IN BLOOD FOR MALE SUBJECTS

Chamber Concentrations: 200 ppm

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> <u>(in mg%)</u>	<u>Range</u> <u>(in mg%)</u>	<u>+ Standard</u> <u>- Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 2, WEEK 2:</u>				
Pre-exposure	-	-		4
Pre-exit	2.22	1.78-2.43	0.31	4
30 min. post exit	2.60	2.38-2.74	0.16	4
1 hr. " "	2.20	1.82-2.43	0.27	4
<u>DAY 5, WEEK 2:</u>				
Pre-exposure	1.10	1.00-1.21	0.09	4
Pre-exit	1.95	1.63-2.33	0.29	4
30 min. post exit	1.96	1.56-2.78	0.56	4
1 hr. " "	1.87	1.83-1.90	0.32	4

GROUP II - 3 Hr. Exposure

<u>DAY 2, WEEK 2:</u>				
Pre-exposure	-	-		4
Pre-exit	1.44	1.20-1.65	0.28	4
30 min. post exit	1.69	1.28-2.08	0.41	4
1 hr. " "	1.41	1.06-1.63	0.25	4
<u>DAY 5, WEEK 2:</u>				
Pre-exposure	1.73	1.52-1.92	0.2	4
Pre-exit	2.43	2.04-2.95	0.38	4
30 min. post exit	2.18	2.04-2.59	0.27	4
1 hr. " "	1.55	1.20-2.02	0.34	4



TABLE III (Continued)

## ACETONE CONCENTRATIONS IN BLOOD FOR MALE SUBJECTS

Chamber Concentrations: 1000 ppm

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> <u>(in mg%)</u>	<u>Range</u> <u>(in mg%)</u>	<u>Standard</u> <u>+ Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 2, WEEK 3:</u>				
Pre-exposure	1.29	1.11-1.61	0.24	4
Pre-exit	7.18	6.49-8.00	0.73	4
30 min. post exit	7.30	6.67-7.72	0.55	3
1 hr. " "	6.62	5.83-7.33	0.79	4
<u>DAY 5, WEEK 3:</u>				
Pre-exposure	2.14	1.35-3.9	1.19	4
Pre-exit	7.69	6.35-9.45	1.31	4
30 min. post exit	6.93	5.25-9.25	1.75	4
1 hr. " "	6.18	5.16-8.16	1.35	4

GROUP II - 3 Hr. Exposure

<u>DAY 2, WEEK 3:</u>				
Pre-exposure	1.23	1.10-1.35	0.18	2
Pre-exit	2.98	2.32-3.64	0.93	2
30 min. post exit	2.97	2.28-3.66	0.98	2
1 hr. " "	2.77	2.20-3.34	0.81	2
<u>DAY 5, WEEK 3:</u>				
Pre-exposure	1.12	0.71-1.53	0.58	2
Pre-exit	3.07	3.07	0	2
30 min. post exit	2.87	2.67-3.07	0.28	2
1 hr. " "	2.81	2.54-3.07	0.38	2

TABLE III (Continued)

## ACETONE CONCENTRATIONS IN BLOOD FOR MALE SUBJECTS

Chamber Concentrations: 1250 ppm

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> (in mg%)	<u>Range</u> (in mg%)	<u>± Standard</u> <u>Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 2, WEEK 4:</u>				
Pre-exposure	0.73	0.55-0.90	0.14	4
Pre-exit	10.01	8.02-10.90	1.36	4
30 min. post exit	9.77	8.37-10.87	1.13	4
1 hr. " "	8.91	7.79-9.64	0.79	4
<u>DAY 5, WEEK 4:</u>				
Pre-exposure	2.80	1.73-3.91	1.07	4
Pre-exit	8.25	6.74-10.43	1.93	3
30 min. post exit	6.95	6.17-8.26	0.97	4
1 hr. " "	6.33	5.54-6.30	0.59	4

GROUP II - 3 Hr. Exposure

<u>DAY 2, WEEK 4:</u>				
Pre-exposure	0.96	0.82-1.18	0.20	3
Pre-exit	3.95	2.04-5.40	1.73	3
30 min. post exit	3.72	1.95-4.87	1.56	3
1 hr. " "	3.43	1.90-4.43	1.35	3
<u>DAY 5, WEEK 4:</u>				
Pre-exposure	1.25	1.20-1.30	0.07	2
Pre-exit	4.37	3.90-4.84	0.67	2
30 min. post exit	4.38	3.66-5.10	1.02	2
1 hr. " "	4.15	3.49-4.80	0.93	2

TABLE III (Continued)

## ACETONE CONCENTRATIONS IN BLOOD FOR MALE SUBJECTS

Chamber Concentrations: Fluctuating 750-1250 ppm

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> <u>(in mg%)</u>	<u>Range</u> <u>(in mg%)</u>	<u>+ Standard</u> <u>- Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 2, WEEK 6:</u>				
Pre-exposure	0.91	0.82-1.00	0.13	3
Pre-exit	10.23	8.65-11.76	1.56	3
30 min. post exit	9.02	8.82-10.11	1.01	3
1 hr. " "	8.65	8.00-9.65	0.88	3
<u>DAY 5, WEEK 6: Last day - zero exposure</u>				
Pre-exposure	0.76	0.48-0.9	0.242	3

GROUP II - 3 Hr. Exposure

<u>DAY 2, WEEK 6:</u>				
Pre-exposure	1.32	1.29-1.35	0.04	2
Pre-exit	4.92	4.47-5.59	0.59	3
30 min. post exit	4.91	4.41-5.41	0.71	2
1 hr. " "	4.32	3.76-4.88	0.79	2
<u>DAY 5, WEEK 6: Last day - zero exposure</u>				
Pre-exposure	0.95	0.71-1.19	0.34	2

TABLE III (Continued)

## ACETONE CONCENTRATIONS IN BLOOD FOR FEMALE SUBJECTS

Chamber Concentrations: 1000 ppm

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> <u>(in mg%)</u>	<u>Range</u> <u>(in mg%)</u>	<u>+ Standard</u> <u>- Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 1:</u>				
Pre-exposure	2.862	1.83-4.17	0.998	4
Pre-exit	16.905	12.99-21.1	3.394	4
30 min. post exit	12.607	9.52-17.48	3.480	4
1 hr. " "	13.077	9.52-17.14	3.835	4
<u>DAY 5:</u>				
Pre-exposure	3.995	2.65-5.78	1.303	4
Pre-exit	10.177	9.28-11.83	1.434	3
30 min. post exit	9.77	8.77-11.75	1.715	3
1 hr. " "	9.17	8.02-11.36	1.897	3

GROUP II - 3 Hr. Exposure

<u>DAY 1:</u>				
Pre-exposure	3.58	3.33-3.71	0.170	4
Pre-exit	6.705	5.71-8.42	1.291	4
30 min. post exit	5.33	5.14-5.71	0.329	3
1 hr. " "	4.495	4.10-4.77	0.313	4
<u>DAY 5:</u>				
Pre-exposure	2.903	2.56-3.18	0.315	3
Pre-exit	7.253	6.85-7.46	0.349	3
30 min. post exit	7.27	6.71-7.64	0.493	3
1 hr. " "	6.967	6.62-7.29	0.336	3

GROUP III - 1 Hr. Exposure

<u>DAY 1:</u>				
Pre-exposure	2.70	2.29-3.11	0.58	2
Pre-exit	3.25	2.86-3.64	0.552	2
30 min. post exit	2.73	2.60-2.86	0.184	2
1 hr. " "	2.67	2.67	0	1
<u>DAY 5:</u>				
Pre-exposure	4.21	4.10-4.32	0.156	2
Pre-exit	5.01	4.61-5.41	0.566	2
30 min. post exit	5.065	4.89-5.24	0.248	2
1 hr. " "	5.08	4.58-5.58	0.707	2

TABLE IV

ACETONE IN URINE OF SUBJECTS EXPOSED  
TO SEVERAL CONCENTRATIONS OF ITS VAPOR

Exposure for 7-1/2 Hr daily <sup>b</sup>	Urinary Acetone Concentration <sup>a</sup> in mg%			
	(n)	<u>Males</u>	(n)	<u>Females</u>
0 ppm	4	1.32 ± 0.35 (0.83 - 1.64)	3	1.35 ± 0.48 (0.95 - 1.89)
	4	1.37 ± 0.34 (1.14 - 1.87)	4	1.16 ± 0.29 (0.80 - 1.50)
	3	0.74 ± 0.19 (0.57 - 0.95)		
200 ppm	4	3.13 ± 0.13 (2.96 - 3.28)		
1000 ppm	4	6.38 ± 1.82 (5.10 - 9.07)	3	9.51 ± 2.04 (7.85 - 11.79)
	3	5.98 ± 2.29 (3.81 - 8.38)		
1250 ppm	4	6.53 ± 0.66 (5.77 - 7.30)		
Exposure for 3 Hr daily <sup>b</sup>				
0 ppm	3	0.99 ± 0.26 (0.96 - 1.01)	4	0.90 ± 0.41 (0.43 - 1.42)
	2	1.35 ± 0.59 (0.93 - 1.77)	3	1.02 ± 0.38 (0.59 - 1.30)
	2	1.17 ± 0.71 (0.67 - 1.67)		
200 ppm	4	2.26 ± 0.50 (1.67 - 2.89)		
1000 ppm	2	2.53 ± 0.67 (2.06 - 3.00)	3	4.62 ± 1.25 (3.19 - 5.45)
	3	3.95 ± 0.95 (2.90 - 4.76)		
1250 ppm	2	3.11 ± 0.55 (2.72 - 3.50)		

(a) Mean values, ±1 S.D., and range.

(b) All urine samples (except females, 0 ppm) were obtained 30 to 60 min postexposure. Females, 0 ppm, samples were obtained pre-exposure. Values from exposures to > 0 ppm acetone represent those from the 3rd or 4th consecutive day of exposure to that vapor concentration.

TABLE IV (Continued)

## ACETONE CONCENTRATIONS IN RANDOM URINE FOR MALE SUBJECTS

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> <u>(in mg%)</u>	<u>Range</u> <u>(in mg%)</u>	<u>± Standard</u> <u>Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 1, WEEK 1:</u>	<u>Chamber Concentration: Zero</u>			
<u>DAY 5, WEEK 2:</u>	<u>Chamber Concentration: 200 ppm</u>			
Pre-exposure	2.297	2.08-2.59	0.245	4
30 min. post exit	3.13	2.96-3.28	0.132	4
<u>DAY 1, WEEK 3:</u>	<u>Chamber Concentration: Zero</u>			
30 min. post exit	1.317	0.83-1.64	0.345	4
<u>DAY 5, WEEK 3:</u>	<u>Chamber Concentration: 1000 ppm</u>			
Pre-exposure	2.247	0.85-4.19	1.406	4
30 min. post exit	6.38	5.10-9.07	1.817	4
<u>DAY 1, WEEK 4:</u>	<u>Chamber Concentration: Zero</u>			
30 min. post exit	1.367	1.14-1.87	0.338	4
<u>DAY 5, WEEK 4:</u>	<u>Chamber Concentration: 1250 ppm</u>			
Pre-exposure	3.742	2.05-5.87	1.617	4
30 min. post exit	6.532	5.77-7.30	0.655	4
<u>WEEK 5:</u>	<u>Chamber Concentration: Zero</u>			
<u>Day 4, WEEK 6:</u>	<u>Chamber Concentration: Fluctuating 750-1250 ppm</u>			
Pre-exposure	2.717	1.86-4.43	1.484	3
30 min. post exit	5.983	3.81-8.38	2.293	3
<u>DAY 5, WEEK 6:</u>	<u>Chamber Concentration: Zero</u>			
30 min. post exit	0.743	0.57-0.95	0.192	3

TABLE IV (Continued)

## ACETONE CONCENTRATIONS IN RANDOM URINE FOR MALE SUBJECTS

GROUP II - 3 Hr. Exposure

	<u>Mean</u> <u>(in mg%)</u>	<u>Range</u> <u>(in mg%)</u>	<u>+ Standard</u> <u>- Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 1, WEEK 1:</u>	<u>Chamber Concentration: Zero</u>			
<u>DAY 5, WEEK 2:</u>	<u>Chamber Concentration: 200 ppm</u>			
Pre-exposure	2.237	1.64-2.80	0.475	4
30 min. post exit	2.257	1.67-2.89	0.499	4
<u>DAY 1, WEEK 3:</u>	<u>Chamber Concentration: Zero</u>			
30 min. post exit	0.99	0.96-1.01	0.26	3
<u>DAY 5, WEEK 3:</u>	<u>Chamber Concentration: 1000 ppm</u>			
Pre-exposure	1.35	0.86-1.84	0.693	2
30 min. post exit	2.53	2.06-3.00	0.665	2
<u>DAY 5, WEEK 4:</u>	<u>Chamber Concentration: 1250 ppm</u>			
Pre-exposure	1.275	1.17-1.38	0.148	2
30 min. post exit	3.11	2.72-2.50	0.552	2
<u>DAY 1, WEEK 5:</u>	<u>Chamber Concentration: Zero</u>			
30 min. post exit	1.35	0.93-1.77	0.594	2
<u>DAY 4, WEEK 6:</u>	<u>Chamber Concentration: Fluctuating 750-1250 ppm</u>			
Pre-exposure	0.903	0.62-1.14	0.263	3
30 min. post exit	3.95	2.90-4.76	0.953	3
<u>DAY 5, WEEK 6:</u>	<u>Chamber Concentration: Zero</u>			
30 min. post exit	1.17	0.67-1.67	0.707	2

TABLE IV (Continued)  
ACETONE CONCENTRATIONS IN RANDOM URINE FOR FEMALE SUBJECTS

GROUP I - 7 1/2 Hr. Exposure

	<u>Mean</u> (in mg%)	<u>Range</u> (in mg%)	<u>+ Standard</u> <u>- Deviation</u>	<u>Number of</u> <u>Subjects</u>
<u>DAY 1, WEEK 1:</u>	<u>Chamber Concentration: Zero</u>			
Pre-exposure	1.353*	0.95 - 1.89	0.484	3
<u>DAY 5, WEEK 1:</u>	<u>Chamber Concentration: 1000 ppm</u>			
	(1.1)	(1.0 - 1.2)	(0.141)	(2)
Pre-exposure	2.857*	1.0 - 6.37	3.044	3
30 min. post exit	9.513	7.85 - 11.79	2.040	3
<u>DAY 1, WEEK 2:</u>	<u>Chamber Concentration: Zero</u>			
Pre-exposure	1.162	0.8 - 1.5	0.286	4

GROUP II - 3 Hr. Exposure

<u>DAY 1, WEEK 1:</u>	<u>Chamber Concentration: Zero</u>			
Pre-exposure	0.898	0.43 - 1.42	0.405	4
<u>DAY 5, WEEK 1:</u>	<u>Chamber Concentration: 1000 ppm</u>			
Pre-exposure	1.06	0.96 - 1.16	0.141	2
30 min. post exit	4.623	3.19 - 5.45	1.246	3
<u>DAY 1, WEEK 2:</u>	<u>Chamber Concentration: Zero</u>			
Pre-exposure	1.017	0.59 - 1.3	0.376	3

GROUP III - 1 Hr. Exposure

<u>DAY 1, WEEK 1:</u>	<u>Chamber Concentration: Zero</u>			
Pre-exposure	0.75	0.47 - 1.03	0.396	2
<u>DAY 5, WEEK 1:</u>	<u>Chamber Concentration: 1000 ppm</u>			
Pre-exposure	0.835	0.71 - 0.96	0.177	2
30 min. post exit	2.38	2.26 - 2.5	0.17	2
<u>DAY 1, WEEK 2:</u>	<u>Chamber Concentration: Zero</u>			
Pre-exposure	1.515	0.58 - 2.45	1.322	2

\*One subject had positive acetone in the urine.



TABLE V

THE SUMMED AMPLITUDE OF THE 2,3,4,5 - COMPLEX OF THE VER  
DURING MALE EXPOSURE TO ACETONE

Date: Day	Concentration ppm	#169 - - -	#229 Mean of Total	#230 Amplitude	#231 - - -
Control	0	52.5	82.70	31.49	46.76
11/6/74, W	200	58.58	86.77	39.39	50.19
11/8/74, F	200	--	--	33.33	43.83
11/11/74, M	0	49.08	81.45	35.42	42.00
11/13/74, W	1000	--	96.78	41.78	43.25
11/15/74, F	1000	38.58	90.00	39.25	41.75*
11/18/74, M	0	66.67	74.43	41.63	49.67
11/20/74, W	1250	53.67	96.56	45.75*	58.33
11/22/74, F	1250	57.33	100.89*	53.00*	55.92
11/25/74, M	0	--	78.67	42.89	54.42
12/2/74, M	0	--	71.33	45.42	55.11
12/4/74, W	1000 fluc	--	48.78*	37.11	52.58
12/6/74, F	0	--	82.78	41.31	52.08

\*.05 Level of Significance

TABLE VI

THE SUMMED AMPLITUDE OF THE 2,3,4,5 - COMPLEX OF THE GROUP VER  
DURING MALE EXPOSURE TO ACETONE AND PAIRED-T TEST

Date	Concentration ppm	t	Mean Amplitude	df
Control	0	-	53.36	-
11/6/74, W	200	-5.292	58.73	3
11/8/74, F	200	.229	N/A	1
11/11/74, M	0	.720	51.99	3
11/13/74, W	1000	-1.301	60.60	2
11/15/74, F	1000	.185	52.40	3
11/18/74, M	0	-.963	58.10	3
11/20/74, W	1250	-3.324*	63.58	3
11/22/74, F	1250	-3.464*	66.79	3
11/25/74, M	0	-1.078	58.66	2
11/2/74, M	0	-.474	57.29	2
12/4/74, W	1000 fluc	.567	46.16	2
12/6/74, F	0	-1.803	58.72	2

\*.05 Level of Significance

TABLE VII

THE SUMMED AMPLITUDE OF THE 2,3,4,5 - COMPLEX OF THE VER  
DURING FEMALE EXPOSURE TO ACETONE

Date: Day	Concentration ppm	#237 - - -	#238 Mean of Total	#239 Amplitude	#240 - - - - -
12/9/74, M	0	50.60	58.20	57.89	51.58
12/11/74, W	1000	47.47	45.13	57.45	54.58
12/13/74, F	1000	42.67*	62.60	66.67	--
12/16/74, M	0	47.67	54.93	49.89	45.17

\*.05 Level of Significance

FEMALE ACETONE EXPOSURE

FIGURE 13

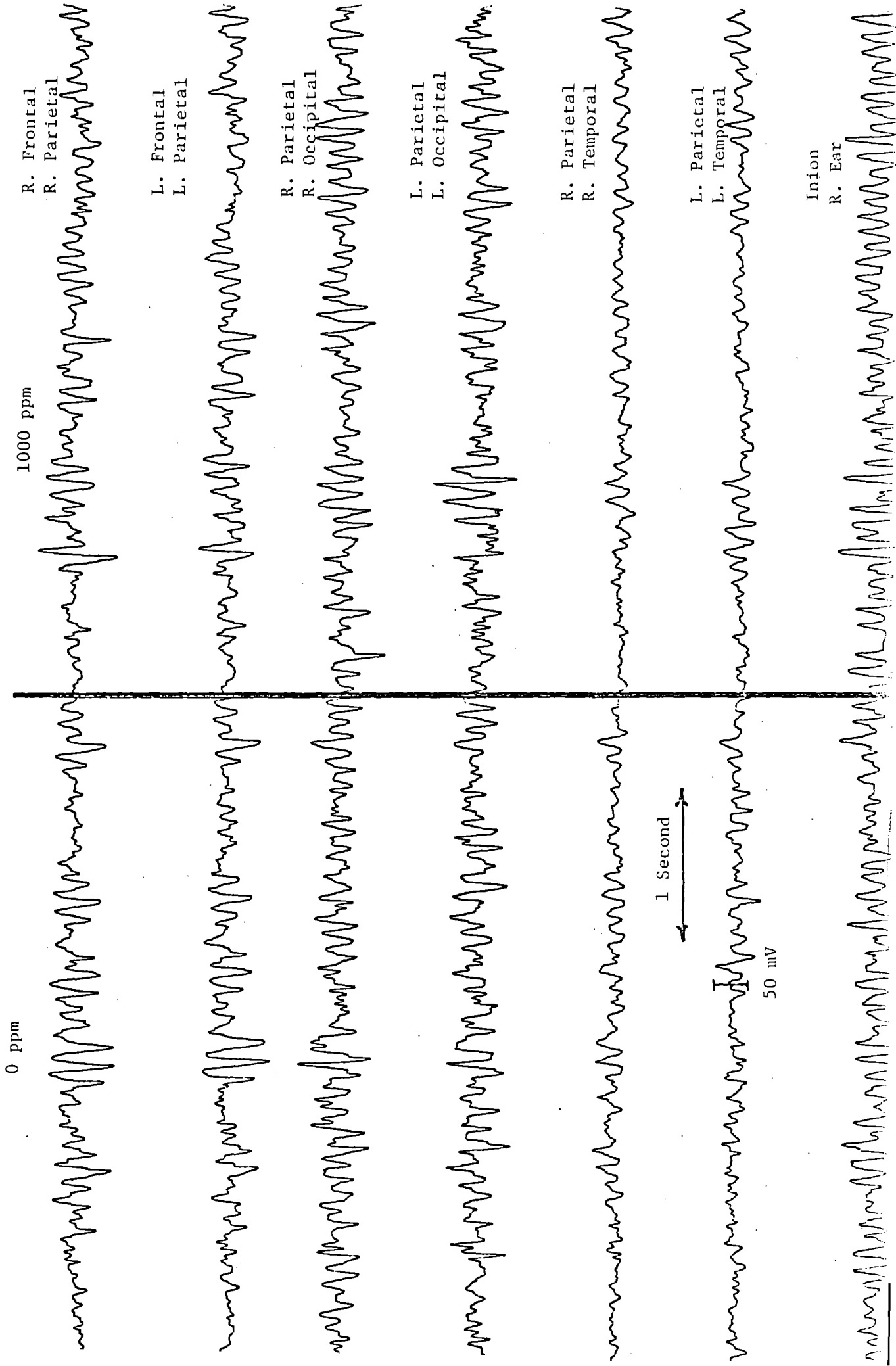


FIGURE 14

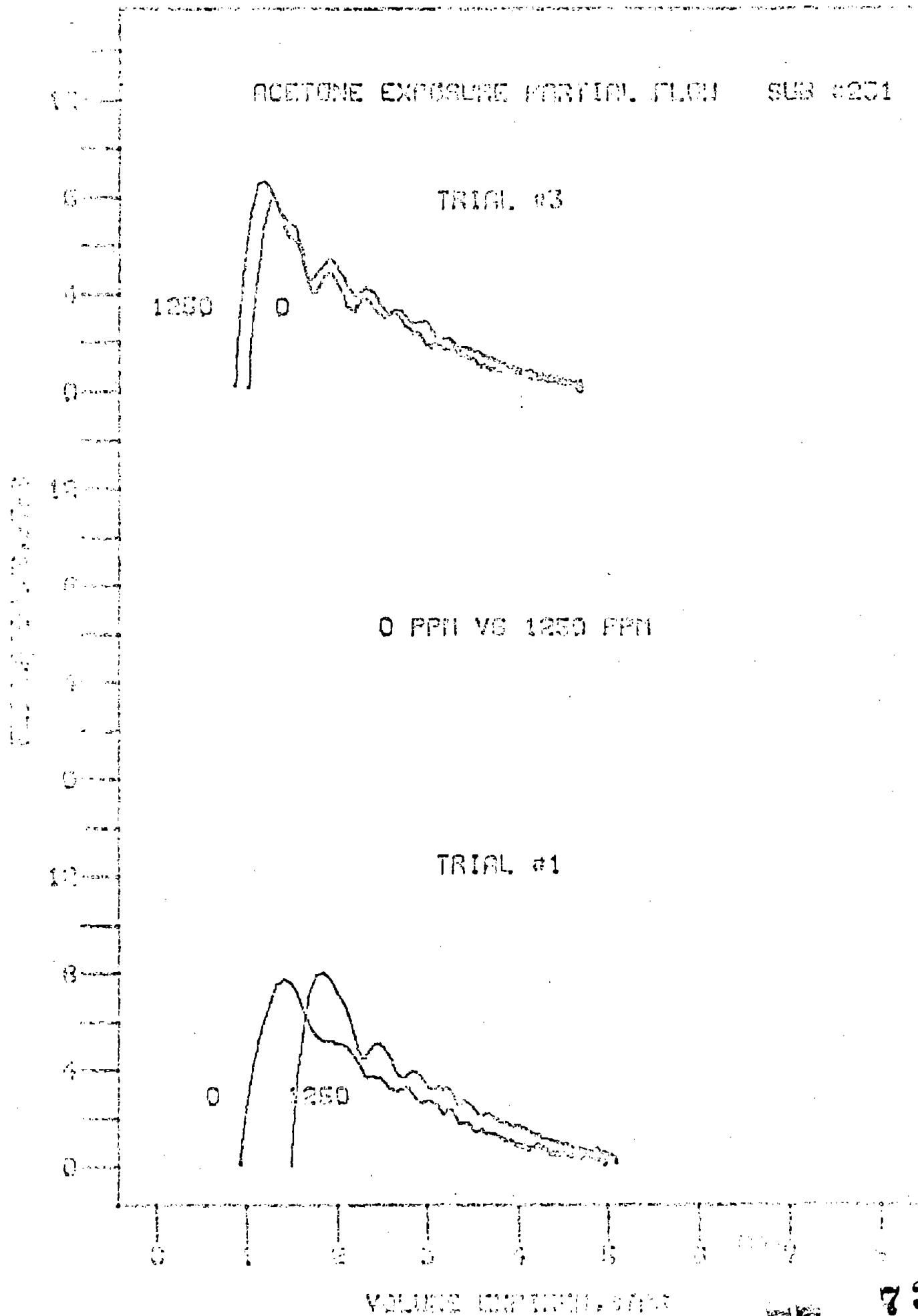


FIGURE 15

THE EFFECT OF EXPOSURE (7-1/2 HRS/DAY) TO ACETONE ON THE COORDINATION TEST

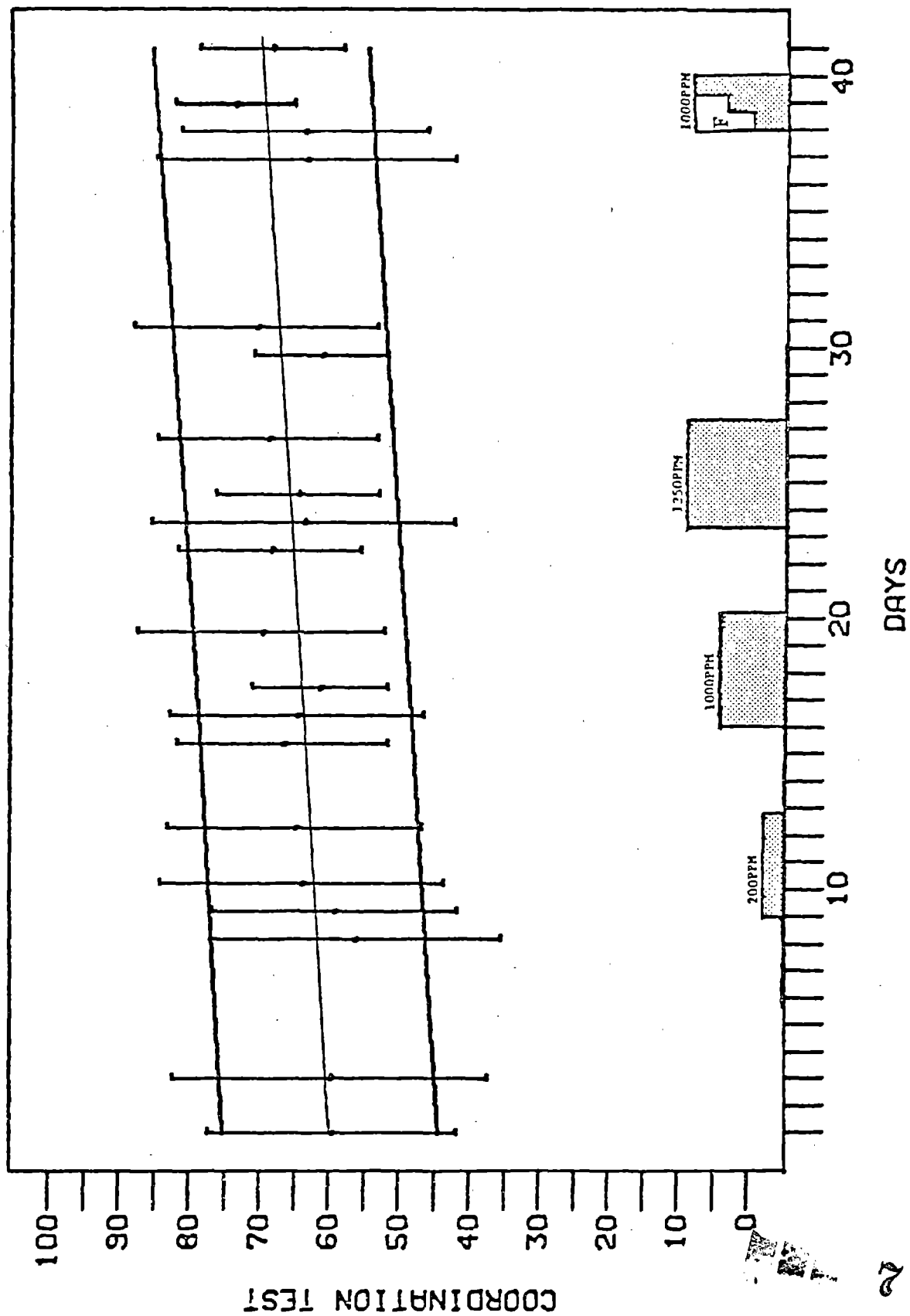


FIGURE 16

THE EFFECT OF EXPOSURE (7-1/2 HRS/DAY) TO ACETONE ON THE INSPECTION TEST

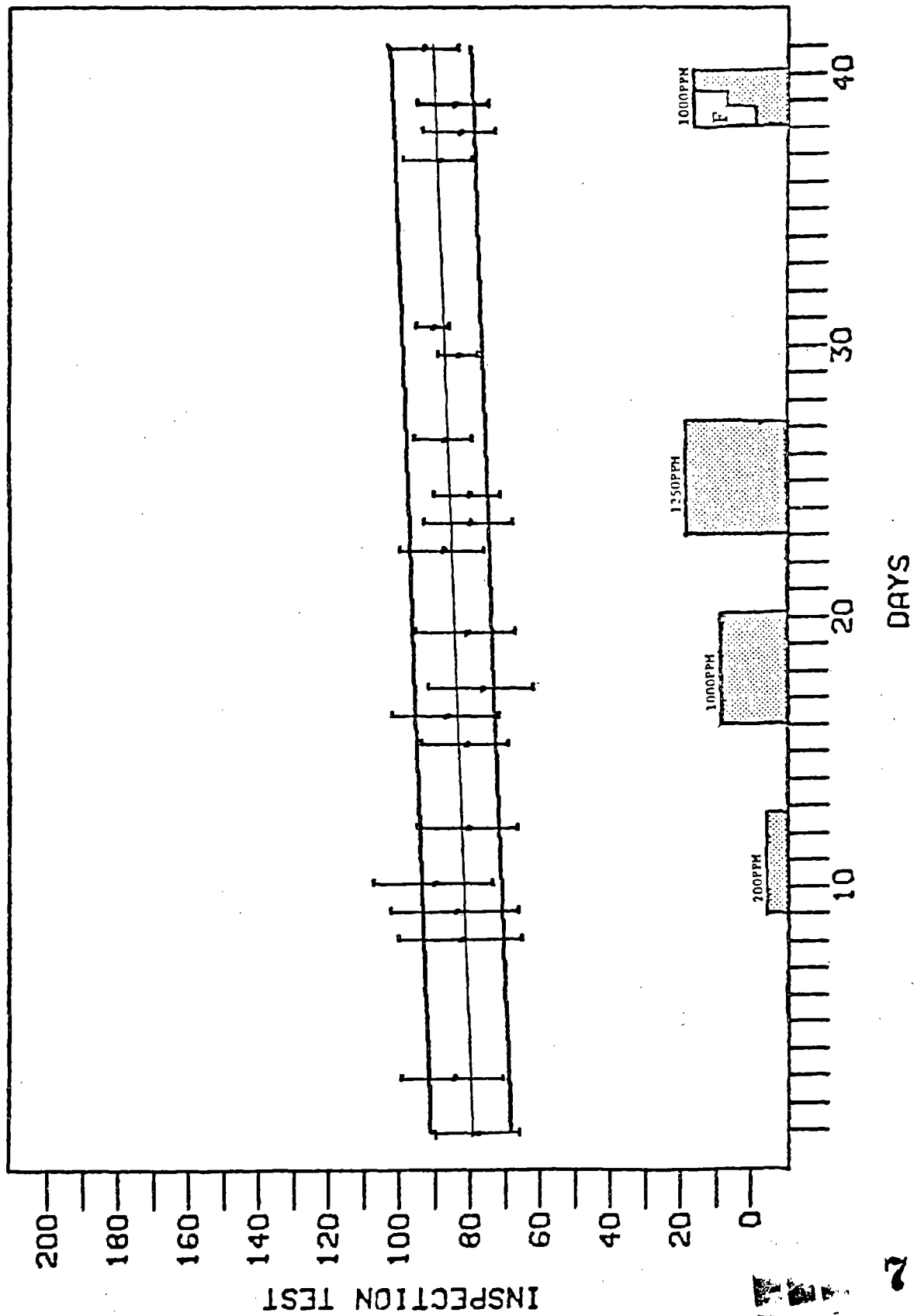


FIGURE 17

THE EFFECT OF EXPOSURE (7-1/2 HRS/DAY) TO ACETONE ON THE ARITHMETIC TEST

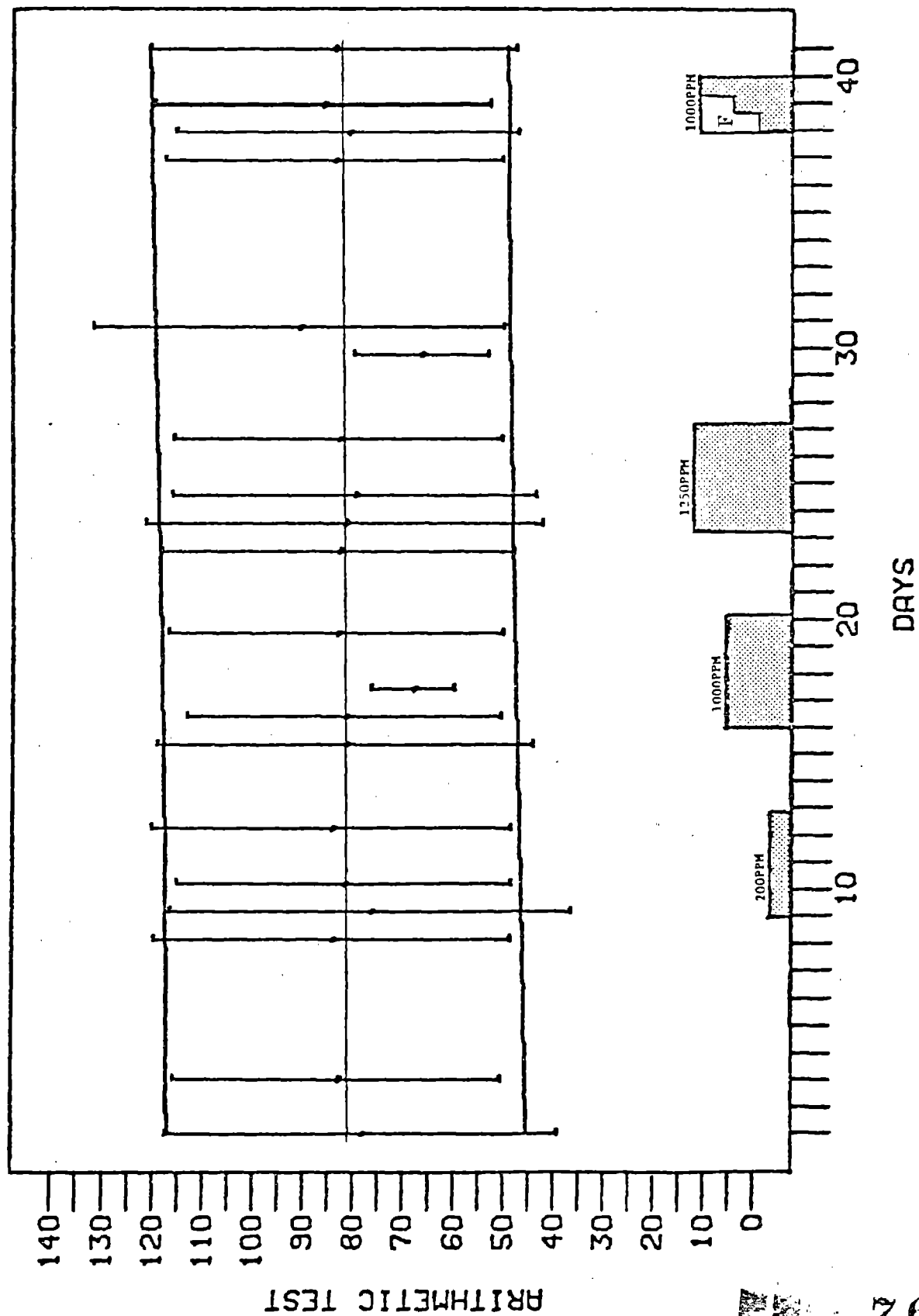
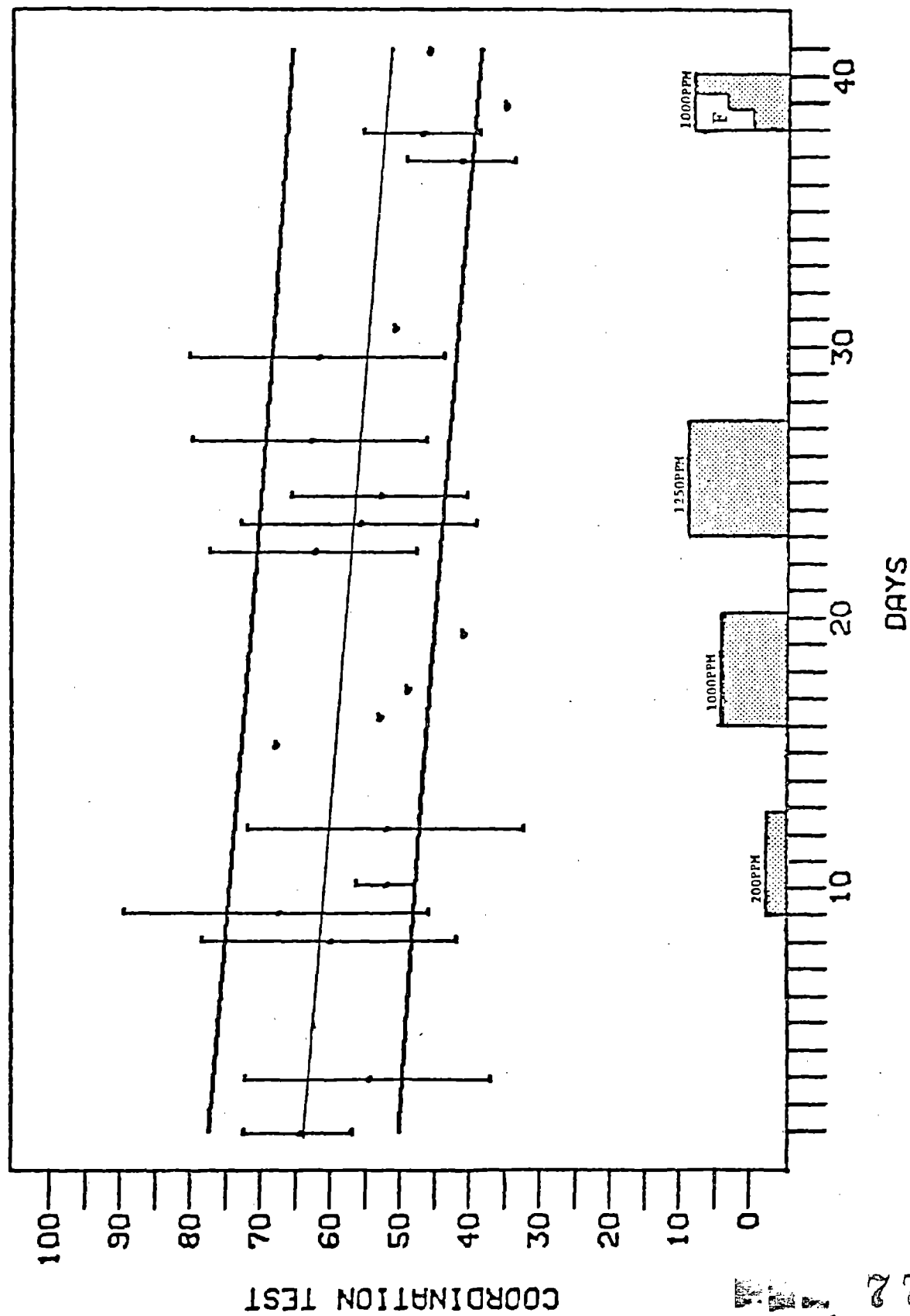




FIGURE 18

THE EFFECT OF EXPOSURE ( 3 HRS/DAY) TO ACETONE ON THE COORDINATION TEST



THE EFFECT OF EXPOSURE (3 HRS/DAY) TO ACETONE ON THE INSPECTION TEST

FIGURE 19

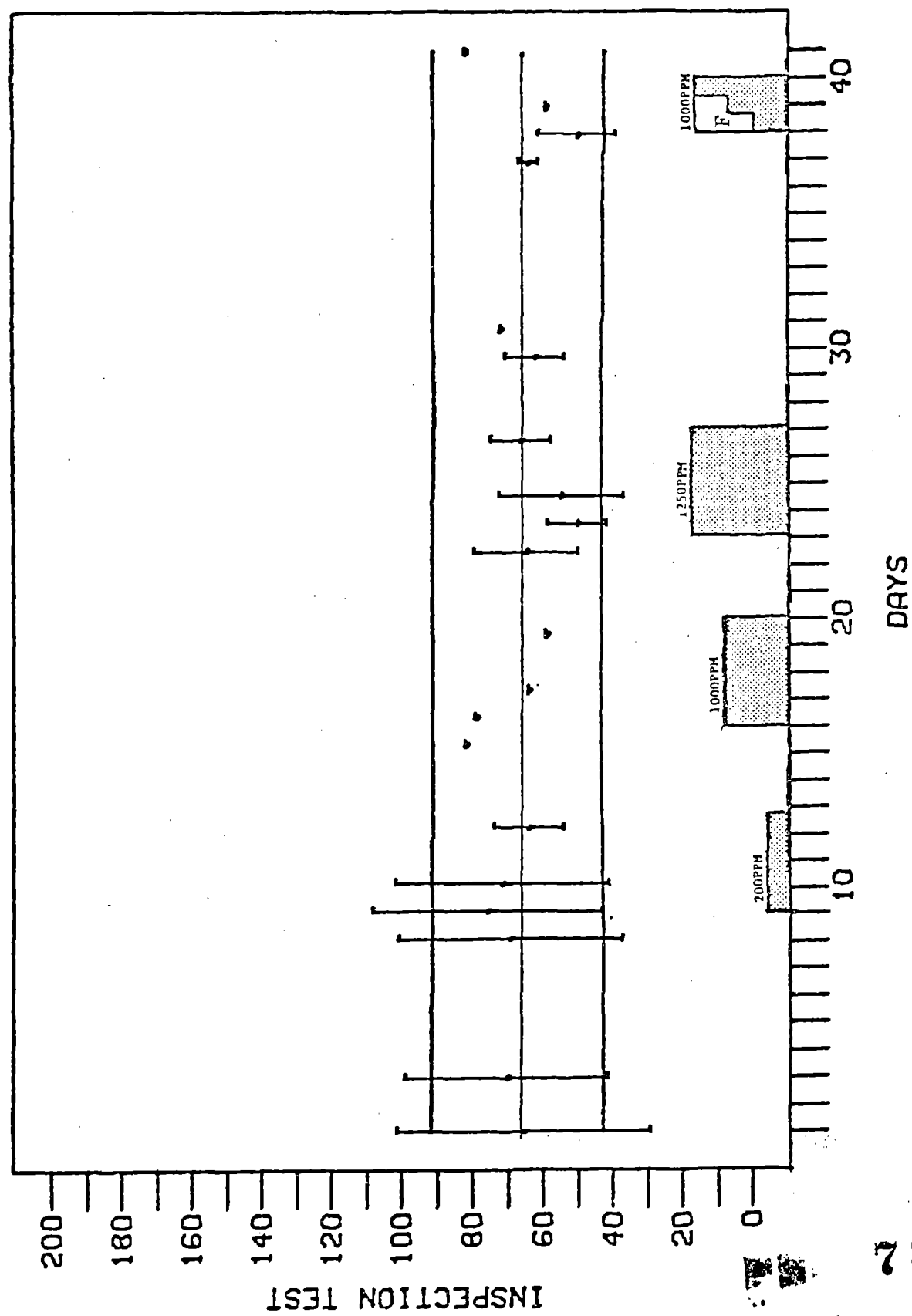


FIGURE 20

THE EFFECT OF EXPOSURE (3 HRS/DAY) TO ACETONE ON THE ARITHMETIC TEST

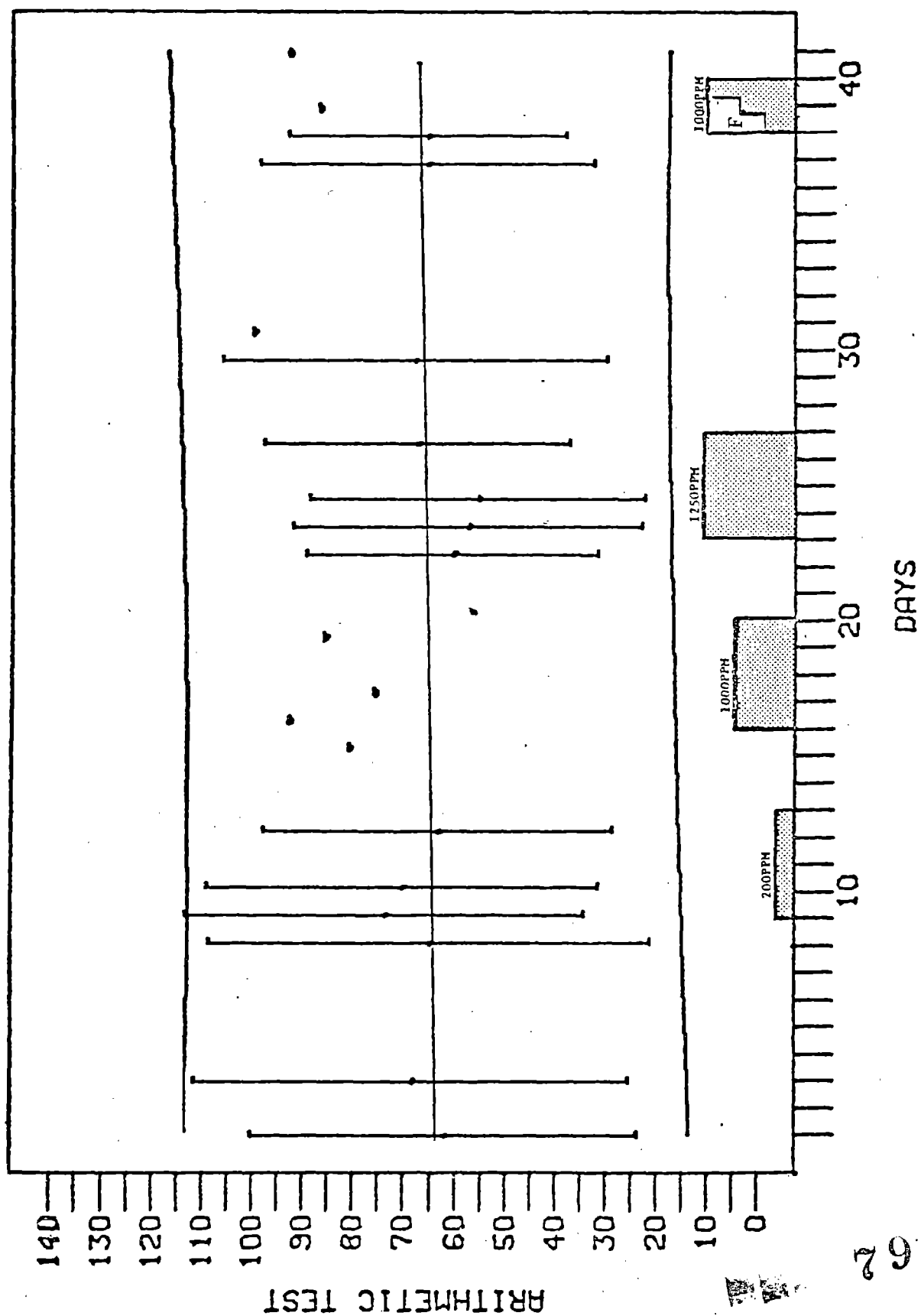


TABLE XIII

## TREND ADJUSTED t-TESTS

## 7-1/2 HOUR EXPOSURE

<u>TEST</u>	<u>0 PPM</u>	<u>200 PPM</u>	<u>1000 PPM</u>	<u>1250 PPM</u>
Arithmetic	0/9*	0/3	0/5	0/3
Coordination	0/9	0/3	0/5	0/3
Inspection	0/9	0/3	0/5	0/3

## 3 HOUR EXPOSURE

<u>TEST</u>	<u>0 PPM</u>	<u>200 PPM</u>	<u>1000 PPM</u>	<u>1250 PPM</u>
Arithmetic	0/9*	2/3	0/5	1/3
Coordination	0/9	0/3	0/5	0/3
Inspection	0/9	0/3	0/5	0/3

\*Number Significant ( $p \leq .05$ )/number of testing days