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EFFECTS OF PERCHLOROETHYLENE/DRUG INTERACTION ON BEHAVIOR AND NEUROLOGICAL FUNCTION

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ABSTRACT

Perchloroethylene (PCE, tetrachloroethylene) vapor is commonly found in the workers' environment in dry cleaning establishments and industrial degreasing operations. Since many of these workers are sometimes additionally exposed to drugs which might exacerbate any effects of PCE on the central nervous system, a study was conducted to evaluate the potential interaction of PCE and such drugs on the behavioral and neurological function of volunteer subjects.

Six volunteers of each sex were examined and found to be in good health both mentally and physically. Alcohol in the form of 100-proof vodka and a mild antidepressant in the form of diazepam were chosen as the two drugs to be added one at a time to the PCE vapor exposures. All high dose levels were selected on the basis of an expectant mild but measurable behavioral or neurological effect: 0, 25, or 100 ppm PCE; 0, 6, or 10 mg/day diazepam, and 0.0, 0.75, or 1.5 ml vodka/kg body weight. All exposures were replicated, and testing was performed in a double-blind mode. Biologic sampling and analysis confirmed the body burdens of PCE, ethanol, and diazepam during testing.

A battery of neurological and behavioral tests, comprised of the following, were administered at the peak blood levels of the drugs: Michigan eye-hand coordination, rotary pursuit, Flanagan coordination, saccade eye velocity, and dual-attention tasks. In the midst of these tests, the subjects completed the Lorr-McNair mood evaluation test. In addition, electroencephalograms were recorded for spectral density analysis during the exposures.

Data analysis revealed that subjects exhibited a decrement in performance of at least one test while on each drug alone at the highest dose level, but no interaction with PCE could be demonstrated in any test for either combination. In addition, there was no consistent effect of PCE alone on the EEG of any subject, as had been previously reported for a different group of subjects. These results lead us to conclude that under the conditions studied, which simulated worker exposures to PCE and the drugs diazepam or alcohol, the subjects demonstrated no decrements in neurological or behavioral performance that could be attributed to the addition of PCE exposure to drug consumption.

Decrements in performance of the Michigan eye-hand coordination, rotary pursuit, and Flanagan coordination tests due to alcohol consumption reinforce the known hazard of the use of this drug in the workplace. Decrements in performance associated with diazepam dosing were more subtle, with a significant effect on the performance of the rotary pursuit test only. A repeat finding of a slight but statistically significant detrimental effect upon the performance of the Flanagan coordination test at the highest level of PCE exposure was noted.

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INTRODUCTION

Perchloroethylene (PCE), chemically named tetrachloroethylene, is widely used in industry as a dry cleaning and degreasing agent. Its lipophilic character, stability, and relatively high boiling point of 121° C make it an ideal solvent for these uses as far as its physical properties are concerned. However, its pharmacologic property of central nervous system depression, or narcotic effect, requires that a value be set for the maximum time-weighted average exposure during which a worker inhaling its vapor can work safely and free from hazard. The documentation (American Conference of Governmental Industrial Hygienists, 1971) for setting the Threshold Limit Value (TLV) for PCE in workroom air at 100 ppm suggests that this concentration will prevent serious narcotic effect. More recent work from this laboratory (Stewart, et al., 1974) suggests that the margin of safety of this TLV is rather minimal, even in sedentary workers, if coordination tests and subjective EEG analysis of volunteer subjects are used as criteria for measuring narcotic effect. The question then arises as to the degree of hazard the workman presents to himself and others if the effect of another "depressant" is added to any central nervous system depression experienced as a result of the TLV (OSHA standard) exposure to PCE vapor. The objective of this study was to answer this question in a laboratory setting.

Ethanol, in the form of alcohol in commercial vodka, was chosen as a central nervous system "depressant" which is sometimes consumed by workers and therefore could increase the hazard of simultaneous exposure to PCE. A second "depressant" drug chosen to be given during PCE exposures was diazepam (VALIUM® - Roche). It is widely prescribed on an outpatient basis for relief of tension and anxiety (Roche Laboratories, 1975) and thus is also available to workers exposed to PCE. Obviously there are several other drugs that are general depressants of the central nervous system (Levine, 1973), but these two were the best candidates for this study because of their widespread use and their predictable action. They were given singly, and in combination with PCE exposure, but never in combination with each other.

Volunteer subjects of both sexes were recruited from the general population, and after it was determined that they were medically, physically, and neurologically healthy, they were asked to participate in biochemical, behavioral, and neurological testing while being exposed to no chemicals, PCE alone at two concentrations, ethanol alone at two dose levels, PCE plus ethanol, both at two levels, diazepam medication alone at two levels, and PCE plus diazepam medication, both at two levels.

The Occupational Safety and Health Agency (OSHA) standard of 100 ppm was chosen as the maximum PCE exposure level, and, in order to equilibrate the body burden rapidly rather than over several hours, subjects exercised

moderately (approximately 50W) on bicycle ergometers for 1/2-hr early in each exposure day. The lower level of exposure chosen, wherein no depressant effect would be expected yet the odor would be detected, was 25 ppm PCE (Stewart, et al., 1974). The two dosages of vodka, given as approximately 10 to 20% in juice, were selected for each subject individually by a physician. The desired blood alcohol levels were 40 and 80 mg/dl, the lower level selected to assure an alcohol taste in the "cocktail", and the upper level one after which the subjects would not be inebriated to the point of being ill. These levels were attained with dosages of approximately 0.75 and 1.50 ml 100-proof vodka/kg body weight. Diazepam dosages of 6 and 12 mg/day were originally selected as no-effect and low-effect doses for this medication (Roche Laboratories, 1975). When it was found that the 6 mg/day (2 mg t.i.d.) may have caused measurable central nervous system depression, the high dose was reduced by the attending physician to 10 mg/day (5 mg b.i.d.).

The original schedule for the repeated exposures to the PCE, alcohol, diazepam, and combinations is shown in Table I. As required for any behavioral testing, control and high dose exposures were replicated in order to make it possible to estimate any interactive effect on a statistically reliable basis (Crow, Davis, and Marfield, 1960). The procedures used for testing are described in detail in the following section on METHODOLOGY. In the subsequent section on TEST CONDITIONS, the conditions that existed as the subjects underwent behavioral and neurological testing are described, while the next section reveals the results of this testing. The final section, entitled DISCUSSION, assimilates the results of the many tests carried out and puts them into a proper perspective regarding the overall CONCLUSIONS of the study.

METHODOLOGY

SUBJECTS

Recruitment of volunteer subjects was carried out by placing a notice in the College's What's Happening sheet, contacting former subjects, and by a commercial temporary help organization. Prospective volunteers were briefly informed of the purposes and terms of the study and then given comprehensive medical examinations. This examination included the following: the completion of a health questionnaire by the prospective subject; a history and physical examination completed by the examining physician; an ORTHO-RATER visual performance profile; a 12-lead electrocardiogram; a neurological examination including cranial nerves, muscles, reflexes, gait, alternating motor rate, and coordination, by the physician; a complete blood count; a urinalysis (COMBISTIX® - Ames); a pregnancy test (PREGNOSIS) for females; and a battery of clinical chemistries (CHEM-SCREEN-25, Medpath, Inc., including calcium, phosphorus, BUN, creatinine, BUN/creatinine ratio, glucose, uric acid, total protein, albumin, A/G ratio, SGOT, SGPT, LDH, total bilirubin, direct bilirubin, alkaline phosphatase, gamma glutamyl-trans-peptidase, amylase, sodium, potassium, chloride, cholesterol, beta-lipoproteins, total lipids, and thymol turbidity).

Prospective subjects who were found to be physically fit for the study by the passing of the comprehensive medical examination were then oriented more completely by a faculty member regarding the purpose, procedures, risks, benefits, and alternatives of this study. In addition, they were told that they could withdraw from the study without prejudice at any time. Each prospective subject received a compilation of printed information. They were encouraged to ask questions if there were unresolved problems. They were then asked to complete the Informed Consent Questionnaire (Appendix I) and NIOSH Participant Document giving informed consent. All volunteers participated in a pulmonary function test (computerized expirogram) and neurological test (electroencephalogram) before the exposures began in order to obtain their baseline values.

The health of each subject was continually monitored with daily, brief medical examinations prior to exposure, including blood pressure, temperature, subjective signs or symptoms, numbers of hours sleep the previous night, alcohol consumption since the previous exposure, and urinalysis (COMBISTIX® - Ames), and with weekly complete blood counts and clinical chemistries (CHEM-SCREEN-25). Whenever any out-of-normal range values appeared, additional testing was carried out as necessary.

The electrocardiogram (EKG) of each subject was monitored intermittently while in the chamber and continuously while exercising. This was

accomplished with telemetered lead II EKGs using SPACELABS, INC. Biotel 170 transmitters and receiver/cardiotachometers, and a single channel recorder for permanent recordings.

Subjects were paid weekly for the total number of hours spent at the laboratory. At the end of the study, each subject who had completed the study was paid a bonus.

EXPOSURE LEVELS

The exposures to PCE were conducted in a controlled-environment chamber 6.1 x 6.1 x 2.4 m in size, which was adjoined by a 1 x 1.5 x 2.4 m toilet facility and a 2.1 x 2.3 x 2.4 m 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 own independent air handling system and all outside doors were self-sealing when closed. Air flow through the complex was approximately 42 cu m 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 21-22° C while relative humidity ranged between 45-55%. The PCE 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 (MODERN METALCRAFT) maintained a steady flow of liquid PCE into the flask. A manually operated set of coordinated valves in the air handling system was used to control the concentration of PCE in the chamber atmosphere. This concentration was continuously recorded by an infrared spectrometer (MIRAN I, Wilks Scientific Corporation) equipped with a 20-m path-length gas cell which was continuously flushed with air drawn from the chamber through a 6.35-mm diameter polyethylene tubing. The absorbance at 10.9 μ was measured through a path-length of 5.25 m. The infrared signal to the recorder was monitored each second by an on-line PDP-12 (Digital Equipment Corp.) computer, which displayed the mean vapor concentration, as compared to standards, for each 30-sec time interval of exposure and calculated the daily time-weighted average exposure for each individual subject. Calibration standards of PCE in purified air were prepared in saran bags and analyzed before and hourly during each daily exposure.

A second independent chamber monitoring system using the gas chromatograph (GC) as the measuring instrument was used for back-up of the infrared system. The GC system was equipped with an automatic sampling device that swept a sample of the chamber atmosphere into the carrier gas (N_2) of the chromatograph every three min. The Varian Aerograph Model 900 GC was fitted with a stainless steel column, 36 x 0.32 cm, packed with Porapak Q, 60/80 mesh. The column was preconditioned at 200° C for 24 hr prior to its use. Throughout the study, the column was kept at 180° when it was not in use. The operating conditions of the GC were: carrier gas flow rate of 35 ml/min, column temperature, 180° C; injection port, 150° C; and flame ionization detector, approximately 250° C. Peak heights of chamber atmosphere samples were compared to peak heights of calibration standards prepared in saran bags and swept through the system from the chamber. Calibration standards were prepared independently by two individuals, and the measured concentrations of PCE in the

chamber atmosphere by the two monitoring systems had to agree before subjects were allowed to enter the chamber. The two systems were cross-checked frequently during daily exposure to assure that the concentration in the chamber was correct.

A commercial vodka (SMIRNOFF, 100-proof) was added by measuring cylinder to a partial cup of juice (tomato or orange, subject's choice) to give a final ethanol concentration of approximately 20% in each "cocktail". Ice was added. The total dose of ethanol was divided equally between two "cocktails", each given to the subjects for sipping over a 15-min period. On all non-alcohol days, the vodka was replaced with juice.

The diazepam (VALIUM^{R}) dosage and placebo in capsule form were prepared by a registered pharmacist. A number of 2-mg tablets of VALIUM were ground in a mortar and pestle and refilled into an equal number of gelatin capsules for the low dose of 6 mg/day (2 mg t.i.d. at mealtime). Placebo for this dose level was prepared by filling corn starch powder into the same size gelatin capsules. The subjects were given sufficient capsules containing either the diazepam or placebo each Friday afternoon to start dosing that evening and continue through the weekend. Then on Monday morning they were each given an additional number of capsules to last through the week to Friday noon. During the exposure days, the second capsule of the day was consumed with the first glass of juice rather than with lunch. After the first week of study with diazepam at 6 mg/day and resultant drowsiness in some subjects, the decision was made by the physician to reduce the high dose from 12 to 10 mg/day. The Pharmacist prepared 5-mg capsules (5 mg b.i.d.), and similar corn starch placebos, which the subjects were advised to take at breakfast and supper, except for the exposure days when they took the second capsule with the juice while in the chamber. As will be noted in the schedule later, this dose was given to subjects an hour prior to behavioral testing.

EXPOSURE SCHEDULE

As shown in the original schedule (Table I), exposures were to take place over eleven weeks during a three-month period. The timing of the plan required that this schedule be carried out between October 1 and December 25, and allowed only the Thanksgiving week for possible repeats. Fortunately, a minimum of repeats was required. Some of the testing equipment, specifically that for the electroencephalograms, saccade velocity test, and dual-task test, was not totally operable during the first three weeks of the schedule. Because Week 1 was a training week, and Week 2 was scheduled to be repeated as Week 6, these were no problem. Only Week 3 needed to be repeated, and this was accomplished (see Table II) by moving Week 12 to Week 9, moving Week 11 to Week 12 and repeating Week 3 as Week 11.

BIOCHEMICALS

Breath samples were obtained from subjects by the 30-sec breath-holding technique, with subsequent collection of the alveolar breath in SARAN film bags (Stewart, Hake, and Wu, 1976). When collected in the chamber,

care was taken to exclude chamber air. The breath samples were analyzed for PCE, and ethanol when needed, on the same day as collected.

A Varian Aerograph Model 2700 gas chromatograph (GC) equipped with a hydrogen flame ionization detector was used to measure the PCE and ethanol in aliquots removed from the breath bags by syringe. The GC was fitted with a stainless steel column, 1.8 m x 0.32 cm, packed with FFAP on Chromosorb W, 80/100 mesh. The column was preconditioned at 200° C overnight prior to use. The operating conditions of the GC were: helium carrier gas flow rate of 40 ml/min; column temperature, 100° C; injection port temperature, 210° C; and detector temperature, 220° C. Standards at a minimum of three concentrations of PCE, and ethanol when needed, were prepared daily in purified air. A single 1-ml injection was normally made from each breath bag, except when overlapping or poor peaks were encountered. The concentrations of the PCE and ethanol were obtained by direct comparison of peak heights to standards, and were reported in ppm (volume per volume).

All blood samples were withdrawn with Vacutainer^{R} tubes from antecubital veins, filling the tube to equalize the inner pressure to atmospheric. A 2-ml aliquot was removed and introduced into a 40-ml capped (Saran film liner) glass vial containing 1 ml aqueous solution of 1 ppm ethyl benzene as internal standard for PCE, and 50 mg/dl isopropyl alcohol as internal standard for ethanol when needed. The mixture was shaken and warmed to 37° C in a water bath. Two 1-ml aliquots of the headspace were removed for PCE analysis, using the same GC and conditions as for the breath samples. The blood ethanol was assayed by removing two 1-ml aliquots from the head space of the vial and injecting into a second GC with a Porapak Q, 60/80 mesh column. The operating conditions for this GC were slightly different with a column temperature of 180° C; injection port, 180° C; and detector, 250° C. A second GC was needed for the ethanol assay because of the much higher concentration of this volatile in the blood. Calibration curves (peak height ratio of PCE or ethanol to appropriate internal standard versus concentration) were prepared daily. The concentration of PCE and ethanol in the unknown were obtained directly from the calibration curves and reported as ppm (by weight, assuming sp. gr. of blood equals one) of PCE and mg/dl of ethanol.

The method of Garriott (1975) was followed for the analysis of diazepam in blood. Five ml of blood was assayed in duplicate for this medication. The procedure involved an extraction with n-butyl chloride from blood made basic with conc. ammonium hydroxide, re-extraction into aqueous HCl, and final extraction by chloroform from the alkalinized aqueous solution. Aliquots of the chloroform extract were injected into a GC and peak heights were compared directly to standards. Diazepam blood levels were reported in µg/dl.

BEHAVIORAL

Behavioral testing was carried out immediately upon entry into the chamber (saccade velocity and Michigan eye-hand coordination) and again 50 min after exercise (complete battery). The Michigan eye-hand

coordination, rotary pursuit, and Flanagan coordination tests were carried out in the environmentally-controlled chamber, but they were separated by carrel walls or a curtain, while the saccade velocity and dual-attention tasks tests were carried out in isolation in the shielded room adjacent to the chamber.

The Michigan eye-hand coordination test was developed by Pook (1967). The hardware consisted of a flat, eight-inch square board with 119 0.32-cm diameter holes which were connected by a zig-zag line (see Figure 1). The subject, following the line from start to finish, placed a stylus to the bottom of each hole as rapidly as possible. Timing with an electrical stop clock was started with the withdrawal of the stylus from the S hole, and the elapsed time to the insertion into the F hole was recorded. A subject who missed a hole in the zig-zag line was required to start over. Each session consisted of four trials from which the elapsed times were totaled for that session's score. The instructions for the staff person giving the test are given in Appendix II. Each session took approximately 5 min to complete and record the testing.

The rotary pursuit test was carried out with a photoelectric rotary pursuit apparatus with a circular template (Lafayette Instrument Co., Model 30013). In this test, the subject, standing at a comfortable distance from the table on which the apparatus was placed, was required to follow the light in its horizontal, clockwise, circular path on the top of the apparatus with a wand containing an electric eye. The wand was held in the hand used for writing. The sensitivity setting of the light was always at 10 units. After a 30-sec warm-up at 10 rpm, the subject "pursued" the light for 45-sec intervals at 15, 30, 45, and 60 rpm. The apparatus measured the time-off target in hundreths of a second, and the "errors" or number of times off and back on the target, during each 45-sec trial. The staff operator recorded these numbers for each 45-sec interval. The instructions for the staff persons giving the test are given in Appendix III. Each session took approximately 5 min to complete and record the testing.

The Flanagan coordination test used is published by Science Research Associates, Inc., 259 E. Erie St., Chicago (Flanagan Aptitude Classification Test, 7A, Coordination). This test required that the subject rapidly follow a spiral pathway (see Figure 2) with a pencil, touching the sides of the pathway as few times as possible. The staff operator started each trial with the words "pencil down, ready, begin." The subject was allowed 40 sec to complete each of six spirals. The first two were considered practice and the last four 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. Scoring was carried out by visual inspection of each spiral, and though done by several staff persons, the same person scored all of the tests for a given subject throughout the entire study.

The saccade velocity test, which used electrooculography (EOG), was furnished by NIOSH. The design was based upon work by Dr. Robert Baloh and associates at UCLA (1976). Horizontal eye movements were

differentially recorded from electrodes fixed lateral to both outer canthi and to the forehead for reference ground while the subject's head was mechanically fixed using a bite bar. The stimulus used to elicit eye movement was a semi-circular array of 32 small red lights, 15 cm apart, arranged on a black plywood stand and approximately 76 cm from the subject's eyes. A programmable digital-logic system was used to control the lighting of the stimuli, and a FM tape recorder was used to record the amplified electrooculogram. This test was carried out in a completely isolated, weakly lit room adjacent to the chamber, with the subject only required to stay alert and turn the eyes to the red stimulus light as rapidly as possible. This test required approximately 5 min.

The dual-attention tasks test used the same room and equipment setting as the saccade velocity test. The semicircular array of red lights included one white light at the center of the arc directly in front of the subject. The two tasks, as reported by Moskowitz and Sharma (1974), were differentiated by the blinking or non-blinking of the white light. The blinking task required that the subject count the random number of times the white light blinked, and release a hand-held microswitch as rapidly as possible when a peripheral red light appeared (1 sec duration). A tone signaled the start and the stop of each trial, and there were ten trials in each session. Programmed equipment allowed the center white light to blink randomly 11 to 19 times during each 20-sec trial, and a peripheral red light to light at random two to four times. Timing instrumentation recorded the red light response time, and the subject entered the number of blinks of the white light on a 10-digit keyboard. The non-blinking white light task simply required the subject to release the hand-held microswitch as rapidly as possible when a peripheral red light came on, meanwhile focusing the eyes on the white light. Again, the peripheral red lights appeared two to four times over each of ten 20-sec trials. The timing instrument recorded the response time. The total elapsed time for this test was approximately 10 min.

NEUROLOGICAL

Within five min of entry into the environmental chamber, and within ten 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 1.5 m. This was first done with the eyes open and then repeated with eyes shut. A staff person, viewing the performances from outside the chamber, recorded each subject's performance as +, ±, or -.

For the spontaneous electroencephalagrams (EEGs), the subject sat upright in a comfortable recliner chair with a back high enough to fully support the head and neck. The chair was located in isolation in the shielded room adjacent to the chamber. There was no room lighting during the tests. The EEGs were recorded on an eight-channel GRASS Model 7 polygraph using gold-plated silver electrodes oriented on the scalp according to the 10-20 International System (Jasper, 1958). The

leads utilized and their corresponding electrode geometry are shown in Figure 3.

The first four channels listed in Figure 3 were linked to the analog/digital converters of a PDP-12 computer (Digital Equipment Corp.). Power spectral analyses of these channels were obtained by taking fast Fourier transforms of the data sampled at a rate of 256 Hz for four pairs of four-sec epochs, or a total of 32 sec. The frequency range of the spectra was 0 - 31.75 Hz in 1/4 Hz intervals. The computer program printed and plotted the spectral energy within 1.75-Hz bands from 0 to 31.75 Hz, the spectral energy within the alpha (8 - 13.75 Hz), delta (0.25 - 3.75 Hz), theta (4.00 - 7.75 Hz), and beta (14.00 -30.00 Hz) EEG bands, and the "dominant frequency," or the frequency that had the maximum spectral amplitude. A three-point moving average smoothing filter was applied to the raw spectral estimates prior to any computations.

The power spectra were generated three times during the exposure day, once shortly after entry into the chamber and twice approximately four hours later. During each session, three 32-sec periods were analyzed and stored on tape for later processing. These sessions were conducted with the eyes closed, and were each preceded by having the subject quietly relax in the darkened room for two min, after which he or she clapped the hands loudly five times. This procedure standardized the alertness of the subject. Each session required approximately ten min.

PHYSIOLOGICAL

Exercise was carried out on four MONARK (GCI, Stockholm) bicycle ergometers at a pedal rate of 60 rpm. Loads were individualized prior to exposure in order to increase the average heart rate by 30 beats/min over each subject's normal resting heart rate. Total ventilation could be expected to increase three- to four-fold over sedentary levels (Robinson, 1974). Heart rates were determined by EKG telemetry as described earlier. Subjects used the same bicycle each day, adjusting the seat height to comfort for the 30-min session.

SUBJECTIVE RESPONSES

Mood assessment by completion of a subjective feeling inventory form based upon the Lorr-McNair mood adjective checklist (McNair and Lorr, 1964) was measured on a daily basis. Each subject selected a personal psuedonym for the study, and entered this psuedonym and the date at the top of the form. The form contained 56 adjectives or phrases to describe mood and four phrases that required the following of simple directions (see Appendix IV). Five variations of adjective sequence were used in order to prevent memorization. Choice of boxes to be checked for each adjective were "not at all, a little, quite a bit, and extremely." The subjects were advised to "check the appropriate box - which indicates how you feel at that moment. Use your first response." This form took approximately 3 min to complete.

For scoring, the adjectives were arranged into nine groups according to Davis (1971); depression (9 adjectives), carefree (9), friendliness (6),

hostility (5), anxiety (7), cognitive gain (5), guilty-ashamed (3), fatigued (3), and miscellaneous (9), and the group of simple directions (4). In the last group, a correct answer was simply scored one point, and zero if incorrect. In all other groups, "not at all" received 0 value; "a little" - 1; "quite a bit" - 2; and "extremely" - 3. The psuedonym code was broken by subject number only after the entire testing and scoring were completed.

The subjective response form completed each hour when in the chamber is shown in Appendix V. Rows were provided for the keywords: headache, nausea, dizziness, abdominal pain, chest pain, ENT irritation, other, and odor, with the adjectives mild, moderate, and strong. Columns were addressed: immediate, 1/2, 1, 2, 3, 4, and 5 hr, and 1/2 hr post. The subjects were advised to record only abnormalities with an appropriate adjective, drawing a line through all rectangles when no abnormal subjective response was present. These responses were checked daily by a physician, and the forms were scored simply by noting the number of subjects marking a specific response and the total times a response was noted.

The form used for staff assessment of the subjects' mood and behavior in the environmentally-controlled chamber is found in Appendix VI. These were completed at the end of each day, starting on Day 5 of Week 3 by five staff persons who worked with the subjects but were not informed of the PCE concentration or drug- or alcohol-dose levels.

DATA ANALYSIS

Methods used for the analysis of the voluminous data generated in this study were several in number, depending upon circumstances. Data to establish the TWA of the PCE exposures was handled by computer fitting of standard curves and subsequent calculation of each 30-sec unknown and averaging during chosen time periods. PCE, ethanol, and diazepam biochemical levels were treated by computerized two-tail t-test to determine interactive and gender effects.

Data from the subjective feeling inventory were entered into the computer and analyzed for variance from the control mean by the t-test method. Subjective response and staff assessment of subjects' mood comparisons were made by simple calculation of means for each of the 18 exposure conditions.

All of the behavioral responses were quantitated by individual subject and day of study (1 through 74). Concentration codes were as follows: PCE - 000, 025, and 100, corresponding to 0, 25, and 100 ppm PCE; diazepam - 00, 01, 06, and 10, corresponding to no capsules, placebo capsules, 6, and 10 mg/day; and alcohol - 000, 075, and 150, corresponding to doses of none, 0.75, and 1.5 ml 100-proof vodka/kg body weight. The compiled raw data for the Michigan eye-hand coordination, Flanagan coordination, and the rotary pursuit tests were keypunched and analyzed by computer at the Medical College of Wisconsin Computer Center, while the data from the saccade velocity and dual-attention tasks

tests were sent to NIOSH (Cincinnati) for analysis,as per the contract.* EEG power spectra tapes were first analyzed in the Department to prepare visual spectra and compute summary descriptors and then the resultant descriptors were statistically analyzed by the Computer Center. Missing data were supplied by the usual method (Yates) of handling missing data. Only the responses from the nine subjects who finished the study were analyzed.

Computerized programs computed mean group responses for the behavioral tests for each day of testing. Because of the learning or conditioning which occurred during the three-month period of testing, a "trend adjusted t-test" was used to plot the means versus each daily exposure condition. For the trend adjusted t-test, a linear trend line was fit for each subject using the control days data only. The regression response for each day was subtracted from the observed response. Then, for each day the mean of adjusted observations was tested versus zero. Since each subject had an equal number of observations on each day, the overall trend line represented the (unweighted) average trend line of the nine subjects. This overall trend line, with 95% confidence bands for a future average of nine subjects, was drawn on the three month graph, along with the daily means.

The continuous variables were assessed by analysis of variance techniques. Multiple regression equations, using the baseline or control trends data, were used to evaluate the treatment effects. Analysis of variance tables were used to display the results of significance testing and the multiple regression equations were used to depict the PCE, diazepam, and alcohol interactions, both significant and nonsignificant. Using a block-design type of analysis, with the subjects as blocks (random) and treatments specified by combinations of PCE with diazepam or PCE with alcohol (fixed effects), separation of the interaction effects was achieved.

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*The analysis of the dual-attention task data is found in the Addendum. Technical difficulties to date have precluded NIOSH analysis of saccade velocity, the analysis of which will be reported separately.

TEST CONDITIONS

SUBJECTS

Eight males and six females were judged by the examining physician to be those best qualified for the study from nine males and eleven females who were given comprehensive medical examinations. Neurological examination, eye tests, physical condition, past medical and work history, EKG, and pulmonary function tests revealed that each of these persons was qualified to carry out the behavioral/neurological testing under the required testing conditions. All personal medical data concerning these persons are secured in the Department's confidential files, available upon written request to the individual concerned. One male person failed to appear for the orientation and another failed to return after the first day of training. All persons present for orientation signed the Participant Document form. Table III lists the ages, heights and weights of the six males and six females who volunteered for and then began the study. All were Caucasian. They were assigned subject numbers, three having been subjects in previous studies (more than six months previous) and these retained their original subject number. All data generated in the study were collected by subject number, or pseudonym (mood evaluation only).

The six male and six female subjects were further divided into Groups A and B for study purposes. As seen in Table III, there were three subjects of each sex in each Group, selected simply by consecutively assigned subject numbers.

There were 55 training and exposure days during the study. Table IV gives the attendance summary of each subject. Subject 326 withdrew from the study when her previous job again became available, and subject 331 withdrew when his spouse suffered an injury that forced him to stay at home. Subject 123 was withdrawn from the study after a week's absence with no excuse. All other subjects finished the study. Three subjects, 329, 330, and 334, were present but not participating on four days while medical problems were being resolved. Absences were most often due to the subject's reporting by phone of bad colds or flu-like symptoms. Several absences were due to trips out-of-town for personal reasons. Only one subject, 330, was present for all 55 training and exposure days.

Daily medical surveillance by the attending physician, using the testing procedures listed in the METHODOLOGY section and further follow-up when necessary, provided assurance that each subject entering the exposure chamber each day for testing was in good health. Weekly laboratory studies and final comprehensive physical examination confirmed that each subject remained in good health throughout the study. Surveillance

of EKG's on the scope during subject exercise and daily review of intermittent EKG tracings revealed no deleterious effect of the study upon the electrical activity of the heart of any subject.

EXPOSURE LEVELS

The PCE used for this study was obtained from the Aldrich Chemical Co., Inc. (catalog no. T750-0, tetrachloroethylene, 99%, MW 165.83, d 1.623, bp 121°) in 4-kg bottles. Each bottle was sampled for identity confirmation by infrared spectroscopy. Table V lists the time-weighted average (TWA) PCE concentrations, and the standard deviations (SD), that were measured in the controlled-environment chamber by the infrared monitoring system. Each pair of subjects entered the chamber at 10-min intervals, thus the 5-1/2-hr TWA for each pair differed slightly from that found in the table, but the difference from that reported was never more than 0.5%.

Table VI lists the daily total ml of 100-proof vodka consumed in two "cocktails" by each subject during the two weeks that ethanol was studied. These levels were chosen by the physician based upon weight and probable blood levels of ethanol that would be attained. Subject 326 had already withdrawn from the study at Week 5, and subject 123 and 331 had withdrawn by Week 10. Although the amount of conversation in the chamber was greater during these two weeks, no subject became nauseated or ill from this dose of vodka. All subjects were encouraged not to consume any form of alcohol outside of the tests. However, most of the subjects reported drinking socially in moderation after the test day was completed. Blood and breath ethanol levels found during the test day will be discussed in a later section on Biochemical Measurements, as will the blood diazepam levels.

Although subjects were continually reminded to take the diazepam doses that were required while away from the laboratory, many forgot or were unable to comply. Listed in Table VII are the exceptions to the prescribed diazepam and placebo dosages. Every dose that was to be ingested while in the chamber was ingested unless the subject was absent. In some cases the breakfast dose was taken when the subject arrived at the laboratory because there was no "convenient" time beforehand. During the high dose diazepam and placebo weeks (Weeks 7 and 8) and the high ethanol and last diazepam weeks (Weeks 10 and 11), all subjects were transported between their place of residence and the laboratory by taxi.

DAILY SCHEDULE

The schedule for the 55 training and exposure days that were included in this study was described under METHODOLOGY, Exposure Schedule; therefore, this section will deal with the daily schedules.

During the 2-1/2 days of training, all subjects carried out the Michigan eye-hand coordination test six times, the rotary pursuit test six times, and the Flanagan coordination test seven times. They were oriented on each of the other tests by practical demonstrations, and rode the bicycle ergometer while heart rates were determined. These training days allowed

each subject to become thoroughly acquainted with the testing procedures, and brought them near their individual plateau performance on those tests where practice affected the performance.

It was determined before the exposure days began that it would be difficult for all 12 subjects to be involved in every test on a daily basis for two reasons: 1) there was insufficient time, and 2) it was objectionable to the subjects to have both the saccade velocity and EEG electrodes attached every day for 53 days. Therefore, the 12 subjects were divided into Groups A and B, as noted in the Subjects section. Group A subjects underwent EEG testing and Group B the EOG during the alcohol (ethanol) dose weeks and certain control and placebo days, while the reverse was true during diazepam dosing and alternate control and placebo days. The schedule shown in Table II includes the notations for which Group was scheduled to undergo EEG testing. The other Group automatically underwent EOG testing. Another complication to overcome was the fact that, for almost all the behavioral and neurological testing, only one piece of equipment was available, and only one person at a time could be tested in the isolation booth for EEG, EOG, or the dual tasks test. Therefore, each Group was further divided into three subgroups of a male and female (subgroups 1 and 2, 3 and 4, 5 and 6). Alternate subgroups from A and B entered the chamber at 10-min intervals in the same order on a daily basis.

The first pair of subjects (1 and 2, EOG) entered the chamber at 8:30 AM and exited at 2:00 PM with an elapsed time of 5-1/2 hr or 330 min. Their schedule using elapsed time in min was as follows: 0 to 5, Romberg and heel-to-toe and EKG strip; 5 to 35, saccade velocity (EOG) and Michigan eye-hand; 35 to 65, exercise with EKG monitoring; 65 to 95, "cocktails"; 95 to 115, rest with blood and breath sample at 112; 115 to 130, Michigan eye-hand and rotary pursuit; 130 to 140, mood and Flanagan coordination; 140 to 170, saccade velocity (EOG) and dual tasks; EKG strip at 250; 225 to 255, lunch; 320 to 325, Romberg and heel-to-toe and EKG strip; 330, exit chamber. The second pair of subjects (1 and 2, EEG) entered the chamber at 8:40 AM and exited at 2:10 PM. Their schedule was as follows: 0 to 5, Romberg and heel-to-toe and EKG strip; 10 to 20, EEG; 25 to 40, Michigan eye-hand; 40 to 70, exercise with EKG monitoring; 70 to 100, "cocktails"; 100 to 120, rest with blood and breath sample at 118; 120 to 135, Michigan eye-hand and rotary pursuit; 135 to 145, mood and Flanagan coordination; EKG strip at 240; 215 to 245, lunch; 260 to 320, two sets of EEGs; 320 to 325, Romberg and heel-to-toe and EKG strip; 330, exit chamber. The alternating subgroup entry by twos each 10 min continued through 9:20 AM, and subsequent testing followed the alternating schedules (see Appendix VII).

In summary, each subject was in the chamber 5-1/2 hr daily. Within 5 min of entry and 10 min of exit, each subject performed a Romberg and heel-to-toe equilibrium test. Within 30 to 60 min of entry, each subject carried out the Michigan eye-hand coordination test. During this same 30-60 min, before exercise, "alcohol" subjects had an EEG while "diazepam" subjects had an EOG. After this 30-60 min period, each subject carried out the following sequence: 30 min of exercise on a bicycle ergometer; 30 min of sipping two "cocktails," with medication

during the first if it was a diazepam or placebo week; 20 min of rest, with a blood and breath sample at 18-20 min; 15 min of Michigan eye-hand coordination and rotary pursuit tests; and 10 min of Flanagan coordination and mood tests. The "diazepam" subjects then repeated the EOG and carried out the dual tasks test over the next 30 min, while the "alcohol" subjects were given EEGs after lunch.

BIOCHEMICAL

The results of the biochemical measurements made on blood and breath samples revealed that all subjects carried significant body burdens of the chemical or chemicals under test at the time that behavioral studies were carried out.

Because of the voluminous nature of the individual analyses, the daily results were averaged by sex for this report. The results of the analysis of PCE in the venous blood samples taken just prior to behavioral testing (2' of exposure) are given by week in Tables VIII to XVIII, along with pre-exposure (baseline) levels on many days. As had been expected, exercise had a marked effect upon the PCE blood levels. These values at 50 min after exercise were found to be three to six times higher than the venous blood levels of sedentary subjects exposed to equivalent levels of PCE vapor in this laboratory previously (Stewart, et al., 1974) (8.25 vs 1.12 to 2.95 ppm). As was also noted previously, PCE is measureable in the venous blood for many hours after exposure; however, the levels were generally below 0.5 ppm 18 hr after a 5-1/2 hr exposure to 100 ppm.

Mean PCE breath concentrations, baseline, after two hr of exposure, and at 15 and 30 min post exposure, are given by week in Tables XIX through XXIX. Breath concentrations of PCE at 50 min after exercise were elevated approximately 50% over those from previous studies with sedentary subjects exposed for 3 hr to 100 ppm PCE. The post exposure breath levels were unaffected by the exercise early in the exposure period. They fell between levels from 3- and 7-1/2-hr exposures of sedentary subjects tested previously (Stewart, et al., 1974).

The mean blood and breath ethanol concentrations found in the samples taken just prior to behavioral testing during Weeks 5 and 10 are listed in Tables XXX and XXXI, respectively. The individual values varied considerably as noted by the ranges, also listed. During Week 5, the low dose week, both male and female subjects averaged just under 50 mg % ethanol in blood, except on Day 1 when both were much lower. During the higher dose week, Week 10, male subjects averaged 61, while female subjects averaged 65 mg % ethanol in blood. There was a larger difference in the breath ethanol levels between the low and high doses, an average of 150 vs 255 ppm, respectively. The latter is more representative of the general difference in doses during these two weeks.

The mean diazepam blood concentrations for the weeks of diazepam dosage are given in Tables XXXII, XXXIII, and XXXIV. The blood levels of diazepam were generally in the same range during Week 7 as during Week 3 despite a 66% increase in daily dose. However, the return to the

lower dose during Week 11 resulted in lower blood levels than during the first week of identical dosing. This phenomenon is probably related to the induction of enzymes that metabolize diazepam, giving the lower levels during the weeks after induction (Sellman, et al., 1975). Included in each table are the results of spot checking of diazepam blood levels during the week after dosing. None was ever detected during those weeks. However, it should be pointed out that we were operating near the lower detection limits of the analysis procedure for diazepam, even during the weeks of diazepam dosing. It can be assumed from the results, but not proven, that no mistake in dosing with the wrong capsules occurred.

In the tables already discussed, means were derived from all analytical data that were available each day. In further development of the effects of the combined treatments upon each biochemical level in order to determine whether there was an interaction between PCE blood levels and alcohol or diazepam consumption, blood values from the four male subjects who finished the study (nos. 117, 332, 333, and 334), and the four female subjects who had the best attendance record (nos. 95, 328, 329, and 330) were studied. Values for blood and breath when no diazepam or alcohol were given, including placebo days, were meaned, and compared to either all alcohol days, regardless of dose, or all diazepam days, regardless of dose. The results are shown in Table XXXV. At 25 ppm exposure concentration, alcohol significantly increased the PCE blood level ($p < 0.01$), but did not increase it at 100 ppm. Diazepam had no effect upon PCE blood levels at 25 or 100 ppm PCE exposure. A similar picture emerged when comparing breath levels from samples taken at the same time as the blood samples (2 hr into the exposure). Breath sample values from 30-min post exposure indicated a significant effect of alcohol at both levels of PCE exposure; however, the 100 ppm PCE and alcohol combination resulted in a significantly lower breath PCE level in contrast to the 25 ppm where it was higher. The meaning of these results is unclear. Because the alcohol was consumed almost five hours earlier, it certainly was all metabolized by the time of this breath sample and should have had no direct effect. If the effect is real, it must be an indirect effect.

The difference of blood levels between male subjects and female subjects at two hours into the daily study was calculated for all treatments combined and neither blood nor breath levels were statistically different ($p > 0.10$) by the two-tailed t-test (8 pairs of means, $t = 0.623$).

Alcohol blood and breath levels of the eight subjects were found to both be significantly greater during the higher alcohol versus the lower alcohol week (bloods: means of 43.9 and 60.9 mg/dl, $\Delta = 17$ mg/dl, $t = -3.79$, $p < 0.01$; and breaths: means of 149 and 256 ppm, $\Delta = 108$ ppm, $t = -6.10$, $p < 0.0005$). However, diazepam blood levels were highest the first week of the lower dosage (Week 3), the mean being 18.46 ± 4.76 µg/dl. During the week of higher dosage (Week 7), the mean dropped to 17.51 ± 6.65 µg/dl. However, by paired t-test, this mean was significantly higher ($p < 0.05$) than the second week of lower dosage (Week 11), the mean for this week falling to 12.07 ± 4.52 µg/dl. This response was assumed to be due to more rapid metabolism of the diazepam

after enzyme induction during the first week of dosage (Sellman, et al., 1975).

BEHAVIORAL

As noted in previous sections, a great amount of effort was made to reduce the variations in the parameters, other than PCE, ethanol, and diazepam levels, that might affect test scores. In addition, efforts were made to keep the "double-blind" aspects of the study intact, with both the staff supervising the testing and the subjects unaware of the exposure conditions. As with any study of this magnitude and length, certain unavoidable problems presented themselves that may have had some unknown affect on the individual's particular performance, or the group's performance. Deviations that could affect performance were noted each day by the staff psychologist and the physician. A list of these is presented in Table XXXVI. Also noted are equipment failures. Data known to be affected were removed from further analysis.

Problems with the equipment during behavioral testing usually invalidated the data obtained. One particular problem was the dual-attention tasks test wherein the paper tape reader that presented the stimuli to the subjects malfunctioned randomly through Day 2 of Week 4. All of the previous data were invalidated. Even after repair, there were problems with the recording of the number of times a subject noted that the white light blinked. Therefore additional data were discarded. Another instrument that malfunctioned occasionally was the rotary pursuit, where unpredictable stoppage of the rotating light occurred on a few days.

Also noted in Table XXXVI are minor medical problems and some outside influences that may have had some bearing on behavioral test scores.

On the last day of the study, all the remaining nine subjects were asked to complete a debriefing questionnaire after testing was completed and prior to actual debriefing. The questionnaire and the results are shown in Appendix VIII.The last page of the questionnaire was completed after debriefing. It is apparent from the results that the presence or absence of alcohol in the "cocktail" was easily established by the subjects, and therefore that part of the study was not blinded. However, only two of the nine were accurate in distinguishing the two dosages. Subjects' accuracy in determining when they received diazepam versus placebo was only about half accurate, and only one subject could distinguish the low from the high dose accurately. Excess noise from conversation, laughing, joking, etc. during the alcohol days had some influences upon the behavioral testing according to this questionnaire.

NEUROLOGICAL

Test conditions that varied during the Romberg and heel-to-toe equilibrium testing just after entry and before exit from the controlled-environment chamber were the PCE concentration and the presence or absence of diazepam. Any ethanol effect would have been mitigated by the four-hour time period between alcohol consumption and chamber exit. Because diazepam dosage was on a more continuous basis over a week's period, any differences

between the entry and exit performance would most likely have been due to PCE.

Table XXXVI also lists the deviations that occurred in EEG testing. Unfortunately, the computer program that recorded the EEG epochs on tape was unavailable until the third day of Week 4. However, with the repeat of Week 3, all types of exposure combinations were eventually put on tape and therefore were studied. The accidental blinking of a strobe light in the EEG room during days 3 and 4 of Week 8 may have inadvertently affected some subjects EEGs during those days (placebo plus 100 ppm and plus 25 ppm PCE).

PHYSIOLOGICAL

Pulse rates were recorded in the resting state three times daily, and three times during the 30 min of daily exercise. Bicycle ergometer loads were set individually to cause an approximate increase of 30 beats per min during the exercise period. Loads had to be adjusted at least once for all subjects as their physical performance usually improved during the study.

SUBJECTIVE

Each subject completed a Lorr-McNair mood adjective checklist in the midst of the behavioral testing on a daily basis. As noted under Methodology, the 56 adjectives or phrases to assess mood were divided into categories for analysis to indicate depression, carefree, friendliness, hostility, anxiety, cognitive gain, guilty-ashamed, fatigued, and miscellaneous (see Table XXXVII). Four direction phrases were also included for a total of 60 multiple-choice questions. A visual assessment of the answers to the four direction-type questions showed that all subjects had no problem on any day with following these simple directions.

Two of the nine categories of mood need some explanation. As seen in Table XXXVII, the cognitive gain category included the terms confused, able to think clearly, forgetful, able to concentrate, and alert. Obviously some of these terms are opposite in effect and therefore a change in score was difficult to assess. The miscellaneous category included nine mostly unrelated adjectives, again making scoring almost meaningless. In all other categories, an increase in score could be directly related to an increase of this particular mood.

Figures 4 through 12 relate the daily mean scores (± SD) of each of the nine groups of mood assessment to treatment. The straight lines describe the trend of scores for zero exposure conditions and the outer lines the 95% confidence limits of the zero exposure means. Unfortunately, there was a wide range of responses for all categories, with no change easily relatable to exposure condition. This was confirmed with the trend adjusted t-test where no significant differences ($p < 0.05$) from zero exposure scores were found for any treatments in any categories. The analysis of variance approach, using individual differences from predicted values in the paired t-test to compare treatments, also revealed a low level of significant changes in mood with treatment. On high level

alcohol days, scores on the cognitive gain decreased ($p < 0.005$) and the miscellaneous category increased ($p < 0.05$). Unfortunately, neither of these two categories included a well-defined mood. Diazepam treatment also resulted in a significant increase ($p < 0.005$) in score of the miscellaneous category. During the diazepam treatment weeks, the analysis of variance revealed a significant increase ($p < 0.025$) in friendliness due to PCE, and an interactive effect of PCE and diazepam to significantly decrease ($p < 0.025$) friendliness.

Subjects noted subjective symptoms on the subjective reponse forms eight times per exposure day, and PCE odor perception seven times. The number of subjects per day who noted a given symptom or perceived the odor of PCE (responders), and the total number of times each were noted per day (responses), were totaled for each different type of exposure. Because there were often different numbers of subjects and, therefore, different numbers of subjective response forms returned under different conditions, total numbers of responders and responses were divided by the number of forms returned in order to give a rate per subject report. These rates are listed by type of response as "incidence" and "persistence," responders and responses, respectively, in Tables XXXVIII and XXXIX. There was no suggestion of a trend to a greater rate of any symptom when exposures to increasing concentrations of PCE alone took place. However, as expected, the PCE odor perceived became stronger and persisted longer as the PCE concentration increased. Table XXXVIII shows the results for the addition of placeb mg, and 10 mg of diazepam to each level of PCE. Again there seems to be no dose-response relationship regarding untoward symptoms, and only the odor perception increases with increasing PCE concentration. Table XXXIX demonstrates similar responses for addition of alcohol to the PCE exposures. It appears that the alcohol may have actually decreased the number of symptoms in some areas. As a whole, it can be concluded that, despite the increase in PCE odor perception with increasing PCE concentration, PCE, diazepam, alcohol, or the combinations of these at the levels studied had no discernible effect upon the subjective symptoms of the subjects.

The staff assessments of the subjects' mood and behavior while they were in the controlled-environment chamber are summarized in Tables XL and XLI. Five staff members who worked with the subjects, but were not informed of the PCE concentrations or the drug and alcohol dosages, completed the mood and behavior assessment daily. The scales between opposite types of behavior ranged from +5 through 0 to -5 (see Appendix VI). The means for each condition are listed in the tables. PCE concentration alone had no effect on these assessments, while the higher dose of alcohol was assessed to <u>increase</u> the subjects' happy, at ease, friendly, carefree, full of pep, giddy, talkative, active, and staggering images, and the higher dose of diazepam <u>decreased</u> the subjects' alert, concentration (able to think clearly), happy, full of pep, talkative and active images, as assessed by the staff.

RESULTS OF BEHAVIORAL AND NEUROLOGICAL TESTING

BEHAVIORAL MEASUREMENTS

Michigan Eye-Hand Coordination Test

The Michigan eye-hand coordination test required the subjects to follow a weaving maze-like path with an electronic recording stylus. At each of the 119 points in the path, changing direction at each point, the stylus was fully inserted to the bottom of the hole. The response measured at each trial was the total elapsed time in seconds required for the completion of the entire path tracing. The final score was the total of four path tracings. Thus, a higher score indicated a slower response time. This test incorporated many of the eye-hand coordination movements encountered in manual work tasks requiring hand and arm dexterity. Each subject performed the test twice daily, once within 60 min of entry into the chamber and prior to exercise and dosing (labeled AM), and again 1-1/2 hr later after exercise and dosing (labeled PM). The two daily test scores were analyzed separately.

Figure 13 displays the mean scores (± one SD) for both AM and PM tests. Even though the subjects were trained before the exposure sequence was initiated, the general improvement in performance is quite noticeable, especially during the first few weeks. Inspection of Figure 13 reveals that the higher level of alcohol (ca 1.50 ml/kg) produced the greatest variation in the PM scores.

Analysis of the data from weeks pertaining to PCE exposure and alcohol yielded the following multiple regression equations:

$$\text{AM score} = 47.67 - \underline{0.1199\ D} + 0.0016\ P - 0.1196\ A - 0.0091\ (P \times A) + \text{subject effects}$$

$$\text{PM score} = 45.90 - \underline{0.1089\ D} + 0.0037\ P + \underline{1.7529\ A} - 0.0023\ (P \times A) + \text{subject effects}$$

Where: D = day number (0 through 75)
P = level of PCE (0, 25, or 100 ppm)
A = level of Alcohol (0, 0.75, or 1.5 ml/kg)

Analysis of variance summaries for these two multiple regressions are given in Tables XLII and XLIII. Results indicate the highly significant improvement trend (linear day effect). Alcohol manifested its significant effect in the PM scores. PCE showed no significant (linear) effect and no significant interaction effect with alcohol. Trend adjusted t-tests (Table XLIV), which were designed to correct for individual improvement in scores, showed that PM scores yielded significant increases (decrements) in test completion time on two days (56 and 58). Fortuitously, these t-tests showed a significant improvement in AM score

during the first week in which alcohol was used (0.75 ml/kg). This is not an alcohol effect because it was administered after the test. The improvements could have been due to some subjects performing well in anticipation of their alcohol "cocktail" and/or a reflection of the general point in the study where further baseline improvement subsided and, since overall improvement was accounted for by a straight-line relationship for the entire study, one would expect deviations from the assumed linear zero-exposure trend.

Subparts of the study encompassing PCE exposure and diazepam combinations produced the following multiple regression equations:

$$\text{AM score} = 47.91 - \underline{0.1322\ D} - 0.0041\ P + 0.0861\ V + 0.9428\ (P \times V) + \text{subject effects}$$
$$\text{PM score} = 46.62 - \underline{0.1257\ D} - 0.0024\ P + 0.0874\ V - 0.0010\ (P \times V) + \text{subject effects}$$

Where: D = day number (0 through 75)
P = level of PCE (0, 25, or 100 ppm)
V = level of diazepam (0, placebo = 0, 6 or 10 mg/day)

The analysis of variance for each multiple regression is given in Tables XLV and XLVI. The linear day trend was the only significant effect. PCE and the interaction with diazepam showed no significant effects. Analysis of all days excluding alcohol (0.75 and 1.5) and diazepam (6 and 10) yielded multiple regression equations:

$$\text{AM score} = 47.59 - \underline{0.1259\ D} - 0.0055\ P + \text{subject effects}$$
$$\text{PM score} = 46.28 - \underline{0.1196\ D} - 0.0032\ P + \text{subject effects}$$

Corresponding analysis of variance tables are not presented, but as indicated by the underlined effects, only the linear day trend was significant. The AM and PM scores for these no ethanol:no diazepam days correlated quite highly ($r = 0.9324$), agreeing with the previous report by Pook (1967).

Flanagan Coordination Test

The Flanagan coordination test required the subjects to draw with a pencil a continuous spiral path between well-marked spiral boundaries. Forty sec were allowed for completion of each of four scored trials and the test score was a function of the greatest distance obtained and the number of spiral borders that were touched (adds negatively to the final score). The scoring was standardized to a 0 to 100 point scale, with 100 points signifying a perfect score. Scores above 100 were impossible and scores of 100 were rarely obtained. However, scores below zero can be observed when subjects are intoxicated (alcohol). Past experience has shown that individuals show marked differences in the Flanagan coordination test. Improvement in score was generally achieved over a period of weeks, particularly for subjects with low initial scores and less frequently for subjects with high initial scores.

The graph in Figure 14 shows the daily Flanagan coordination mean responses for the entire study period. The average trend line shown was obtained only from the zero exposure days of the study (open circles on graph). The trend line reveals only slight improvement for the group of nine subjects. The boundary about the line depicts a region that can be expected to contain about 95% of future coordination score means if experimental conditions remain at zero (no PCE, diazepam, or alcohol). Obvious deviations from the control situation occurred during weeks when subjects received either low alcohol or high alcohol. The trend adjusted t-tests given in Table XLIV show that significant deviations obtained during low alcohol, high alcohol and high PCE, high diazepam, high diazepam and high PCE, and low diazepam and high PCE. All of these deviations resulted in an average reduction in the coordination score. Multiple linear regression analysis performed on zero-exposure days and alcohol exposure weeks yielded multiple regression equations:

$$C = 81.13 + 0.0456\ D - \underline{0.0418\ P} - \underline{7.0537\ A} + \text{subject effects}$$

$$C = 80.83 + 0.0453\ D - 0.0332\ P - \underline{6.2909\ A} - 0.01848\ (P \times A) + \text{subject effects}$$

Where: C = average coordination score
D = day number (0 through 75)
P = level of PCE (0, 25, or 100 ppm)
A = level of Alcohol (0, 0.75, or 1.5 ml/kg)

Underlined coefficients in the above equations correspond to significant effects as determined by the analysis of variance for the multiple regression(s) (Table XLVII). The effect of PCE and alcohol is exhibited by an augmented drop in average score, particularly noticeable on days 58 and 60 (Figure 14). However, the interaction effect was not statistically significant (in the equation above). Alcohol had an extremely significant effect and this is obvious in Figure 14 and in Table XLVII. By focusing only on this subset of the study, the linear effect of PCE indicated a drop in coordination score of three to four units per 100 ppm PCE. A similar effect of PCE was not entirely confirmed for days when alcohol and/or diazepam (including placebo) was absent, but inclusion of placebo (diazepam) days to other zero days yielded a statistically significant linear PCE effect. The corresponding multiple regression equation for the drug non-exposure days are:

$$C = 79.79 + 0.0482\ D - 0.0191\ P + \text{subject effects}$$

$$C = 81.36 + 0.0364\ D - \underline{0.0387\ P} + \text{subject effects (placebo days included)}$$

Analysis of PCE and diazepam exposure revealed similar results. Multiple regression equations reflecting effects of days, PCE and diazepam are:

$$C = 80.10 + \underline{0.0413\ D} - \underline{0.0253\ P} - 0.2265\ V + \text{subject effects}$$

$$C = 80.05 + \underline{0.0413\ D} - 0.0241\ P - 0.2095\ V - 0.00042\ (P \times V) + \text{subject effects}$$

Where: C = average Flanagan coordination score
D = day number
P = level of PCE (ppm)
V = level of diazepam (mg/day)

Table XLVIII gives the corresponding analysis of variance results to multiple regressions. The effect of diazepam was not statistically significant, the interaction of PCE and diazepam (linear interaction) was not statistically significant, and the linear effect of PCE and the linear day trend showed statistical significance only in the first equation above. These results were derived from an analysis that compared exposure factors with smaller measures of random variation (the Residual Mean Square of Table XLVIII is smaller than the Residual Mean Square of Table XLVII) and this accounts for the day trend being declared significant.

The effect of PCE was in the neighborhood of a two to four unit reduction for a 100 ppm exposure to PCE. This effect was not consistently statistically significant for all subparts of the experiment.

Rotary Pursuit Test

The rotary pursuit test required the subjects to maneuver a hand-held electronic recording stylus in a circular pattern so that it "pursued" a one-inch square light that revolved in a 30-cm diameter circle. The rotation of the light for each of four successive trials was fixed at constant speeds of 15, 30, 45, and 60 rpm, with each trial lasting 45 sec. Variables recorded that characterized each subject's performance were (1) the time off target, in seconds, and (2) the number of errors or the number of times the stylus moved off and onto the target while tracking it. This was an eye-hand coordination test similar to the Flanagan coordination test in the sense that circular motion was involved. However, it differed from the Flanagan in several respects, namely (1) the circular pattern was much larger than the series of concentric spirals of the Flanagan, (2) the speed of the rotation was fixed for each trial, and (3) the rotary pursuit was administered in a standing rather than a sitting position as in the Flanagan.

Analysis of the rotary pursuit data revealed that the time off target and the number of errors provided nearly equivalent information with respect to the influence of PCE, alcohol, and diazepam. Figures 15, 16, 17, and 18 depict the daily mean results for each rotation speed. As rotation velocity increased, the time off target also increased; and as the study progressed, the subjects exhibited improved trends in tracking ability at each of the four speeds.

The effects of PCE and alcohol are illustrated in the following multiple regression equations:

$$T_{15} = 1.47 - \underline{0.00321\ D} + 0.00132\ P + \underline{0.73159\ A} + 0.00021\ (P \times A) + \text{subject effects}$$
$$T_{30} = 7.86 - \underline{0.04124\ D} - 0.00281\ P + \underline{2.9837\ A} + 0.00567\ (P \times A) + \text{subject effects}$$
$$T_{45} = 17.08 - \underline{0.08345\ D} + 0.00548\ P + \underline{5.2654\ A} + 0.00836\ (P \times A) + \text{subject effects}$$
$$T_{60} = 26.36 - \underline{0.07443\ D} - 0.01267\ P + \underline{3.6921\ A} + 0.02129\ (P \times A) + \text{subject effects}$$

Where: T_s = time off target at speed s (rpm)
D = day number (from 1 to 75)
A = level of alcohol (0, 0.75, or 1.5 ml/kg)
P = level of PCE (0, 25, or 100 ppm)

Analysis of variance tables that correspond to the above regression equations are given in Tables XLIX, L, LI, and LII. Results indicated a clear day trend that exhibited improvement in performance. Alcohol effects significantly increased the time off target at all four rotation speeds. However, the effect of PCE was not significant at any of the four speeds, and moreover, the alternating signs of the PCE coefficients suggests inconsistent directional effects. The linear by linear interaction of PCE and alcohol was also non-significant, except at 60 rpm trials, where it was significant at the $p = 0.05$ level. The effect of alcohol is quite obvious in Figures 15, 16, 17, and 18. It is noteworthy that the number of errors also showed similar deviations from expected responses during zero exposure conditions, except at the fastest rotation speed, where the number of errors is lower than expected because of the large amount of time spent off the target during high alcohol conditions. The trend adjusted t-tests in Table XLIV demonstrate that the high level alcohol week resulted in the most consistent significant deviations from the expected response of zero exposures. This occurred for all four rotation speeds and also for the number of errors at 15 and 30 rpm. The low alcohol week showed essentially no significant deviations from the expected trend line (Figures 15, 16, 17, 18, and Table XLIV).

Multiple regression equations that display the effects of diazepam, PCE, and day trends in concert are:

$$T_{15} = 1.45 - 0.00233\ D - 0.00082\ P + \underline{0.07149\ V} - 0.00007\ (P \times V) + \text{subject effects}$$
$$T_{30} = 7.33 - \underline{0.03641\ D} - 0.00463\ P + 0.06806\ V + 0.00093\ (P \times V) + \text{subject effects}$$
$$T_{45} = 16.65 - \underline{0.07524\ D} + 0.00130\ P + \underline{0.21287\ V} - 0.00053\ (P \times V) + \text{subject effects}$$
$$T_{60} = 25.61 - \underline{0.06754\ D} - 0.00968\ P + \underline{0.23283\ V} + 0.00053\ (P \times V) + \text{subject effects}$$

Where: V = level of diazepam (0, 6, or 10 mg/day)

Analysis of variance tables that correspond to the above equations are found in Tables LIII, LIV, LV, and LVI. As with the alcohol subset analysis, the diazepam and PCE analysis showed no significant PCE effect and no significant linear by linear interaction effect of PCE and diazepam. This conclusion was made for each of the four rotation speeds. The day trend is significant at speeds of 30, 45, and 60 rpm, and the effect of diazepam is significant at 15, 45, and 60 rpm, in the regressions shown above. If the 30 rpm speed is analyzed ignoring the interaction term, the resulting multiple regression equation becomes:

$$T_{30} = 7.23 - \underline{0.03652\ D} - 0.00182\ P + \underline{0.10602\ V} + \text{subject effects}$$

Now the diazepam effect reappears with a larger coefficient and also tests to be statistically significant ($p < 0.005$). (The corresponding analysis of variance is not presented.) The diazepam effect indicates that time off target increased as the dose of diazepam was increased. Trend adjusted t-tests show no significant deviations for the 6 mg dose of diazepam during Week 2, and a few significant deviations at the 30 rpm speed at the identical dose level during Week 11 (see Table XLIV). The high dose diazepam week, Week 7, showed essentially no significant deviations from the expected zero exposure trend line. Oddly though, the placebo diazepam exposure (Week 4) produced significant deviations from the expected responses for the 15, 30, and 45 rpm speeds on no PCE and PCE days. Some deviations from control levels would be expected.

The summary of the multiple regression analyses of the rotary pursuit data is as follows: (1) PCE did not exhibit a statistically significant effect for time off target, (2) its interaction with alcohol or diazepam also showed no statistical significance, and (3) alcohol and diazepam alone each produced significant effects that increased the time off target.

NEUROLOGICAL MEASUREMENTS

Only once during the three-month study did a subject perform abnormally on the equilibrium test. This occurred on a high-dose diazepam combined with 100 ppm PCE day in the test given just prior to leaving the chamber. Subject 95 could not perform a normal heel-to-toe walk with eyes closed. Because all other subjects performed the dual test (Romberg and heel-to-toe) normally, this single abnormal result of 18 tests performed under these conditions was considered as spurious.

The subjects were divided into Groups A and B as explained earlier, Group A undergoing electroencephalographic tests on ethanol, placebo, and certain control days while Group B underwent EEG testing on diazepam, alternate placebo, and alternate control days. Figures 19 through 24 and 25 through 30 are plots of each subjects' EEG power spectra which are representative of those generated during each treatment condition for the PCE-ethanol (Group A) and PCE-diazepam (Group B) subject groups, respectively. Table LVII presents the results of the analysis of variance for shifts in the dominant frequency from each of the four leads over all the treatment conditions. Tables LVIII and LIX present the results of the analysis of variance for changes in the percent relative activity in the α, β, θ and δ bands for each of the four leads over all the treatment conditions.

Visual comparison of the three power spectra derived from subjects in Group A (Figures 19, 20, and 23) showed that subjects 117 and 327 had no shifts in the distribution during treatment days that did not also occur on control days. Subject 95, however, did show increased α activity in lead 3 (F7-F8) and increased δ activity in lead 2 (F8-02) after ingesting

alcohol during Week 5, but this did not occur consistently over all the days of that week. Neither did it occur at the higher level of alcohol ingestion. The peak that appears in these power spectra at 4 Hz is an artifact of 60 Hz noise. The noise appeared at 4 Hz due to the sampling rate, and while it appeared in some of the spectra, it was not visible in the EEG tracings themselves.

The one-way analysis of variance for the three subjects in Group A showed no significant effects on the dominant frequency for any subject (Table LVII), but did show an effect in the percent relative amount of activity in the α band for subject 95 (Table LVIII). This effect was a significant decrease in the relative amount of α activity in lead 2 (F8-O2) during the high alcohol alone, and the high PCE plus placebo, treatment days.

Visual comparison of the power spectra of the six subjects in Group B (Figures 25 through 30) show no consistent changes between treatment conditions. The one-way analysis of variance tests showed several significant shifts in the dominant frequency in one of six subjects (Table LVII) and percent relative activity of bands from four leads (Table LIX) in four of the six subjects. These shifts are correlated with the corresponding treatment conditions in Table LX. Although no consistent pattern emerged, a majority of them occurred on a combined PCE exposure and diazepam ingestion day, and was elicited as increased β activity. Only one of these (subject 333, increased β activity in lead 1) can be attributed to a deviation in conditions, as this occurred on the day a light inadvertently blinked in the darkened testing room.

DISCUSSION

The discussion of the voluminous bank of data obtained in this study is divided into four main parts: (1) the effect of perchloroethylene (PCE) alone, (2) the effect of alcohol alone and in combination with PCE, (3) the effect of diazepam alone and in combination with PCE, and (4) the comparison of behavioral tests.

A comprehensive study on the total effect of repeated exposure to PCE alone has been reported from this laboratory (Stewart, et al., 1974). The following conclusions were advanced in that final report:

> 1. Repeated daily exposures to PCE result in a tachyphylactic type of response regarding subjective feelings and odor detection. Therefore, both of these parameters are unreliable measures of exposure concentration.
>
> 2. There is considerable individual difference in subjective response to PCE vapor exposures.
>
> 3. EEG analyses indicate that the preliminary signs of narcosis are present in most subjects exposed to 100 ppm PCE for 7-1/2 hours per day.
>
> 4. Impairment of coordination may occur at 150 ppm exposure for 7-1/2 hours.
>
> 5. Because there is very little metabolism of PCE by humans, the CNS response is probably due to the PCE itself.
>
> 6. Analysis of the chemical in the postexposure expired breath provides an excellent tool for estimating the magnitude of the body burden of PCE.
>
> 7. Physical activity (exercise) during exposure to PCE dramatically increases the body burden of the chemical. Therefore, the time-weighted average concentration to which a male or female human is exposed may not reflect the true body burden attained by that individual.
>
> 8. Postexposure levels of the chemical in the breath are an accurate reflection of the body burden and thus provide a "biologic threshold limit value" for worker exposure to this chemical.

None of the above conclusions need be abrogated from the results of the present study; however, several require further clarification. None of the twelve subjects exposed to PCE in the present study was unusually susceptible to PCE vapors as related to objective tests. However, as in the previous study, one subject reported many more subjective symptoms than all others. This subject accounted for 1/3 of the incidence of headache and 2/3 of the nausea reported by the nine subjects who completed

the study. This subject also reported ENT irritation on all but 8 of the 55 exposure days. Upon analysis of the times of reporting these subjective symptoms, it was found that there was no relationship to PCE vapor exposure; in fact, the incidence decreased somewhat when the 100 ppm PCE exposure concentrations were compared to non-PCE exposures.

The preliminary signs of narcosis, as indicated by EEG changes found by subjective review of tracings in most subjects exposed to 100 ppm PCE for 7-1/2 hr in the previous study, were not found with PCE alone in the present study. In this study, the EEG power spectra analyzed were obtained by averaging six power spectra generated from four 4-sec epochs for a total of 96 sec. This should have been sufficient time to demonstrate any significant changes in the spectra had they occurred. The conditions and subjects for the two studies were different, therefore, one cannot assume that either study was in error regarding EEG changes from exposure to 100 ppm PCE. However, it appears that EEG testing is an unreliable test for the early detection of narcosis due to PCE exposure.

Of great interest is the fact that PCE alone caused a significant decrement in the Flanagan coordination scores on some of the 100-ppm exposure days. This confirms the finding in the previous study wherein the group of male subjects exposed to 150 ppm for 7-1/2 hr per day had a significant decrement in performance on the same test. There were no significant decrements in performance in the Michigan eye-hand or rotary pursuit tests due to PCE alone.

The assessment of effects of PCE upon any change from control in mood of the subjects during exposure to 100 ppm revealed almost no effect either by the subjects own assessment or by the assessment of staff personnel. Analysis of variance did reveal that during the diazepam treatment weeks, PCE exposure caused the subjects to feel more friendly than expected. In looking at the weekly data, this appears to have been due to a "more friendly" attitude during Week 3 when the subjects may have first felt "better acquainted."

Analysis of the blood and breath levels for PCE after 30 min of exercise confirmed the rather dramatic effect that exercise confers upon body burden of PCE. The previous study had indicated that an increase would occur and this was confirmed. The similarities in blood and breath PCE levels between male and female subjects found in this study are different from the previous study. However, it was theorized that the lower levels found in female subjects previously could have been due to the fact that they did not exercise during the exposures, while male subjects exercised, though minimally.

Post exposure breath analysis at 30 min revealed that 5-1/2 hr of exposure to PCE vapor resulted in a mean breath level of 17.6 $\pm$ 3.3 ppm ($n = 64$) PCE for all subjects exposed to PCE alone or PCE and placebo. This compares favorably to the previous study of male subjects where a similar exposure to PCE vapor for 7-12 hr resulted in a mean PCE breath

concentration of 26.5 $\pm$ 3.2 ppm (n = 40) 30 min post exposure. These results further confirm that "post exposure expired breath provides an excellent tool for estimating the magnitude of the body burden of PCE."

In summary, we found no effects from the exposure of twelve human subjects to PCE vapor at 25 or 100 ppm concentration for 5-1/2 hr that were either unpredictable or unexpected.

Turning to the effects of alcohol, it has been impossible to review all of the myriad of previous publications on the behavioral effects of alcohol. In our own laboratory, we have found in previous studies that blood alcohol levels of > 50 mg/dl caused a significant decrement in performance scores of the Flanagan coordination test. Moskowitz and Sharma (1974) reported a decrement in the dual-attention tasks test, if the central white light was blinking, with blood alcohol levels of 0.06%. (Breathalyzer test. This is equivalent to ca. 60 mg/dl.) Using the rotary pursuit test, Kalant, et al., (1975) found a decrement in performance, measured by time on target at 30 rpm for 1 min, in both male and female subjects when blood levels reached 50 to 70 mg/dl. These levels were similar to our high dose levels. Sidell and Pless (1971) found the "greatest decrement in performance was on the test requiring hand-eye coordination; lesser decrements were produced on tests of cognitive ability" when subjects ingested from 0.5 to 2.0 ml ethanol/kg body weight. Serial blood alcohol levels revealed a rather level concentration from 0.5 to 2 hr post dosing when the alcohol was consumed as a juice "cocktail" over a half-hour period. At the blood levels equivalent to our low dose, the blood alcohol level was reduced to almost zero at 4 hr post dosing, while the level equivalent to our high dose level neared zero at 6 hr. Jones and Vega (1972) showed that after alcohol consumption, which was slightly higher than our high dose, students demonstrated a poorer performance on cognitive testing only when the blood alcohol concentration was rising. While the concentration was decreasing (about 2 hr post dosing), performance was identical to placebo controls. From these results, it would appear that all of our behavioral testing was carried out during the correct time period post dosing to observe maximum decrement in performance. However, the EEG spectra were obtained on the descending limb of the blood alcohol concentration curve at a time when the expected alcohol effect was past its maximum.

The mood tests completed by the subjects themselves did not confirm the staff assessment that alcohol increased the subjects' general "euphoric" mood. In fact, the consumption of alcohol had a significant effect on only two categories of the subjects' own assessment of their mood. The scores in the cognitive gain category (which included the adjectives confused, able to think clearly, forgetful, able to concentrate, and alert) were significantly lowered due to alcohol, while those for the miscellaneous category (suspicious, feel sexy, need a cigarette, need a drink, taken advantage of, hungry, headache, stomach upset, and trouble seeing) were significantly increased. Although these changes in "mood"

could be expected, the subjects did not see themselves as more carefree and friendly as the staff assessed them. In addition, there was no interactive effect between PCE and alcohol on the subjects' own assessment of their mood.

The Michigan eye-hand coordination test was the only test in which all subjects participated in daily both prior to and after consuming alcohol or a dose of diazepam. Alcohol alone at 1.5 ml/kg had a significant effect, resulting in an increased score (a slowing down), upon the performance of this coordination test. There was no significant interaction with PCE, even at the 100 ppm exposure concentration. A similar picture was obtained with the Flanagan coordination test. Here, a significant reduction in score, equivalent to a poorer performance, was observed with both low and high alcohol alone. Although high PCE also caused an occasionally significant decrement in performance, the interaction effect between alcohol and PCE was not statistically significant due to the extremely significant effect of the alcohol. Alcohol alone also had a significant detrimental effect upon performance of the rotary pursuit test, both in time off target and in number of errors, during the high dose week. However, this was not true during the low dose week, nor was there a statistically significant interaction with PCE. Moskowitz (1974) has observed significant effects of alcohol at low dosage levels on the dual-attention tasks test where divided attention to both signal detection and recall of simultaneously presented digits were required.

Ethanol consumption alone, or with simultaneous exposure to PCE, had little effect on the power spectra generated from the EEGs. One of the three subjects who underwent EEG testing during the ethanol dosing weeks did show significantly increased α activity which would correlate with a more relaxed feeling. It is not surprising that an alcohol effect upon the EEG was not uncovered because the EEG testing was carried out either before the consumption of the "cocktails" or several hours after when blood alcohol levels were probably low or undetectable (Jones and Vega, 1972).

Before leaving the subject of alcohol effects, it must be mentioned that PCE at 25 ppm seemed to have a positive effect on the blood alcohol concentration, particularly at the lower dose level. The average blood alcohol level of eight subjects was 50.7 ± 8.6 mg/dl during the low alcohol, low PCE day, while it was significantly lower, 40.1 ± 12.5 mg/dl on the two low alcohol, zero PCE days. A similar relationship was demonstrated during the high alcohol week, although the difference was not significant (66.1 ± 17.7 vs 58.5 ± 13.2). It may also be recalled that alcohol (both weeks combined) had a statistically significant effect on the blood level of PCE during low PCE (25 ppm) exposure days (Table XXXV). The reason for these increases is uncertain, although they may have simply been due to the physical effects of solubility. However, one would have expected them to also occur at the high dose levels.

Kleinknecht and Donaldson (1975) have recently reviewed the effects of diazepam on cognitive and psychomotor performance. From this review, it

is evident that our dosage regimens of 6 mg or 10 mg per day were on the threshold of impaired performance in many of the various tasks assessed. The review divided the tasks into six major groupings: reflex speed; critical flicker fusion threshold; attention and vigilance; decision making; learning and memory; and psychomotor performance. At 6 mg per day or less, it seems that only the critical flicker fusion threshold was definitively impaired, while reflex speed was unimpaired at doses up to 15 mg/day. In one of the papers, the reviewers report that 10 mg of diazepam administered over a 14-hr period had no effect on the pursuit rotor test. Combination effects of diazepam and alcohol taken together were reported as additive, or occasionally potentiating, although "typically the effects are not dramatic."

A factor that often was not taken into account in the previous studies was the cumulative dose effect. In our studies, diazepam blood levels were generally lowest on Monday, and generally increased during the week, despite the beginning of dosing on the previous Friday evening. Hillstead, Hansen, and Melsom (1974) also reported a cumulation of diazepam, and metabolite, in blood over a period of one week. However, the clinical effects, evaluated somewhat subjectively and classified on a zero to four scale, were not changed greatly during the full two weeks of dosing at 15 mg/day (5 mg t.i.d.). We found a lower mean blood level after 10 mg/day dosage during Week 7 than during Week 3 when the dosage was 6 mg/day. A repeat of the 6 mg/day dosage regime during Week 11 yielded significantly lower mean blood levels. Blood sampling was carried out at the same time period after capsule ingestion all three weeks. The lowered diazepam blood levels we found during the second and third week of dosing corroborate the work of Sellman, et al., (1975) and indicate that metabolic enzyme induction reduced the blood levels of diazepam. The results of the rotary pursuit testing indicate that this reduction in blood level was not associated with a decrement in performance.

Diazepam alone or in combination with PCE had no significant effect upon the performance of the Michigan eye-hand or the Flanagan coordination tests in our studies. However, the drug alone had a significant effect on the time off target, but no interaction effects with PCE, in the rotary pursuit test. The EEG changes seen in this study almost all occurred during a combination of PCE and diazepam. Interestingly, the PCE plus diazepam changes were asymmetrical, generally occurring in only one lead. Although an asymmetrical EEG change is unusual, it is in agreement with the previous PCE study from this laboratory (Stewart, et al., 1974) and the report of Hynek, Tosovský, and Süsová (1975), who related asymmetrical changes to right and left handedness. Contrary to our previous study, the majority of changes seen in the present study were increases in β activity as opposed to θ activity. Montagu (1972) has studied the effects of low doses of diazepam on the EEG of normal subjects and reported decreased theta activity and increased beta activity with eyes open. During the eyes shut testing,his subjects demonstrated typical light sleep and drowsiness in their EEG patterns.

Diazepam also had a visible effect upon the staff's assessment of mood of the subjects. The staff evaluation of the subjects' mood and behavior resulted in decreased alertness, concentration, happiness, peppiness,

giddiness, talkativeness, and activity, all especially noticeable during the high dose week. However, the subjects' themselves revealed only a significant decrease in the miscellaneous mood category attributable to diazepam dosing. This category included the adjectives suspicious, feel sexy, need a cigarette, need a drink, taken advantage of, hungry, headache, stomach upset, and trouble seeing. There was also a significant interactive effect with PCE during the diazepam dosing weeks resulting in a mood of less friendliness. Included in this category were the adjectives good natured, friendly, kind, warmhearted, pleasant, and considerate. From this result, we can assume that the subjects assessed themselves to be less friendly during the diazepam and high PCE exposure days.

The effect on each behavioral test for which the data has been analyzed demonstrates that each test provided slightly different results. However, in none of the behavioral tests was there an interaction effect between PCE and alcohol or PCE and diazepam. The general increases in the average scores of the Michigan eye-hand coordination test were:

EXPOSURE CONDITION	SCORE INCREASE	COMMENT
PCE, 100 ppm	0.25 to 0.50 sec	not significant
Diazepam, 10 mg/day	0.86 sec	not significant
Alcohol, 1.5 ml/kg	3.1 sec	significant

The general reduction in the average scores of the Flanagan coordination test were:

EXPOSURE CONDITION	SCORE REDUCTION	COMMENT
PCE, 100 ppm	2 to 4 units	occasionally significant
Diazepam, 10 mg/day	2 units	not significant
Alcohol, 1.5 ml/kg	9 to 10 units	highly significant

The average changes in time off target in the rotary pursuit test due to exposure conditions were:

EFFECT ON TIME OFF TARGET (SECONDS)

Exposure Condition	15 rpm	30 rpm	45 rpm	60 rpm	Comment
PCE, 100 ppm	.08 to +.3	.28 to .46	+.1 to +.5	.9 to -1.2	all not significant
Diazepam, 10 mg/day	+0.7	+1.1	+2.1	+2.3	all significant decrements
Alcohol, 1.5 ml/kg	+1.1	+4.5	+7.9	+5.5	all significant decrements
74 Days of Testing,	-.2 to -.4	-2.7 to -5.0	-5.6 to -8.0	-5.1 to -6.4	all significant improvements

Comparison of the results from these three behavioral tests show that the high dose of alcohol had a significant detrimental effect on performance in all three tests, the high dose of diazepam had a detrimental effect on performance of only the rotary pursuit test, and high PCE had an occasional detrimental effect only on the Flanagan coordination test.

The correlation of performances on the rotary pursuit test at four speeds to the other two coordination tests during 21 days when complete data for all nine subjects was available resulted in the following levels of correlation:

TEST	15 rpm			30 rpm			45 rpm			60 rpm		
	low	middle	high	low	middle	high	low	middle	high	low	middle	high
Flanagan coordination	-.77	-.53	+.15	-.90	-.60	-.17	-.81	-.62	+.01	-.66	-.45	+.29
Michigan eye-hand, AM	-.37	+.08	+.49	-.29	+.25	+.53	-.40	+.29	+.73	+.01	+.43	+.77
Michigan eye-hand, PM	-.32	+.11	+.83	-.26	+.31	+.78	-.20	+.28	+.86	-.01	+.54	+.88

From these correlations it can be concluded that the rotary pursuit test at all speeds is moderately correlated with the Flanagan coordination test while the Michigan eye-hand coordination test, both AM and PM, correlate best with the rotary pursuit test at high speeds and poorly at low speeds. These results, together with the detrimental differences already noted, suggest that these coordination tests measure similar but not identical tasks.

CONCLUSIONS

A comprehensive study of the behavioral and neurological effects of perchloroethylene (tetrachloroethylene) exposure alone at OSHA standard concentrations, and in combination with low doses of diazepam or alcohol, has been carried out. The result of data analysis from one behavioral test is not yet available. However, the results of all other behavioral testing lead us to conclude that perchloroethylene at its present standard of 100 ppm had no consistent, significant effect upon the performance of four behavioral tests, and the addition of alcohol or diazepam at relatively low levels added no significant decrement to performance over and above that imposed by the alcohol or diazepam itself. There was a non-consistent significant detrimental effect of perchloroethylene alone in the performance of the Flanagan coordination test. However, any additive effect or interaction with alcohol was obscured by the highly significant alcohol effect upon the performance of this test. There was no additive effect by diazepam addition to the PCE exposure. Analysis of neurological data revealed a significant but inconsistent increase in the beta activity of the EEG during combined perchloroethylene exposure and diazepam dosing. We interpret this increased beta activity to be due primarily to the diazepam, although it did not appear consistently with diazepam alone. However, diazepam alone has been reported to have this effect, whereas, perchloroethylene alone has not.

At the levels of dosing studied, there was no exacerbation of the deleterious behavioral and/or neurological effects of either alcohol or diazepam when perchloroethylene was added to the exposure. However, the results emphasize the hazard involved with drinking alcohol during any work situation, as decrements in coordination were found at blood alcohol levels below those generally considered to be legally drunk (100 mg %). Diazepam, at the low dosages generally prescribed for outpatients, caused a significant decrement in only one of three coordination tests. The EEG changes noted are therefore difficult to associate with any projected increased work hazard from these low dosages. In summary, the results from this laboratory study suggest that the degree of hazard the workman presents to himself and others when the effect of low doses of alcohol or diazepam are added to that of breathing OSHA standard PCE vapor levels will be no greater than these attributable to the alcohol or diazepam alone.

REFERENCES

American Conference of Governmental Industrial Hygienists: Documentation of the Threshold Limit Values for Substances in Workroom Air, Third Edition, ACGIH, Cincinnati, 1971, pp. 201-202.

Baloh, R. W., A. W. Sill, W. E. Kumley, and V. Honrubia. 1976. Quantitative measurement of saccade amplitude, duration and velocity. (Manuscript submitted for publication.)

Crow, E. L., F. A. Davis, and M. W. Marfield. 1960. Statistics Manual. Dover Publications, Inc., N.Y. p. 134.

Davis, D. 1971. Mood changes in alcoholic subjects with programmed and free-choice experimental drinking. pp. 496-618. In: N. K. Mello and J. H. Mendelson, Ed. Recent Advances in Studies of Alcoholism. U.S. Government Printing Office.

Garriott, J. C. 1975. Diazepam, Type C Procedure. pp. 121-123. In: I. Sunshine, Ed. Methodology for Analytical Toxicology. CRC Press, Cleveland, Ohio.

Hillstad, L., T. Hansen, and H. Melsom. 1974. Diazepam metabolism in normal man II. Serum concentration and clinical effect after oral administration and cumulation. Clin. Pharmacol. Ther. 16:485-489.

Hynek, K., J. Tosovský and J. Süsová. 1975. Interhemispheral differences in the effect of psychotropic drugs in EEG. Electroencephalogr. Clin. Neurophysiol. (Proceedings). 39:440.

Jasper, H. H. 1958. The 10-20 electrode systems of the international federation. EEG Clin. Neurophysiol. 10:371-375

Jones, B. M., and A. Vega. 1972. Cognitive performance measured on the ascending and descending limb of the blood alcohol curve. Psychopharmacologia (Berl.). 23:99-114.

Kalant, H., A. E. LeBlanc, A. Wilson, and S. Homatidis. 1975. Sensorimotor and physiological effects of various alcoholic beverages. Canad. Med. Assoc. J. 112:953-958.

Kleinknecht, R. A., and D. Donaldson. 1975. A review of the effects of diazepam on cognitive and psychomotor performance. J. Nerv. Ment. Dis. 161:399-414.

Levine, R. R. 1973. Pharmacology. Drug Actions and Reactions. Little, Brown and Co., Boston. p. 333.

McNair, D. M. and M. Lorr. 1964. An analysis of mood in neurotics. J. Abnorm. Soc. Psychol. 69:620-627.

Montagu, J. D. 1972. Effects of diazepam on the EEG in man. Eur. J. Pharmac. 17:167-170.

Moskowitz, H. 1974. Drug effects in relation to industrial safety. pp. 333-347. In: C. Xintaras, B. L. Johnson, and I. de Groot, Ed. Behavioral Toxicology. U. S. Dept. of HEW, NIOSH.

Moskowitz, H., and S. Sharma. 1974. Effects of alcohol on peripheral vision as a function of attention. Human Factors. 16:174-180.

Pook, G. K. 1967. Prediction of Elemental Motion Performance Using Personnel Selection Tests. Ph.D. Thesis. University Microfilms, Inc. Ann Arbor, Michigan

Robinson, S. 1974. Physiology of muscular exercise, In: V. B. Mountcastle, Ed. Medical Physiology. The C. V. Mosby Co., St. Louis, Missouri. 2:1273-1304, 13th ed.

Roche Laboratories. Valium^{R} (Diazepam) tablets, package insert issued January, 1975. Div. of Hoffman-LaRoche Inc., Nutley, N.J.

Sellman, R., J. Kanto, E. Raijola, and A. Pekkarinen. 1975. Induction effect of diazepam on its own metabolism. Acta. Pharmacol. Toxicol. 37:345-351.

Sidell, F. R., and J. E. Pless. 1971. Ethyl alcohol: blood levels and performance decrement after oral administration to man. Psychopharmacologia (Berl.). 19:246-261.

Stewart, R. D., C. L. Hake, H. V. Forster, A. J. Lebrun, J. E. Peterson, A. Wu, and Staff. 1974. Tetrachloroethylene: development of a biologic standard for the industrial worker by breath analysis. Report No. NIOSH-MCOW-ENVM-PCE-74-6. NIOSH. Cincinnati, Ohio

Stewart, R. D., C. L. Hake, and A. Wu. 1976. Use of breath analysis to monitor methylene chloride exposure. Scand. J. Work, Environment, Health. 2:57-70.

TABLE I

PERC/DRUG STUDY
1975

WEEK	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	
1	29	30	1	2 ORIENTATION TRAINING	3 TRAINING	4	
2	6 TRAINING	7 1. 0 ppm * 2. no drug 3. Gp A	8 0 ppm no drug Gp B	9 25 ppm no drug Gp A	10 100 ppm no drug Gp B	11 V - 6 mg	OCTOBER
3	13 0 ppm V- 6 mg Gp B	14 0 ppm V- 6 mg Gp B	15 100 ppm V- 6 mg Gp B	16 25 ppm V- 6 mg Gp B	17 100 ppm V- 6 mg Gp B	18 Placebo	
4	20 0 ppm Placebo Gp A	21 0 ppm Placebo Gp B	22 100 ppm Placebo Gp A	23 25 ppm Placebo Gp B	24 100 ppm Placebo Gp B	25	
5	27 0 ppm Alc.-0.75ml/kg Gp A	28 0 ppm Alc.-0.75ml/kg Gp A	29 100 ppm Alc.-0.75ml/kg Gp A	30 25 ppm Alc.-0.75ml/kg Gp A	31 100 ppm Alc.-0.75ml/kg Gp A	1	
6	3 100 ppm no drug Gp A	4 0 ppm no drug Gp B	5 0 ppm no drug Gp A	6 25 ppm no drug Gp B	7 100 ppm no drug Gp B	8 Placebo	NOVEMBER
7	10 0 ppm Placebo Gp A	11 0 ppm Placebo Gp B	12 100 ppm Placebo Gp A	13 25 ppm Placebo Gp B	14 100 ppm Placebo Gp B	15 V-12 mg	
8	17 0 ppm V-12 mg Gp B	18 0 ppm V-12 mg Gp B	19 100 ppm V-12 mg Gp B	20 25 ppm V-12 mg Gp B	21 100 ppm V-12 mg Gp B	22	
9	24 NO STUDIES THIS WEEK	25	26	27 THANKSGIVING HOLIDAYS	28	29	
10	1 0 ppm Alc.-1.50ml/kg Gp A	2 0 ppm Alc.-1.50 ml/kg Gp A	3 100 ppm Alc.-1.50ml/kg Gp A	4 25 ppm Alc.-1.50ml/kg Gp A	5 100 ppm Alc.-1.50ml/kg Gp A	6	DECEMBER
11	8 100 ppm no drug Gp A	9 0 ppm no drug Gp B	10 0 ppm no drug Gp A	11 25 ppm no drug Gp B	12 100 ppm no drug Gp B	13	
12	15 25 ppm no drug Gp A	16 0 ppm no drug Gp A	17 0 ppm no drug Gp B	18 PHYSICAL EXAMINATIONS	19	20	

* 1. Concentration of PCE in chamber.
2. V = VALIUM® in daily dose, or alc. = ml of 100 proof vodka per kg body weight.
3. Gp of 6 subjects who will have EEG's. Other group of 6 subjects will carry out eye function tests.

TABLE II

PERC/DRUG STUDY
1975

WEEK	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY	SATURDAY	
1	29	30	1	2 ORIENTATION TRAINING	3 TRAINING	4	
2	6 TRAINING	7 1. 0 ppm * 2. no drug 3. Gp A	8 0 ppm no drug Gp B	9 25 ppm no drug Gp A	10 100 ppm no drug Gp B	11 V - 6 mg	OCTOBER
3	13 0 ppm V- 6 mg Gp B	14 0 ppm V- 6 mg Gp B	15 100 ppm V- 6 mg Gp B	16 25 ppm V- 6 mg Gp B	17 100 ppm V- 6 mg Gp B	18 Placebo	
4	20 0 ppm Placebo Gp A	21 0 ppm Placebo Gp B	22 100 ppm Placebo Gp A	23 25 ppm Placebo Gp B	24 100 ppm Placebo Gp B	25	
5	27 0 ppm Alc.-0.75ml/kg Gp A	28 0 ppm Alc.-0.75ml/kg Gp A	29 100 ppm Alc.-0.75ml/kg Gp A	30 25 ppm Alc.-0.75ml/kg Gp A	31 100 ppm Alc.-0.75ml/kg Gp A	1	NOVEMBER
6	3 100 ppm no drug Gp A	4 0 ppm no drug Gp B	5 0 ppm no drug Gp A	6 25 ppm no drug Gp B	7 100 ppm no drug Gp B	8 V - 10 mg	
7	10 0 ppm V-10 mg Gp B	11 0 ppm V-10 mg Gp B	12 100 ppm V-10 mg Gp B	13 25 ppm V-10 mg Gp B	14 100 ppm V-10 mg Gp B	15 Placebo	
8	17 0 ppm Placebo Gp A	18 0 ppm Placebo Gp B	19 100 ppm Placebo Gp A	20 25 ppm Placebo Gp B	21 100 ppm Placebo Gp B	22	
9	24 25 ppm no drug Gp A	25 0 ppm no drug Gp A	26 0 ppm no drug Gp B	27 THANKSGIVING	28 HOLIDAYS	29	
10	1 0 ppm Alc.-1.50ml/kg Gp A	2 0 ppm Alc.-1.50 ml/kg Gp A	3 100 ppm Alc.-1.50 ml/kg Gp A	4 25 ppm Alc.-1.50 ml/kg Gp A	5 100 ppm Alc.-1.50 ml/kg Gp A	6 V - 6 mg	DECEMBER
11	8 0 ppm V- 6 mg Gp B	9 0 ppm V- 6 mg Gp B	10 100 ppm V- 6 mg Gp B	11 25 ppm V- 6 mg Gp B	12 100 ppm V- 6 mg Gp B	13	
12	15 100 ppm no drug Gp A	16 0 ppm no drug Gp B	17 0 ppm no drug Gp A	18 25 ppm no drug Gp B	19 100 ppm no drug Gp B	20 Phys. Exams	

* 1. Concentration of PCE in chamber.
2. V = VALIUM® in daily dose, or Alc. = approx. ml of 100 proof vodka per kg body weight (dose adjusted individually).
3. Gp of 6 subjects who will have EEG's. Other group of 6 subjects will carry out visual function tests.

TABLE III

SUBJECTS PARTICIPATING IN STUDY

SUBJECT NUMBER	ASSIGNED GROUP	AGE	HEIGHT (cm.)	WEIGHT (kg.)
		FEMALE		
95	A	37	164	62.3
326	A	23	170	61.1
327	A	19	165	59.2
328	B	25	162	81.6
329	B	27	172	56.6
330	B	24	160	61.0
		MALE		
117	A	27	171	75.8
123	A	42	173	69.2
331	A	33	182	78.4
332	B	22	170	59.8
333	B	23	180	59.8
334	B	29	178	84.8

TABLE IV

SUMMARY OF SUBJECT ATTENDANCE DURING STUDY

SUBJECT NUMBER & SEX	POTENTIAL DAYS, TOTAL	TOTAL DAYS PRESENT	TOTAL DAYS ABSENT
	GROUP A		
95, F	55	54	1
326, F	19[a]	19	0
327, F	55	45	10
117, M	55	48	7
123, M	32[b]	22	10
331, M	17-1/2[a]	17-1/2	0
	GROUP B		
328, F	55	47	8
329, F	55	54	1
330, F	55	55	0
332, M	55	50	5
333, M	53[c]	51	2
334, M	55	53	2

[a] withdrew from study

[b] withdrawn from study

[c] alternate subject

TABLE V

PCE CONCENTRATION IN EXPOSURE CHAMBER
TWA and SD in ppm

WEEK	ADDIT. EXPOSURE	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
2	none		1 0	2 0	3 25.1 ±0.9	4 100.1 ±3.7	5	6
3	Valium 6 mg	7 0	8 0	9 99.9 ±3.4	10 25.7 ±1.0	11 99.8 ±3.8	12	13
4	Placebo	14 0	15 0	16 101.5 ±4.9	17 25.2 ±0.9	18 100.0 ±2.9	19	20
5	Alcohol 0.75ml/kg	21 0	22 0	23 100.1 ±2.9	24 25.0 ±0.6	25 100.7 ±4.1	26	27
6	none	28 100.3 ±3.4	29 0	30 0	31 25.2 ±1.4	32 99.9 ±2.7	33	34
7	Valium 10 mg	35 0	36 0	37 101.0 ±3.5	38 25.4 ±1.3	39 100.2 ±3.7	40	41
8	Placebo	42 0	43 0	44 99.8 ±3.3	45 25.1 ±1.0	46 99.2 ±2.9	47	48
9	none	49 25.3 ±1.0	50 0	51 0	52	53 THANKSGIVING HOLIDAYS	54	55
10	Alcohol 1.5ml/kg	56 0	57 0	58 100.3 ±4.0	59 25.7 ±1.2	60 99.7 ±3.6	61	62
11	Valium 6 mg	63 0	64 0	65 100.8 ±3.2	66 25.0 ±1.0	67 99.8 ±3.2	68	69
12	none	70 100.0 ±3.5	71 0	72 0	73 25.4 ±1.1	74 100.3 ±3.1		

TABLE VI

ML VODKA CONSUMED BY SUBJECTS DAILY DURING WEEKS 5 & 10

GROUP A

SUBJECT	SEX	WEEK 5	WEEK 10
95	F	64 ml	90 ml
326	F	out of study	out of study
327	F	55 ml	90 ml
117	M	76 ml	110 ml
123	M	65 ml	out of study
331	M	75 ml	out of study

GROUP B

SUBJECT	SEX	WEEK 5	WEEK 10
328	F	60 ml	120 ml
329	F	56 ml	90 ml
330	F	60 ml	90 ml
332	M	62 ml	100 ml
333	M	60 ml	100 ml
334	M	75 ml	100 ml

TABLE VII

DEVIATIONS TO DIAZEPAM AND PLACEBO DOSES

WEEK 3: *Three diazepam capsules/day, with meals, starting on weekend.*

WEEKEND - 328 missed 1 dose; 331 missed 3 doses; 332 missed 1 dose; 334 missed 7 doses (all).

MONDAY - 331 missed breakfast dose; 334 missed breakfast dose.

TUESDAY - 327 missed breakfast dose.

WEDNESDAY - 117 missed breakfast dose.

THURSDAY - 327 missed supper dose; 331 missed supper dose.

FRIDAY - 327 missed breakfast dose.

WEEK 4: *Three placebo capsules/day, with meals, starting on weekend.*

WEEKEND - 326, 328, 331 and 333 missed 1 dose.

MONDAY - 117 and 123 absent.

TUESDAY - 123 absent; 331 missed breakfast dose.

WEDNESDAY - 123 & 327 absent; 329 - no doses after breakfast.

THURSDAY - 123 absent; 329 - no doses.

FRIDAY - 123 absent.

WEEK 7: *Two diazepam capsules/day, w/breakfast and supper, starting on weekend.*

WEEKEND - 327 missed 5 doses (all).

MONDAY - 123 absent.

TUESDAY - 123 absent.

WEDNESDAY - 123 and 332 absent, no doses.

THURSDAY - 123 absent.

FRIDAY - 123 absent; 300 missed chamber dose due to nausea.

TABLE VII (continued)

WEEK 8: *Two placebo capsules/day, w/breakfast and supper, starting on weekend.*

WEEKEND - No recorded deviations.

MONDAY - 117 and 327 absent, missed 2 doses.

TUESDAY - 327 absent, missed 2 doses.

WEDNESDAY - No recorded deviations.

THURSDAY - No recorded deviations.

FRIDAY - 328 absent.

WEEK 11: *Three diazepam capsules/day, with meals, starting on weekend.*

WEEKEND - 327 missed 3 doses; 333 missed 1 dose.

MONDAY - 328 absent, missed 1 dose.

TUESDAY - 328 missed 3 doses; 333 absent, no doses.

WEDNESDAY - 327 and 328 absent; 328 no doses.

THURSDAY - 328 absent.

FRIDAY - 117, 328, and 332 absent.

TABLE VIII

PCE BLOOD CONCENTRATIONS

WEEK: 2 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	no exposure				
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
DAY 4:	Baseline	25				
	2' of Exposure		0.7	0.6-1.0	0.2	6
DAY 5:	Baseline	100				
	2' of Exposure		13.9	7.9-21.0	5.0	5
			FEMALES			
DAY 1:	Baseline	no exposure				
	2' of Exposure					
Day 2:	Baseline	0				
	2' of Exposure					
Day 3:	Baseline	0				
	2' of Exposure					
Day 4:	Baseline	25				
	2' of Exposure		0.6	0.3-0.8	0.2	6
Day 5:	Baseline	100				
	2' of Exposure		7.2	4.0-10.1	2.3	6

TABLE IX

PCE BLOOD CONCENTRATIONS

WEEK: 3 (Valium, 6 mg.)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	0.1	0.0-0.4	0.2	6
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure		0.1	0.0-0.4	0.2	6
DAY 3:	Baseline	100				
	2' of Exposure		8.8	7.0-9.6	1.0	6
DAY 4:	Baseline	25	0.3	0.2-0.7	0.2	6
	2' of Exposure		1.0	0.8-1.2	0.1	6
DAY 5:	Baseline	100	0.1	0.0-0.2	0.1	6
	2' of Exposure		9.7	5.7-12.2	2.6	5
			FEMALES			
DAY 1:	Baseline	0	0.1	0.0-0.2	0.1	6
	2' of Exposure					
Day 2:	Baseline	0	0.2	0.0-0.4	0.1	5
	2' of Exposure					
Day 3:	Baseline	100				
	2' of Exposure		9.0	6.7-11.3	1.8	6
Day 4:	Baseline	25	0.4	0.3-0.8	0.1	6
	2' of Exposure		0.8	0.6-1.0	0.1	6
Day 5:	Baseline	100				
	2' of Exposure		8.2	6.3-10.4	1.5	6

TABLE X

PCE BLOOD CONCENTRATIONS

WEEK: 4 (Placebo)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	0.2	0.1-0.3	0.1	3
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		9.1	7.8-10.8	1.2	5
DAY 4:	Baseline	25				
	2' of Exposure		1.8	1.4-2.2	0.3	5
DAY 5:	Baseline	100				
	2' of Exposure		7.4	7.0-8.6	0.7	5
			FEMALES			
DAY 1:	Baseline	0				
	2' of Exposure		0.4	0.3-0.6	0.1	6
Day 2:	Baseline	0	0.1	0.0-0.8	0.3	6
	2' of Exposure					
Day 3:	Baseline	100	<0.1	0.0-0.2	0.1	6
	2' of Exposure		8.5	7.1-9.2	1.0	4
Day 4:	Baseline	25	<0.1	0.0-0.2	0.1	5
	2' of Exposure		1.4	1.0-1.8	0.3	5
Day 5:	Baseline	100				
	2' of Exposure		6.9	5.9-8.8	1.3	5

TABLE XI

PCE BLOOD CONCENTRATIONS

WEEK: 5 (Alcohol, 0.75 ml/kg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0				
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		7.0	5.6-8.4	1.3	5
DAY 4:	Baseline	25	0.1	0.0-0.3	0.1	5
	2' of Exposure		2.5	1.8-3.2	0.6	5
DAY 5:	Baseline	100				
	2' of Exposure		8.7	6.4-12.0	2.3	5
			FEMALES			
DAY 1:	Baseline					
	2' of Exposure					
Day 2:	Baseline	0				
	2' of Exposure					
Day 3:	Baseline	100				
	2' of Exposure		8.5	7.6-9.2	0.8	4
Day 4:	Baseline	25	0.1	0.0-0.2	0.1	4
	2' of Exposure		2.7	2.1-3.2	0.6	4
Day 5:	Baseline	100	0.1	0.0-0.2	0.1	6
	2' of Exposure		9.6	8.0-12.0	1.8	5

TABLE XII

PCE BLOOD CONCENTRATIONS

WEEK: 6 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	100				
	2' of Exposure		7.3	6.2-9.0	1.1	5
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
DAY 4:	Baseline	25				
	2' of Exposure		1.6	1.4-2.0	0.3	4
DAY 5:	Baseline	100	0.5	0.4-0.7	0.1	4
	2' of Exposure		7.3	6.6-8.8	0.8	5
			FEMALES			
DAY 1:	Baseline	100	0.4	0.4-0.5	<0.1	4
	2' of Exposure		7.8	5.8-9.0	1.3	5
Day 2:	Baseline	0	0.4	0.0-0.7	0.4	5
	2' of Exposure					
Day 3:	Baseline	0				
	2' of Exposure					
Day 4:	Baseline	25				
	2' of Exposure		1.5	1.3-1.7	0.2	4
Day 5:	Baseline	100	0.6	0.3-0.9	0.2	4
	2' of Exposure		7.2	5.8-8.4	1.1	4

TABLE XIII

PCE BLOOD CONCENTRATIONS

WEEK: 7 (Valium, 10 mg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	0.3	0.0-0.4	0.2	3
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		10.5	7.6-13.2	2.8	3
DAY 4:	Baseline	25				
	2' of Exposure		2.2	1.5-2.6	0.5	4
DAY 5:	Baseline	100	0.6	0.4-0.8	0.2	4
	2' of Exposure		12.7	10.8-14.7	1.7	4
			FEMALES			
DAY 1:	Baseline	0	0.5	0.0-0.6	0.3	5
	2' of Exposure					
Day 2:	Baseline	0				
	2' of Exposure					
Day 3:	Baseline	100				
	2' of Exposure		9.4	7.5-11.1	1.5	5
Day 4:	Baseline	25	0.4	0.0-0.8	0.3	5
	2' of Exposure		3.2	2.7-4.2	0.6	5
Day 5:	Baseline	100	0.5	0.3-0.8	0.2	5
	2' of Exposure		10.8	8.2-13.8	2.5	4

TABLE XIV

PCE BLOOD CONCENTRATIONS

WEEK: 8 (Placebo)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	1.1	1.0-1.2	0.1	3
	2' of Exposure					
DAY 2:	Baseline	0	0.2	0.0-0.5	0.2	4
	2' of Exposure					
DAY 3:	Baseline	100	<0.1	0.0-0.2	0.1	4
	2' of Exposure		5.9	4.6-7.3	1.1	4
DAY 4:	Baseline	25	0.4	0.4-0.5	0.1	3
	2' of Exposure		1.3	1.2-1.5	0.1	4
DAY 5:	Baseline	100	0.6	0.5-0.8	0.1	4
	2' of Exposure		7.9	6.5-9.5	1.4	4
			FEMALES			
DAY 1:	Baseline	0	1.2	1.2-1.4	0.1	4
	2' of Exposure					
Day 2:	Baseline	0	0.3	0.2-0.6	0.2	4
	2' of Exposure					
Day 3:	Baseline	100	0.1	0.0-0.4	0.2	5
	2' of Exposure		7.2	5.0-8.6	1.5	5
Day 4:	Baseline	25	0.4	0.3-0.6	0.1	5
	2' of Exposure		1.2	0.9-1.5	0.3	4
Day 5:	Baseline	100	0.5	0.4-0.5	<0.1	3
	2' of Exposure		7.4	6.5-8.4	0.9	4

TABLE XV

PCE BLOOD CONCENTRATIONS

WEEK: 9 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	25	0.4	0.3-0.5	0.1	3
	2' of Exposure		1.7	1.6-1.8	0.2	3
DAY 2:	Baseline	0	0.7	0.7-0.9	0.1	3
	2' of Exposure					
DAY 3:	Baseline	0	0.1	0.1-0.2	<0.1	2
	2' of Exposure					
DAY 4:	Baseline	no exposure				
	2' of Exposure					
DAY 5:	Baseline	no exposure				
	2' of Exposure					
			FEMALES			
DAY 1:	Baseline	25	0.4	0.0-0.8	0.3	5
	2' of Exposure		1.7	1.6-1.8	0.1	5
Day 2:	Baseline	0	0.6	0.4-0.8	0.1	5
	2' of Exposure					
Day 3:	Baseline	0				
	2' of Exposure					
Day 4:	Baseline	no exposure				
	2' of Exposure					
Day 5:	Baseline	no exposure				
	2' of Exposure					

TABLE XVI

PCE BLOOD CONCENTRATIONS

WEEK: 10 (Alcohol, 1.5 ml/kg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0				
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		7.4	7.0-8.4	0.7	4
DAY 4:	Baseline	25	0.7	0.5-0.8	0.2	4
	2' of Exposure		3.0	2.8-3.2	0.2	4
DAY 5:	Baseline	100	0.3	0.2-0.6	0.2	3
	2' of Exposure		6.8	6.0-8.1	1.1	3
			FEMALES			
DAY 1:	Baseline	0				
	2' of Exposure					
Day 2:	Baseline	0				
	2' of Exposure					
Day 3:	Baseline	100				
	2' of Exposure		7.3	6.0-8.5	1.2	4
Day 4:	Baseline	25	0.7	0.6-0.7	<0.1	4
	2' of Exposure		3.0	2.7-3.5	0.3	5
Day 5:	Baseline	100	0.4	0.4-0.5	0.1	4
	2' of Exposure		7.0	6.0-8.3	1.1	4

TABLE XVII

PCE BLOOD CONCENTRATIONS

WEEK: 11 (Valium, 6 mg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	0.3	0.3-0.4	<0.1	3
	2' of Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		3.3	2.5-4.2	0.7	4
DAY 4:	Baseline	25				
	2' of Exposure		1.4	1.1-1.6	0.2	4
DAY 5:	Baseline	100				
	2' of Exposure		8.6	8.0-9.2	0.8	2
			FEMALES			
DAY 1:	Baseline	0	0.4	0.3-0.4	<0.1	4
	2' of Exposure					
Day 2:	Baseline	0				
	2' of Exposure					
Day 3:	Baseline	100				
	2' of Exposure		3.8	3.0-4.9	1.0	3
Day 4:	Baseline	25				
	2' of Exposure		2.0	1.8-2.1	0.1	4
Day 5:	Baseline	100				
	2' of Exposure		8.2	7.5-8.8	0.5	4

TABLE XVIII

PCE BLOOD CONCENTRATIONS

WEEK: 12 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BLOOD CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	100				
	2' of Exposure		10.9	9.9-11.7	0.9	3
DAY 2:	Baseline	0				
	2' of Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
DAY 4:	Baseline	25	2.2	1.6-2.7	0.5	4
	2' of Exposure					
DAY 5:	Baseline	100				
	2' of Exposure		9.8	8.7-11.2	1.1	4
			FEMALES			
DAY 1:	Baseline	100				
	2' of Exposure					
Day 2:	Baseline	0				
	2' of Exposure					
Day 3:	Baseline	0				
	2' of Exposure					
Day 4:	Baseline	25				
	2' of Exposure					
Day 5:	Baseline	100				
	2' of Exposure					

TABLE XIX

PCE BREATH CONCENTRATIONS

WEEK: 2 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	no exposure				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15' Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	25				
	2' of Exposure		6.4	5.7-7.2	0.5	6
	15" Post Exposure		4.4	2.6-4.7	0.8	6
	30" Post Exposure		3.6	2.0-4.3	0.8	6
DAY 5:	Baseline	100	1.7	1.5-1.9	0.2	5
	2' of Exposure		30.8	27.4-32.4	2.1	5
	15" Post Exposure		20.5	17.7-23.1	2.3	5
	30" Post Exposure		16.6	14.6-18.9	2.2	5
			FEMALES			
DAY 1:	Baseline	no exposure				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	25				
	2' of Exposure		6.6	5.5-8.1	0.9	6
	15" Post Exposure		4.1	2.0-5.9	1.5	6
	30" Post Exposure		3.0	1.4-4.1	1.0	6
DAY 5:	Baseline	100	1.7	1.5-1.9	0.2	5
	2' of Exposure		32.9	24.6-39.3	5.8	6
	15" Post Exposure		18.3	13.8-22.5	3.8	6
	30" Post Exposure		15.1	9.7-18.4	3.7	6

TABLE XX

PCE BREATH CONCENTRATIONS

WEEK: 3 (Valium, 6 mg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	1.3	0.8-1.9	0.5	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0	0.9	0.6-1.1	0.2	6
	2' of Exposure					
	15" Post Exposure		0.7	0.5-1.0	0.2	6
	30" Post Exposure					
DAY 3:	Baseline	100	0.6	0.6-0.6	0	6
	2' of Exposure		33.8	29.2-36.7	3.0	6
	15" Post Exposure		20.5	15.8-22.3	2.4	6
	30" Post Exposure		16.8	13.6-20.9	2.6	6
DAY 4:	Baseline	25	3.4	2.9-3.8	0.4	6
	2' of Exposure		12.8	10.5-15.3	1.6	6
	15" Post Exposure		8.8	7.6-10.5	1.1	6
	30" Post Exposure		7.5	6.7-8.8	0.8	6
DAY 5:	Baseline	100	1.3	1.1-1.6	0.3	6
	2' of Exposure		47.0	31.0-59.9	9.9	6
	15" Post Exposure		29.0	25.4-33.8	2.8	6
	30" Post Exposure		23.9	18.3-26.8	3.2	6
			FEMALES			
DAY 1:	Baseline	0	1.9	1.3-2.9	0.6	6
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0	0.8	0.5-1.1	0.2	6
	2' of Exposure					
	15" Post Exposure		1.0	0.8-1.1	0.1	5
	30" Post Exposure					
DAY 3:	Baseline	100	0.6	0.5-0.9	0.1	6
	2' of Exposure		31.7	21.0-38.1	5.9	6
	15" Post Exposure		19.4	15.1-25.2	3.9	6
	30" Post Exposure		15.1	9.4-19.4	3.5	6
DAY 4:	Baseline	25	3.2	2.3-4.1	0.6	6
	2' of Exposure		12.0	9.1-14.1	1.8	6
	15" Post Exposure		8.1	6.8-9.4	1.0	5
	30" Post Exposure		6.4	4.1-7.3	1.1	6
DAY 5:	Baseline	100	1.0	0.9-1.0	0.1	6
	2' of Exposure		51.4	43.7-57.7	6.6	6
	15" Post Exposure		29.6	19.7-40.8	7.0	6
	30" Post Exposure		22.3	17.7-27.5	3.4	6

TABLE XXI

PCE BREATH CONCENTRATIONS

WEEK: 4 (Placebo)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	1.2	1.1-1.5	0.2	4
	2' of Exposure					
	15" Post Exposure		0.9	0.7-1.2	0.2	4
	30" Post Exposure					
DAY 2:	Baseline	0	1.0	1.0-1.1	0	5
	2' of Exposure					
	15" Post Exposure		0.9	0.7-1.1	0.2	3
	30" Post Exposure					
DAY 3:	Baseline	100	0.9	0.5-1.0	0.2	5
	2' of Exposure		34.6	29.2-39.6	3.8	5
	15" Post Exposure		21.1	16.7-23.4	2.8	5
	30" Post Exposure		18.0	14.1-19.8	2.5	5
DAY 4:	Baseline	25	3.3	2.2-4.4	0.8	5
	2' of Exposure		12.7	12.1-14.3	0.9	5
	15" Post Exposure		6.1	4.7-7.7	1.1	5
	30" Post Exposure		6.1	5.2-7.2	0.8	5
DAY 5:	Baseline	100	2.7	2.3-3.7	0.6	5
	2' of Exposure		38.9	33.2-44.2	4.2	5
	15" Post Exposure		22.0	19.4-26.7	2.9	5
	30" Post Exposure		19.5	14.7-22.1	3.1	5
			FEMALES			
DAY 1:	Baseline	0	1.4	1.2-1.8	0.2	6
	2' of Exposure					
	15" Post Exposure		1.3	1.2-1.8	0.3	5
	30" Post Exposure					
DAY 2:	Baseline	0	1.0	0.8-1.1	0.2	6
	2' of Exposure					
	15" Post Exposure		0.9	0.7-1.1	0.2	3
	30" Post Exposure					
DAY 3:	Baseline	100	0.9	0.8-1.0	0.1	6
	2' of Exposure		35.9	28.1-41.6	6.8	4
	15" Post Exposure		21.8	19.2-27.1	4.6	3
	30" Post Exposure		18.7	15.6-23.4	4.1	3
DAY 4:	Baseline	25	2.7	2.2-3.9	0.7	5
	2' of Exposure		11.4	9.9-12.1	0.9	5
	15" Post Exposure		6.1	4.9-8.2	1.3	5
	30" Post Exposure		5.1	3.8-6.0	0.9	4
DAY 5:	Baseline	100	2.4	1.8-2.8	0.5	5
	2' of Exposure		36.9	27.6-46.1	6.6	6
	15" Post Exposure		20.8	17.1-28.1	4.4	6
	30" Post Exposure		19.2	14.7-25.8	4.4	6

TABLE XXII

PCE BREATH CONCENTRATIONS

WEEK: 5 (Alcohol, 0.75 ml/kg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	1.8	0 -2.6	1.1	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		32.3	23.1-36.5	5.6	5
	15" Post Exposure		16.5	10.6-22.1	4.2	5
	30" Post Exposure		14.7	10.1-20.2	4.3	5
DAY 4:	Baseline	25	3.8	3.0-4.5	0.6	4
	2' of Exposure		15.2	14.9-16.4	0.7	5
	15" Post Exposure		9.5	7.5-11.2	1.3	5
	30" Post Exposure		8.3	6.3-9.7	1.5	5
DAY 5:	Baseline	100	2.7	2.5-3.1	0.3	5
	2' of Exposure		36.3	32.5-42.5	3.8	5
	15" Post Exposure		16.5	13.1-20.0	2.7	5
	30" Post Exposure		12.5	11.3-13.8	1.1	4
			FEMALES			
DAY 1:	Baseline	0	1.9	1.2-2.3	0.4	6
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		31.3	25.0-38.5	5.5	4
	15" Post Exposure		16.9	14.4-20.2	2.7	5
	30" Post Exposure		15.4	11.5-18.8	3.0	4
DAY 4:	Baseline	25	3.9	3.0-4.5	0.7	4
	2' of Exposure		13.4	10.4-14.9	2.1	4
	15" Post Exposure		9.8	8.2-11.9	1.6	4
	30" Post Exposure		8.2	6.0-9.7	1.6	4
DAY 5:	Baseline	100	2.3	1.8-2.5	0.3	5
	2' of Exposure		34.5	25.0-40.0	5.7	5
	15" Post Exposure		16.5	13.8-18.8	2.6	5
	30" Post Exposure		13.1	11.3-16.3	2.3	5

TABLE XXIII

PCE BREATH CONCENTRATIONS

WEEK: 6 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	100	3.1	2.5-4.5	1.0	4
	2' of Exposure		33.1	28.2-39.5	4.4	5
	15" Post Exposure		18.8	13.6-22.1	3.3	5
	30" Post Exposure		16.1	11.8-20.5	3.3	5
DAY 2:	Baseline	0	4.1	3.8-4.5	0.3	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	25	1.4	1.1-1.8	0.3	5
	2' of Exposure		11.6	10.8-12.9	0.9	4
	15" Post Exposure		7.9	7.5-8.1	0.3	4
	30" Post Exposure		7.1	6.9-7.3	0.2	4
DAY 5:	Baseline	100	2.6	1.3-3.4	0.9	5
	2' of Exposure		30.5	28.1-34.9	2.6	5
	15" Post Exposure		18.5	16.2-20.8	1.8	5
	30" Post Exposure		16.4	14.1-17.7	1.5	5
			FEMALES			
DAY 1:	Baseline	100	3.2	2.8-3.4	0.3	5
	2' of Exposure		35.6	27.1-39.0	4.9	5
	15" Post Exposure		19.8	18.4-22.1	1.4	5
	30" Post Exposure		17.2	15.4-19.0	1.4	5
DAY 2:	Baseline	0	3.5	3.0-3.8	0.3	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	25	1.4	1.1-1.8	0.3	4
	2' of Exposure		11.2	10.5-12.5	0.9	4
	15" Post Exposure		8.5	8.1-8.6	0.3	4
	30" Post Exposure		7.5	7.3-7.8	0.2	4
DAY 5:	Baseline	100	2.4	1.9-3.4	0.6	5
	2' of Exposure		26.3	19.3-34.9	6.6	4
	15" Post Exposure		18.0	13.6-23.2	4.1	4
	30" Post Exposure		17.0	13.6-20.8	3.0	4

TABLE XXIV

PCE BREATH CONCENTRATIONS

WEEK: 7 (Valium, 10 mg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	2.2	2.1-2.3	0.1	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0	1.1	0.9-1.5	0.2	4
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100	1.5	1.4-1.7	0.2	3
	2' of Exposure		27.5	24.0-31.1	3.6	3
	15" Post Exposure		18.7	15.0-21.2	3.3	3
	30" Post Exposure		16.4	13.7-18.5	2.5	3
DAY 4:	Baseline	25	3.0	1.8-4.1	0.9	4
	2' of Exposure		11.1	9.3-12.3	1.4	4
	15" Post Exposure		8.2	6.7-8.8	1.0	4
	30" Post Exposure		7.4	5.3-9.2	1.6	4
DAY 5:	Baseline	100	3.0	2.7-3.4	0.3	4
	2' of Exposure		33.1	31.3-34.2	1.4	4
	15" Post Exposure		18.0	16.6-20.2	1.7	4
	30" Post Exposure		16.2	13.6-19.0	2.6	4
			FEMALES			
DAY 1:	Baseline	0	2.1	1.4-2.5	0.5	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0	1.2	0.9-1.5	0.2	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100	1.5	0.7-2.0	0.6	5
	2' of Exposure		28.4	23.3-31.1	3.2	5
	15" Post Exposure		16.6	14.6-19.2	2.1	5
	30" Post Exposure		14.64	13.0-16.4	1.7	5
DAY 4:	Baseline	25	3.2	2.8-3.7	0.3	5
	2' of Exposure		11.9	10.2-13.0	1.1	5
	15" Post Exposure		8.1	6.5-9.5	1.1	5
	30" Post Exposure		7.1	6.0-8.1	1.0	5
DAY 5:	Baseline	100	3.5	3.1-4.3	0.5	5
	2' of Exposure		31.9	29.9-35.7	2.6	4
	15" Post Exposure		15.5	14.0-16.3	1.1	4
	30" Post Exposure		14.2	12.0-17.1	2.3	4

TABLE XXV

PCE BREATH CONCENTRATIONS

WEEK: 8 (Placebo)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	3.2	3.0-3.5	0.2	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0	2.3	2.1-2.6	0.3	4
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100	1.9	1.6-2.3	0.3	4
	2' of Exposure		30.3	27.5-32.1	1.9	4
	15" Post Exposure		19.4	18.3-21.9	1.7	4
	30" Post Exposure		16.3	15.0-18.3	1.6	4
DAY 4:	Baseline	25	3.0	2.8-3.2	0.2	4
	2' of Exposure		10.0	9.1-11.2	0.9	4
	15" Post Exposure		7.3	6.7-8.0	0.5	4
	30" Post Exposure		6.9	6.6-7.1	0.2	4
DAY 5:	Baseline	100	3.0	2.9-3.1	0.1	4
	2' of Exposure		27.6	25.8-30.9	2.4	4
	15" Post Exposure		16.7	12.0-21.1	4.0	4
	30" Post Exposure		14.7	11.4-17.5	2.8	4
			FEMALES			
DAY 1:	Baseline	0	3.9	3.5-4.3	0.4	4
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0	2.5	1.5-3.0	0.7	4
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100	1.7	1.3-2.6	0.6	5
	2' of Exposure		29.72	25.6-32.7	2.8	5
	15" Post Exposure		16.2	13.4-19.0	2.7	5
	30" Post Exposure		15.5	13.8-17.7	2.0	3
DAY 4:	Baseline	25	3.0	2.7-3.2	0.2	5
	2' of Exposure		11.3	10.7-12.6	0.8	5
	15" Post Exposure		7.9	7.5-9.4	0.8	5
	30" Post Exposure		6.6	6.2-7.0	0.3	5
DAY 5:	Baseline	100	3.0	2.6-3.3	0.3	4
	2' of Exposure		26.9	23.7-32.0	3.7	4
	15" Post Exposure		16.2	14.0-18.6	1.9	4
	30" Post Exposure		14.5	11.4-16.5	2.3	4

TABLE XXVI

PCE BREATH CONCENTRATIONS

WEEK: 9 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	25	2.5	1.8-3.6	1.0	3
	2' of Exposure		8.8	6.2-10.3	2.3	3
	15" Post Exposure		6.9	6.3-7.6	0.6	3
	30" Post Exposure		5.6	4.1-6.7	1.4	3
DAY 2:	Baseline	0	2.3	2.0-2.5	0.3	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0	1.4	1.3-1.5	0.1	2
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	no exposure				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 5:	Baseline	no exposure				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
			FEMALES			
DAY 1:	Baseline	25	2.4	2.1-2.8	0.3	5
	2' of Exposure		1.0	8.0-11.6	1.3	5
	15" Post Exposure		7.0	5.7-8.0	0.9	5
	30" Post Exposure		5.9	5.1-6.4	0.5	5
DAY 2:	Baseline	0	2.2	1.9-2.7	0.3	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0	1.4	1.2-1.7	0.2	5
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	no exposure				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 5:	Baseline	no exposure				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					

TABLE XXVII

PCE BREATH CONCENTRATIONS

WEEK: 10 (Alcohol, 1.5 ml/kg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		30.0	25.0-34.2	4.7	3
	15" Post Exposure		15.3	11.0-19.7	3.6	4
	30" Post Exposure		12.1	7.6-14.9	4.0	3
DAY 4:	Baseline	25	3.4	2.2-5.2	1.4	4
	2' of Exposure		11.5	11.0-12.3	0.6	4
	15" Post Exposure		7.9	6.8-8.9	0.9	4
	30" Post Exposure		6.7	6.5-6.8	0.2	3
DAY 5:	Baseline	100	2.3	1.6-3.0	0.7	3
	2' of Exposure		33.5	26.5-37.0	6.1	3
	15" Post Exposure		17.9	16.5-19.1	1.3	3
	30" Post Exposure		13.3	10.4-18.0	4.1	3
			FEMALES			
DAY 1:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		28.5	28.6-32.3	3.3	5
	15" Post Exposure		15.8	14.5-17.1	1.0	5
	30" Post Exposure		11.6	9.6-13.5	1.4	5
DAY 4:	Baseline	25	4.1	3.4-5.2	0.8	4
	2' of Exposure		10.0	8.2-11.6	1.2	5
	15" Post Exposure		6.8	5.5-8.2	1.1	5
	30" Post Exposure		5.8	4.8-6.5	0.7	5
DAY 5:	Baseline	100	2.9	2.7-3.3	0.3	4
	2' of Exposure		30.5	27.5-33.5	2.5	5
	15" Post Exposure		17.5	14.7-21.8	3.1	5
	30" Post Exposure		12.9	9.8-14.7	1.8	5

TABLE XXVIII

PCE BREATH CONCENTRATIONS

WEEK: 11 (Valium, 6 mg)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	0	2.4	1.7-2.9	0.6	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		32.1	31.1-32.4	0.7	4
	15" Post Exposure		17.7	13.0-20.0	3.3	4
	30" Post Exposure		16.2	12.7-18.4	2.5	4
DAY 4:	Baseline	25	3.3	2.4-3.9	0.8	3
	2' of Exposure		11.3	10.4-12.6	0.9	
	15" Post Exposure		6.1	5.8-6.7	0.6	4
	30" Post Exposure		6.1	4.3-7.5	1.3	4
DAY 5:	Baseline	100	3.8	3.2-4.3	0.8	2
	2' of Exposure		41.3	33.3-49.3	11.3	2
	15" Post Exposure		17.7	17.3-18.0	0.5	2
	30" Post Exposure		16.8	16.0-17.5	1.1	2
			FEMALES			
DAY 1:	Baseline	0	2.0	1.7-2.7	0.4	4
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 2:	Baseline	0				
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	100				
	2' of Exposure		36.0	35.1-37.8	1.6	3
	15" Post Exposure		21.3	20.3-21.9	0.9	3
	30" Post Exposure		18.6	18.4-18.9	0.3	3
DAY 4:	Baseline	25	3.3	2.6-4.1	0.8	3
	2' of Exposure		10.4	9.3-11.2	0.8	4
	15" Post Exposure		7.0	4.5-8.3	1.7	4
	30" Post Exposure		6.4	4.3-7.5	1.4	4
DAY 5:	Baseline	100	3.5	3.2-4.0	0.4	4
	2' of Exposure		38.0	30.0-45.3	6.3	4
	15" Post Exposure		18.6	12.7-21.0	4.0	4
	30" Post Exposure		17.1	12.3-20.7	3.6	4

TABLE XXIX

PCE BREATH CONCENTRATIONS

WEEK: 12 (Control)

	TIME OF SAMPLE	PCE CHAMBER CONC., PPM	PCE BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
			MALES			
DAY 1:	Baseline	100	3.9	3.6-4.1	0.3	3
	2' of Exposure		36.6	32.0-39.5	4.1	3
	15" Post Exposure		23.5	18.2-28.3	5.1	3
	30" Post Exposure		16.9	13.9-22.4	4.8	3
DAY 2:	Baseline	0	3.9	3.4-4.3	0.5	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0	2.3	1.4-3.1	0.9	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	25				
	2' of Exposure		11.4	10.2-13.6	1.6	4
	15" Post Exposure		6.5	5.4-8.9	1.6	4
	30" Post Exposure		6.1	5.3-7.2	0.9	4
DAY 5:	Baseline	100	2.3	1.8-2.7	0.4	4
	2' of Exposure		41.5	35.7-46.3	5.2	4
	15" Post Exposure		25.7	20.4-29.0	3.9	4
	30" Post Exposure		20.5	14.9-25.9	4.6	4
			FEMALES			
DAY 1:	Baseline	100	4.1	3.7-4.3	0.3	4
	2' of Exposure		35.2	34.1-37.9	1.8	4
	15" Post Exposure		22.2	19.2-24.8	2.5	4
	30" Post Exposure		18.2	13.9-21.1	3.1	4
DAY 2:	Baseline	0	3.7	3.4-3.8	0.2	4
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 3:	Baseline	0	3.1	2.6-3.4	0.4	3
	2' of Exposure					
	15" Post Exposure					
	30" Post Exposure					
DAY 4:	Baseline	25				
	2' of Exposure		9.9	6.4-11.6	2.4	4
	15" Post Exposure		6.2	3.8-8.3	1.9	4
	30" Post Exposure		5.7	4.5-7.1	1.1	4
DAY 5:	Baseline	100	2.4	1.8-2.9	0.6	3
	2' of Exposure		37.0	31.4-40.4	3.9	4
	15" Post Exposure		22.1	16.5-28.6	5.0	5
	30" Post Exposure		18.4	10.0-23.9	6.9	5

TABLE XXX

ETHANOL BLOOD* CONCENTRATIONS

DAY OF WEEK	PCE CHAMBER CONC., PPM	ETHANOL BLOOD CONC., mg/dl MEAN	RANGE	±S.D.	NO. OF SUBJECTS
		WEEK 5			
Dose: Approximately 0.75 ml vodka/kg body weight					
		MALES			
1	0	35.6	28.5-42.5	5.1	5
2	0	50.6	31.7-64.3	13.8	4
3	100	44.1	25.5-56.4	11.5	5
4	25	50.0	41.0-63.2	9.1	5
5	100	50.7	39.2-59.1	8.1	5
		FEMALES			
1	0	32.1	13.6-42.1	10.9	5
2	0	48.5	33.7-58.6	11.2	4
3	100	43.1	20.7-56.9	14.5	5
4	25	54.8	45.9-64.9	8.0	4
5	100	46.8	23.9-60.3	15.0	5
		WEEK 10			
Dose: Approximately 1.5 ml vodka/kg body weight					
		MALES			
1	0	62.6	40.0-90.5	20.8	4
2	0	51.7	44.6-58.4	6.2	4
3	100	58.8	44.1-66.1	10.0	4
4	25	65.5	54.0-81.0	13.2	4
5	100	69.2	65.0-72.0	3.7	3
		FEMALES			
1	0	63.3	41.1-85.5	15.9	5
2	0	64.1	44.0-74.1	12.6	5
3	100	54.2	36.8-71.4	15.0	5
4	25	74.4	34.0-105.0	26.7	5
5	100	70.1	47.5-95.0	21.8	5

*Sampled 15-20 min after dosage that was consumed over 30-min period

TABLE XXXI

ETHANOL BREATH* CONCENTRATIONS

DAY OF WEEK	PCE CHAMBER CONC., PPM	ETHANOL BREATH CONC., PPM MEAN	RANGE	±S.D.	NO. OF SUBJECTS
WEEK 5					
Dose: Approximately 0.75 ml vodka/kg body weight					
MALES					
1	0	130	102-154	26	3
2	0	181	144-245	48	4
3	100	153	118-181	27	4
4	25	156	130-180	23	4
5	100	156	106-200	38	5
FEMALES					
1	0	118	82-170	41	4
2	0	136	125-147	10	4
3	100	131	75-200	62	4
4	25	198	160-270	63	3
5	100	148	96-192	48	3
WEEK 10					
Dose: Approximately 1.5 ml vodka/kg body weight					
MALES					
1	0	209	162-255	38	4
2	0	241	201-313	50	4
3	100	218	206-247	20	4
4	25	250	202-304	43	4
5	100	194	160-226	33	3
FEMALES					
1	0	341	240-465	111	4
2	0	335	262-480	85	5
3	100	277	182-352	71	4
4	25	279	223-324	41	5
5	100	213	173-246	30	4

*Sampled 15-20 min after dosage that was consumed over 30-min period

TABLE XXXII

DIAZEPAM BLOOD* CONCENTRATIONS

DAY OF WEEK	PCE CHAMBER CONC., PPM	DIAZEPAM BLOOD CONC., µg/dl MEAN	RANGE	±S.D.	NO. OF SUBJECTS
		WEEK 3			
Dose: 6 mg/day (2 mg t.i.d.)					
		MALES			
1	0	12	9-16	2.9	6
2	0	19	14-25	3.8	6
3	100	19	14-24	4.7	6
4	25	25	20-32	4.5	6
5	100	24	21-29	2.9	6
		FEMALES			
1	0	12	9-17	2.7	6
2	0	17	14-22	2.8	6
3	100	17	13-21	2.9	6
4	25	21	20-22	0.6	6
5	100	21	16-27	3.7	6
		WEEK 4			
Dose: Placebo					
		MALES			
1	0	<5**			4
2	0	<5			1
3	100	<5			2
4	25	<5			1
5	100	<5			1
		FEMALES			
1	0	<5			6
2	0	<5			3
3	100	<5			2
4	25	<5			1
5	100	<5			2

*Sampled approximately 45 min after second dose
**Detection limit = 5 µg/dl

TABLE XXXIII

DIAZEPAM BLOOD* CONCENTRATIONS

DAY OF WEEK	PCE CHAMBER CONC., PPM	DIAZEPAM BLOOD CONC., µg/dl MEAN	RANGE	±S.D.	NO. OF SUBJECTS
		WEEK 7			
Dose: 10 mg/day (5 mg b.i.d.)					
		MALES			
1	0	19	17-21	1.7	4
2	0	13	10-18	3.6	4
3	100	18	14-21	3.5	3
4	25	21	11-41	13.5	4
5	100	30	20-42	9.3	4
		FEMALES			
1	0	16	12-23	4.4	5
2	0	13	8-19	4.2	5
3	100	19	14-28	4.6	5
4	25	17	9-26	6.2	5
5	100	23	13-30	6.3	5
		WEEK 8			
Dose: Placebo					
		MALES			
1	0	--			
2	0	<5**			2
3	100	<5			2
4	25	<5			2
5	100	<5			1
		FEMALES			
1	0	<5			3
2	0	<5			2
3	100	<5			2
4	25	<5			1
5	100	--			

*Sampled approximately 45 min after second dose
**Detection limit = 5 µg/dl

TABLE XXXIV

DIAZEPAM BLOOD* CONCENTRATIONS

DAY OF WEEK	PCE CHAMBER CONC., PPM	DIAZEPAM BLOOD CONC., µg/dl MEAN	RANGE	±S.D.	NO. OF SUBJECTS
		WEEK 11			
Dose: 6 mg/day (2 mg t.i.d.)					
		MALES			
1	0	8	6-9	1.4	4
2	0	12	11-14	1.5	3
3	100	11	7-16	4.4	3
4	25	19	11-25	7.0	4
5	100	8	8-8	0.0	2
		FEMALES			
1	0	8	5-10	2.1	4
2	0	15	11-20	3.3	5
3	100	12	9-15	3.0	3
4	25	13	8-18	4.1	4
5	100	16	10-20	4.2	4
		WEEK 12			
Dose: Control					
		MALES			
1	0	<5**			3
2	0				
3	100	<5			1
4	25				
5	100				
		FEMALES			
1	0	<5			4
2	0	<5			1
3	100				
4	25				
5	100				

*Sampled approximately 45 min after second dose
**Detection limit = 5 µg/dl

TABLE XXXV

ALCOHOL AND DIAZEPAM EFFECTS UPON PERCHLOROETHYLENE
BLOOD AND BREATH LEVELS, 5-1/2 HOUR EXPOSURE

PCE in Chamber, PPM	PPM PCE in Blood			PPM PCE in Breath					
	@ 2 hours into exposure			@ 2 hours into exposure			@ 30 minutes post exposure		
	PCE alone	PCE + alcohol[a]	PCE + diazepam[b]	PCE alone	PCE + alcohol[a]	PCE + diazepam[b]	PCE alone	PCE + alcohol[a]	PCE + diazepam[b]
25	1.65 (35)	2.92** (15)	1.76 (23)	11.03 (35)	12.35* (15)	11.72 (23)	6.40 (35)	7.49** (14)	6.96* (22)
100	8.25 (63)	7.96 (29)	8.47 (41)	33.2 (68)	32.3 (28)	35.5 (44)	17.62 (64)	13.83** (29)	17.35 (42)

a Alcohol blood levels of 30 to 100 mg%

b Diazepam blood levels of 7 to 30 mcg%

* Significantly different from PCE alone at $p<.05$

** Significantly different from PCE alone at $p<.01$

(n) Number of determinations

TABLE XXXVI

DEVIATIONS NOTED IN PERC/DRUG STUDY

WEEK	DAY	PCE, PPM	OTHER	GENERAL, BEHAVIORAL, NEUROLOGICAL, SUBJECTIVE, MEDICAL DEVIATIONS
2	2	0	--	General - all ss learning schedule. Medical - ss117 and 329 have viral infections. Neurological - computer EEG program not working.
	3	0	--	Behavioral - all ss told to hold arms parallel to table in Michigan eye-hand, mechanical problems with rotary pursuit and dual-tasks tests. Neurological - no PM EEG tracings for s334.
	4	25	--	Behavioral - saccade velocity test equipment problems.
	5	100	--	Medical - s326 mildly nauseated in AM.
3	1	0	diazepam, daily, 6 mg	General - s327 tired.
	2	0		Behavioral - s330 had difficulty during Flanagan Coordination due to coughing. Subjective - s333 was clarified re. "check" questions on mood test.
	3	100		General - physician noted altered mood in chamber. Behavioral - staff operator noted problems with dual-attention task equipment.
	4	25		--
	5	100		General - s329 upset due to involvement in car accident previous PM. Behavioral - ss327, 330, and 334 rotary pursuit tests invalid due to mechanical problems. Medical - s326 has URI.
4	1	0	placebo daily	Behavioral - still having problems with dual-tasks test.
	2	0		Medical - ss330 & 333 have URI.
	3	100		General - all testing started 40 min later than normal. Behavioral - dual-task test equipment repaired. Neurological - EEG computer program repaired. Medical - s327 sent home, URI. s329 not exposed due to medical problem.
	4	25		General - all testing started 20 min later than normal. Medical - s329 still held out from study resolving medical problem.
	5	100		Medical - s329 back in study.

(continued)

TABLE XXXVI(continued)

DEVIATIONS NOTED IN PERC/DRUG STUDY

WEEK	DAY	PCE, PPM	OTHER	GENERAL, BEHAVIORAL, NEUROLOGICAL, SUBJECTIVE, MEDICAL DEVIATIONS
5	1	0	alcohol, daily, 0.75 ml per kg	General - control day for s326. s331 called home on emergency (last day exposed).
	2	0		General - last control day for s326. Medical - s117 sent home due to flu-like symptoms. Behavioral - s329 given second saccade velocity test.
	3	100		--
	4	25		Medical - s327 has URI.
	5	100		--
6	1	100	--	Behavioral - ss95, 327, and 332 rotary pursuit mechanical problems. Medical - s327 has soft tissue bruise on leg, s334 GI problems.
	2	0	--	Behavioral - rotary pursuit data all invalid.
	3	0	--	Medical - s334 held out of study due to medical problem.
	4	25	--	Medical - s334 held out of study due to medical problem.
	5	100	--	Medical - s334 had medical problem resolved, back in study.
7	1	0	diazepam, daily, 10 mg	General - s117 ingested 2 beers prior to coming to work, all data invalid.
	2	0		Subjective - ss all seem tired and subdued.
	3	100		Behavioral - rotary pursuit data for s327 invalid.
	4	25		Behavioral - dual tasks test data invalid for s95.
	5	100		General - s123 withdrawn from study because of unexcused absences. Medical - s330 taken out of chamber at 1.5 hr due to nausea.
8	1	0	placebo, daily	--
	2	0		Medical - s332 has URI.
	3	100		Neurological - ss may have noted accidental blinking of strobe light during EEG. Medical - ss95, 330, 332 have cough or sore throat.
	4	25		Neurological - ss328 and 330 reported light flash during EEG, corrected today.

(continued)

TABLE XXXVI (continued)

DEVIATIONS NOTED IN PERC/DRUG STUDY

WEEK	DAY	PCE, PPM	OTHER	GENERAL, BEHAVIORAL, NEUROLOGICAL, SUBJECTIVE, MEDICAL DEVIATIONS
8	5	100		Medical - s330 has URI.
9	1	25	--	Medical - s328 has some "flu -like" symptoms.
	2	0	--	Behavioral - s334 had finger injury and tetanus shot, therefore, Flanagan coordination, rotary pursuit, Michigan eye-hand data invalid. Medical - s330 has URI.
	3	0	--	Behavioral - s117 repeated rotary pursuit test.
	4	holiday		
	5	holiday		
10	1	0	alcohol, daily,	--
	2	0	1.5 ml per kg	--
	3	100		--
	4	25		--
	5	100		Behavioral - s329 had invalid rotary pursuit test.
11	1	0	diazepam, daily, 6 mg	Subjective - s330 upset due to multiple sticks upon blood withdrawal. Medical - s333 has URI.
	2	0		General - s332 entered study 40 min late, all data invalid.
	3	100		--
	4	25		--
	5	100		Behavioral - s330 Flanagan coordination invalid. Subjective - all mood tests invalid due to random answering w/o pseudonyms.
12	1	100	--	General - all ss entered chamber 15 min later than normal.
	2	0	--	--
	3	0	--	General - s333 entered chamber 20 min late.
	4	25	--	General - all ss received debriefing in PM - s333 entered chamber 15 min late.
	5	100	--	Behavioral - all rotary pursuit data probably invalid due to mechanical difficulties.

TABLE XXXVII

MOOD ASSESSMENT CONTEXT ARRANGED IN NINE GROUPS
ACCORDING TO DAVIS(1971)

DEPRESSSION	CAREFREE	FRIENDLINESS
sad	happy	goodnatured
downhearted	full of pep	friendly
worthless	carefree	kind
unhappy	at ease	warmhearted
useless	active	pleasant
depressed	cheerful	considerate
blue	satisfied	
troubled	lively	
lonely	efficient	MISCELLANEOUS
		suspicious
HOSTILITY	ANXIETY	feel sexy
		need a cigarette
angry	tense	need a drink
irritable	on edge	taken advantage of
annoyed	fearful	hungry
rude	impatient	headache
sarcastic	restless	stomach upset
	nervous	trouble seeing
COGNITIVE GAIN	jittery	
		FATIGUED
confused	GUILTY-ASHAMED	
able to think clearly		tired
forgetful	troubled by conscience	sleepy
able to concentrate	sorry for things done	worn out
alert	weary	

TABLE XXXVIII

EFFECT OF PCE AND DIAZEPAM UPON SUBJECTIVE SYMPTOMS AND PCE ODOR PERCEPTION
MEAN PER SUBJECT REPORT

PCE Conc, ppm		0	25	100	0	25	100	0	25	100	0	25	100
Drug Dose, mg/day		0	0	0	Plac	Plac	Plac	6	6	6	10	10	10
No. of Subject Reports		71	35	46	35	19	38	40	20	37	18	9	16
SYMPTOM		Mean Number Per Subject Report											
HEADACHE	incidence	0.14	0.11	0.09	0.20	0.11	0.08	0.05	0.05	0.08	0.06	0.11	0.06
	persistence	0.42	0.34	0.09	0.43	0.21	0.08	0.13	0.05	0.30	0.06	0.11	0.06
NAUSEA	incidence	0.03	0.03	0.09	0.0	0.05	0.0	0.0	0.0	0.03	0.06	0.11	0.13
	persistence	0.07	0.03	0.28		0.11				0.05	0.28	0.22	0.38
DIZZINESS	incidence	0.01	0.06	0.07	0.03	0.05	0.05	0.05	0.0	0.03	0.06	0.22	0.13
	persistence	0.01	0.14	0.07	0.03	0.11	0.16	0.10		0.11	0.06	0.44	0.50
CHEST PAIN	incidence	0.03	0.03	0.02	0.06	0.0	0.0	0.03	0.05	0.03	0.0	0.0	0.0
	persistence	0.10	0.06	0.15	0.31			0.18	0.40	0.22			
ABDOM. PAIN	incidence	0.0	0.03	0.07	0.14	0.11	0.03	0.05	0.0	0.03	0.06	0.0	0.0
	persistence		0.23	0.28	0.46	0.11	0.13	0.40		0.08	0.44		
ENT IRRIT.	incidence	0.42	0.49	0.35	0.34	0.26	0.37	0.30	0.45	0.38	0.28	0.33	0.31
	persistence	1.93	2.11	1.91	1.80	1.16	1.89	1.05	0.50	1.73	0.72	0.89	1.06
OTHER	incidence	0.28	0.37	0.24	0.43	0.42	0.34	0.35	0.40	0.32	0.44	0.56	0.56
	persistence	1.06	1.51	0.83	1.54	1.47	0.97	1.35	1.50	1.05	2.00	2.00	2.13
ODOR													
MILD	incidence	0.21	0.66	0.59	0.17	0.79	0.55	0.15	0.80	0.57	0.06	0.67	0.44
	persistence	0.44	1.71	1.67	0.26	1.47	2.00	0.28	1.85	1.68	0.17	1.33	1.31
MODERATE	incidence	0.03	0.60	0.65	0.0	0.26	0.47	0.0	0.35	0.70	0.06	0.22	0.56
	persistence	0.04	0.89	1.15		0.26	1.08		0.50	1.97	0.06	1.22	0.63
STRONG	incidence	0.01	0.20	0.48	0.0	0.16	0.61	0.0	0.05	0.57	0.0	0.11	0.50
	persistence	0.01	0.26	0.98		0.16	0.89		0.10	0.68		0.11	1.06

TABLE XXXIX

EFFECT OF PCE AND ALCOHOL UPON SUBJECTIVE SYMPTOMS AND PCE ODOR PERCEPTION
MEAN PER SUBJECT REPORT

PCE Conc, ppm		0	25	100	0	25	100	0	25	100
Alcohol Dose, ca. ml/kg		0	0	0	0.75	0.75	0.75	1.5	1.5	1.5
No. of Subject Reports		71	35	46	19	9	20	17	9	17
SYMPTOM		Mean Number Per Subject Report								
HEADACHE	incidence	0.14	0.11	0.09	0.26	0.11	0.10	0.24	0.11	0.06
	persistence	0.42	0.34	0.09	1.05	0.22	0.10	0.53	0.33	0.12
NAUSEA	incidence	0.03	0.03	0.09	0.05	0.22	0.15	0.06	0.0	0.0
	persistence	0.07	0.03	0.28	0.05	0.67	0.80	0.18		
DIZZINESS	incidence	0.01	0.06	0.07	0.0	0.22	0.05	0.0	0.0	0.0
	persistence	0.01	0.14	0.07		0.33	0.10			
CHEST PAIN	incidence	0.03	0.03	0.02	0.0	0.0	0.0	0.0	0.0	0.0
	persistence	0.10	0.06	0.15						
ABDOM. PAIN	incidence	0.0	0.03	0.07	0.05	0.11	0.05	0.0	0.0	0.0
	persistence		0.23	0.28	0.16	0.22	0.15			
ENT IRRIT.	incidence	0.42	0.49	0.35	0.42	0.22	0.40	0.24	0.33	0.47
	persistence	1.93	2.11	1.91	1.32	0.89	1.20	1.12	1.67	2.12
OTHER	incidence	0.28	0.37	0.24	0.21	0.44	0.35	0.41	0.33	0.47
	persistence	1.06	1.51	0.83	1.05	1.22	1.30	1.18	0.89	1.29
ODOR										
MILD	incidence	0.21	0.66	0.59	0.11	0.44	0.65	0.0	0.78	0.47
	persistence	0.44	1.71	1.67	0.21	1.22	1.70		1.22	1.29
MODERATE	incidence	0.03	0.60	0.65	0.0	0.56	0.60	0.0	0.33	0.59
	persistence	0.04	0.89	1.15		1.67	1.25		0.33	1.47
STRONG	incidence	0.01	0.20	0.48	0.0	0.0	0.45	0.0	0.22	0.47
	persistence	0.01	0.26	0.98			0.75		0.33	0.59

TABLE XL

EFFECT OF PCE AND DIAZEPAM UPON STAFF ASSESSMENT
OF SUBJECTS' MOOD AND BEHAVIOR

PCE Conc, ppm	0	25	100	0	25	100	0	25	100	0	25	100
Drug Dose, mg/day	0	0	0	Plac	Plac	Plac	6	6	6	10	10	10
Days	6	3	4	4	2	4	2	1	3	2	1	2
DIMENSION												
Alert	0.86	0.62	1.02	0.64	1.63	1.06	0.82	0.83	0.97	-1.00	-1.00	-0.24
Concentration	0.72	0.49	0.73	0.66	1.09	1.00	1.12	0.83	1.04	-0.41	0.33	-0.17
Happy	0.67	0.02	1.21	0.31	1.38	1.12	0.21	1.33	1.36	-0.61	-0.67	-0.25
At Ease	0.75	0.33	0.79	0.71	1.27	1.03	0.59	1.00	1.82	1.08	0.33	0.33
Friendly	0.97	0.30	0.77	0.65	1.34	1.11	0.72	1.33	1.22	0.34	1.00	0.59
Carefree	0.72	0.27	0.93	0.51	1.42	0.83	0.59	1.17	1.23	0.59	0.67	0.34
Full of Pep	0.18	0.33	0.40	-0.56	1.05	0.13	-0.34	0.0	-0.16	-1.92	-1.83	-1.75
Giddy	-0.56	-0.54	-0.18	-1.01	0.57	-0.25	-0.90	0.0	0.24	-1.00	-0.83	-1.34
Talkative	0.22	-0.16	0.77	-0.68	1.20	0.63	-0.68	1.00	0.55	-1.50	-1.00	-1.17
Active	0.19	0.21	0.56	-0.85	0.92	0.17	-0.85	0.83	0.54	-1.50	-0.67	-1.25
Cooperative	0.59	0.37	0.87	0.94	0.84	0.80	0.94	0.67	1.07	0.25	0.33	0.67
In Balance	0.11	0.06	0.27	0.46	0.68	0.33	0.46	0.33	0.32	0.0	0.17	0.17

TABLE XLI

EFFECT OF PCE AND ALCOHOL UPON STAFF ASSESSMENT
OF SUBJECTS' MOOD AND BEHAVIOR

PCE Conc, ppm	0	25	100	0	25	100	0	25	100
Alcohol Dose, ca. ml/kg	0	0	0	0.75	0.75	0.75	1.5	1.5	1.5
Days	6	3	4	2	1	2	2	1	2
DIMENSION									
Alert	0.86	0.62	1.02	0.67	0.80	1.17	1.04	0.50	1.41
Concentration	0.72	0.49	0.73	0.72	0.80	0.83	-0.34	0.0	1.10
Happy	0.67	0.02	1.21	1.02	1.40	1.67	3.46	2.75	3.10
At Ease	0.75	0.33	0.79	1.12	0.40	1.00	2.37	2.50	2.42
Friendly	0.97	0.30	0.77	1.20	0.80	1.67	2.42	2.75	2.81
Carefree	0.72	0.27	0.93	0.98	0.60	1.08	3.12	3.00	2.66
Full of Pep	0.18	0.33	0.40	0.48	0.20	1.08	3.09	1.50	2.25
Giddy	-0.56	-0.54	-0.18	0.30	-0.40	0.42	2.87	1.50	1.95
Talkative	0.22	-0.16	0.77	0.97	0.40	1.33	3.42	3.25	2.86
Active	0.19	0.21	0.56	0.48	0.0	0.83	3.09	2.25	2.58
Cooperative	0.59	0.37	0.87	0.99	0.20	0.83	0.72	1.25	1.27
In Balance	0.11	0.06	0.27	0.19	-0.20	0.25	-0.40	-0.25	-0.16

TABLE XLII

ANALYSIS OF VARIANCE FOR A.M. MICHIGAN EYE-HAND COORDINATION TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	4222.7027			
Linear Day (adj.)	1	1651.7111	1651.7111	329.04643	<.005
Linear PCE (adj.)	1	.67672	.67672	.13481	ns
Linear Alcohol (adj.)	1	.59577	.59577	.11869	ns
Linear PCE x Linear Alc.	1	13.17060	13.17060	2.62379	ns
People Effects	8	1512.4522	189.05652		
Residual	208	1044.09644	5.01969		

TABLE XLIII

ANALYSIS OF VARIANCE FOR P.M. MICHIGAN EYE-HAND COORDINATION TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	3837.4377			
Linear Day (adj.)	1	1362.7621	1362.7621	243.85332	<.005
Linear PCE (adj.)	1	3.76556	3.76556	.67381	ns
Linear Alcohol (adj.)	1	128.04042	128.04042	22.91162	<.005
Linear PCE x Linear Alc.	1	.82714	.82714	.14801	ns
People Effects	8	1179.6459	147.45573		
Residual	208	1162.39673	5.58845		

TABLE XLIV

RESULTS OF TREND ADJUSTED t-TESTS FOR EACH STUDY DAY

Day No.	Exposure Level PCE	Diazepam	Alcohol	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
1	0	0	0	ns	ns	ns	ns	ns	ns	.025	ns	.005	.05	ns
2	0	0	0	ns	.025	.025	ns	ns	ns	ns	ns	ns	ns	ns
3	25	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
4	100	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	.05
7	0	6	0	ns	.02	.001	ns	ns	ns	ns	ns	ns	ns	ns
8	0	6	0	ns	.05	.02	ns	ns	ns	ns	ns	ns	ns	ns
9	100	6	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
10	25	6	0	ns	ns	ns	ns	.05	ns	ns	ns	.05	ns	ns
11	100	6	0	.05	ns	ns	ns	ns	ns	ns	.005	ns	.01	ns
14	0	P	0	ns	ns	ns	ns	.02	ns	.02	ns	ns	ns	ns
15	0	P	0	ns	ns	ns	.005	.05	.025	ns	ns	ns	.02	ns
16	100	P	0	ns	ns	ns	ns	ns	.01	ns	ns	ns	.02	.05
17	25	P	0	ns	.02	.001	ns	.02	.001	ns	ns	.005	ns	ns
18	100	P	0	.02	.005	.005	.05	.01	.02	.05	.05	.02	ns	ns
21	0	0	.75	.05	.05	ns	ns	ns	ns	ns	ns	ns	ns	ns
22	0	0	.75	ns	.02	ns	ns	ns	ns	ns	ns	ns	ns	ns
23	100	0	.75	ns	.001	ns	ns	ns	.05	ns	ns	ns	ns	ns
24	25	0	.75	ns	.005	ns	ns	ns	ns	ns	ns	ns	ns	ns
25	100	0	.75	ns	.05	ns	ns	ns	ns	.05	.05	ns	ns	ns
28	100	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
29	0	0	0	ns	.01	.005	ns	ns	ns	ns	ns	ns	.02	ns
30	0	0	0	ns	.005	.02	ns	.02	ns	ns	ns	.005	ns	ns
31	25	0	0	ns	.005	.01	ns	ns	ns	ns	.05	ns	ns	ns
32	100	0	0	ns	.01	.05	ns	ns	ns	.005	ns	ns	.05	ns
35	0	10	0	ns	ns	ns	.02	ns	ns	ns	ns	ns	.05	.02
35	0	10	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	.025
37	100	10	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	.01
38	25	10	0	ns	ns	.02	ns	ns	ns	ns	ns	ns	ns	ns
39	100	10	0	.001	.05	ns	ns	ns	ns	ns	ns	ns	ns	ns

(continued)

TABLE XLIV (continued)

RESULTS OF TREND ADJUSTED t-TESTS FOR EACH STUDY DAY

Day No.	Exposure Level			(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
	PCE	Diazepam	Alcohol											
42	0	P	0	.05	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
43	0	P	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
44	100	P	0	ns	.01	ns	ns	ns	ns	ns	ns	ns	ns	ns
45	25	P	0	ns	.005	ns	ns	.02	ns	.05	ns	.02	ns	ns
46	100	P	0	ns	.02	ns	ns	ns	ns	ns	ns	ns	ns	ns
49	25	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	.025	ns
50	0	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
51	0	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
56	0	0	1.5	.005	ns	.05	.02	.01	.001	.005	.005	.005	ns	.05
57	0	0	1.5	.01	ns	ns	.025	.02	.005	.001	.025	.005	ns	ns
58	100	0	1.5	.01	ns	.01	.005	.01	.001	.005	.005	.001	ns	ns
59	25	0	1.5	ns	ns	ns	.05	.02	.001	.005	.05	.005	ns	ns
60	100	0	1.5	.05	ns	ns	.05	.01	.005	.05	.05	.005	ns	ns
63	0	6	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	.02	ns
64	0	6	0	ns	ns	ns	ns	.01	ns	ns	ns	.01	ns	ns
65	100	6	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
66	25	6	0	ns	ns	ns	ns	.005	.01	ns	ns	ns	ns	ns
67	100	6	0	ns	ns	ns	ns	.025	ns	.005	ns	.02	ns	ns
70	100	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
71	0	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
72	0	0	0	ns	.02	ns	ns	ns	ns	ns	ns	ns	.05	ns
73	25	0	0	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns
74	100	0	0	ns	ns	ns	ns	ns	ns	ns	ns	.05	ns	ns

(1) Flanagan Coordination
(2) Michigan EH AM
(3) Michigan EH PM
(4) Time Off Target Rotary Pursuit 15 rpm
(5) " " " 30 rpm
(6) " " " 45 rpm
(7) " " " 60 rpm
(8) Errors Rotary Pursuit 15 rpm
(9) " " 30 rpm
(10) " " 45 rpm
(11) " " 60 rpm

TABLE XLV

ANALYSIS OF VARIANCE FOR A.M. MICHIGAN EYE-HAND COORDINATION TEST: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	F-LEVEL
Total	342	7849.0203			
Linear Day (adj.)	1	3120.5006	3120.5006	519.14551	<.005
Linear PCE (adj.)	1	6.55081	6.55081	1.08983	ns
Linear Diaz. (adj.)	1	17.76346	17.76346	2.95524	ns
Linear PCE x Linear Diaz. (adj.)	1	6.13822	6.13822	1.02119	ns
People Effect	8	2714.4892	339.3415		
Residual	330	1983.57813	6.01084		

TABLE XLVI

ANALYSIS OF VARIANCE FOR P.M. MICHIGAN EYE-HAND COORDINATION TEST: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	342	6938.5674			
Linear Day (adj.)	1	2818.4941	2818.4941	496.35094	<.005
Linear PCE (adj.)	1	2.24162	2.24162	.39476	ns
Linear Diaz. (adj.)	1	18.28790	18.28790	3.22059	ns
Linear PCE x Linear Diaz. (adj.)	1	8.47979	8.47979	1.49333	ns
People Effects	8	2217.1813	271.14766		
Residual	330	1873.88281	5.67845		

TABLE XLVII

ANALYSIS OF VARIANCE FOR FLANAGAN COORDINATION TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	41425.0000			
(1)					
Linear Day (adj.)	1	239.3341	239.3341	2.6455	ns
Linear PCE (adj.)	1	754.0464	754.0464	8.3348	P<.005
Linear Alcohol (adj.)	1	3733.4705	3733.4705	41.2677	P<.005
(2)					
Linear Day (adj.)	1	34.2222	34.2222	.3782	ns
Linear PCE (adj.)	1	300.1192	300.1192	3.3173	ns
Linear Alcohol (adj.)	1	1649.0425	1649.0425	18.2276	P<.005
L.PCE x L.Alc.	1	54.5122	54.5122	.6025	ns
People	8	17437.7052	2179.7131		
Residual	208	18817.6602	90.4695		

Note (1): Assumes Model with absence of PCE-Alcohol interaction.

Note (2): Assumes Model with PCE-Alcohol interaction.

TABLE XLVIII

ANALYSIS OF VARIANCE FOR FLANAGAN COORDINATION TEST: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	342	46231.0000			
(1)					
Linear Day (adj.)	1	305.2656	305.2656	4.6395	P<.05
Linear PCE (adj.)	1	437.127	437.127	6.6436	P<.025
Linear Diaz. (adj.)	1	224.8434	224.8434	3.4172	ns
(2)					
Linear Day (adj.)	1	304.3750	304.3750	4.626	P<.05
Linear PCE (adj.)	1	231.1051	231.1051	3.512	P<.1
Linear Diaz. (adj.)	1	105.1256	105.1256	1.598	ns
L.PCE x L.Diaz. (adj.)	1	1.5345	1.5345	.023	ns
People	8	23353.8864	2919.2358		
Residual	330	21712.7539	65.7962		

Note (1): Assumes Model with absence of PCE-Diazepam interaction.

Note (2): Assumes Model with PCE-Diazepam interaction.

TABLE XLIX

ANALYSIS OF VARIANCE FOR 15 RPM ROTARY PURSUIT TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	324.53203			
Linear Day (adj.)	1	1.19046	1.19046	1.62780	ns
Linear PCE (adj.)	1	.47244	.47244	.64600	ns
Linear Alcohol (adj.)	1	22.32041	22.32041	30.52030	<.005
Linear PCE x Linear Alc. (adj.)	1	.00723	.00723	.00989	ns
People Effects	8	148.42441	18.55305		
Residual	208	152.4708	.73133		

TABLE L

ANALYSIS OF VARIANCE FOR 30 RPM ROTARY PURSUIT TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	4241.2867			
Linear Day (adj.)	1	196.84016	196.84016	29.93380	<.005
Linear PCE (adj.)	1	2.14730	2.14730	.32654	ns
Linear Alcohol (adj.)	1	371.27166	371.27166	56.45987	<.005
Linear PCE x Linear Alc. (adj.)	1	5.13211	5.13211	.78045	ns
People Effects	8	2298.493	284.26491		
Residual	208	1257.77587	6.57585		

TABLE LI

ANALYSIS OF VARIANCE FOR 45 RPM ROTARY PURSUIT TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	11060.588			
Linear Day (adj.)	1	805.91894	805.91894	61.07094	<.005
Linear PCE (adj.)	1	8.18365	8.18365	.62014	ns
Linear Alcohol (adj.)	1	1156.1816	1156.1816	87.61314	<.005
Linear PCE x Linear Alc. (adj.)	1	11.15636	11.15636	.84541	ns
People Effects	8	6334.2962	791.78627		
Residual	208	2744.85938	13.19644		

TABLE LII

ANALYSIS OF VARIANCE FOR 60 RPM ROTARY PURSUIT TEST: PCE AND ALCOHOL

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	220	11295.052			
Linear Day (adj.)	1	641.15817	641.15817	42.93551	<.005
Linear PCE (adj.)	1	43.68820	43.68820	2.92560	ns
Linear Alcohol (adj.)	1	568.47365	568.47365	38.06815	<.005
Linear PCE x Linear Alc. (adj.)	1	72.30947	72.30947	4.84224	<.05
People Effects	8	6862.3499	854.9579		
Residual	208	3106.07422	74.93305		

TABLE LIII

ANALYSIS OF VARIANCE FOR 15 RPM ROTARY PURSUIT TEST: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	342	444.03199			
Linear Day (adj.)	1	.97643	.97643	1.23036	ns
Linear PCE (adj.)	1	.26965	.26965	.35313	ns
Linear Diaz. (adj.)	1	12.23945	12.23945	16.0284	<.005
Linear PCE x Linear Diaz. (adj.)	1	.04245	.04245	.05560	ns
People Effects	8	178.51413	22.31427		
Residual	330	251.98988	0.76361		

TABLE LIV

ANALYSIS OF VARIANCE FOR 30 RPM ROTARY PURSUIT TEST: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	342	3748.5687			
Linear Day (adj.)	1	237.84305	237.84305	52.09664	<.005
Linear PCE (adj.)	1	8.57822	8.57822	1.87896	ns
Linear Diaz. (adj.)	1	11.09247	11.09247	2.42967	ns
Linear PCE x Linear Diaz. (adj.)	1	7.61051	7.61051	1.66699	ns
People Effects	8	1976.8558	247.3397		
Residual	330	1506.58889	4.56542		

TABLE LV

ANALYSIS OF VARIANCE FOR 45 RPM RCTARY PURSUIT TEST: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	342	12874.242			
Linear Day (adj.)	1	1015.6076	1015.6076	94.65598	<.005
Linear PCE (adj.)	1	.69796	.69796	.06505	ns
Linear Diaz. (adj.)	1	108.51152	108.51152	10.11342	<.005
Linear PCE x Linear Diaz. (adj.)	1	2.42981	2.42981	.22646	ns
People Effects	8	8206.2754	1025.7844		
Residual	330	3540.72266	10.72946		

TABLE LVI

ANALYSIS OF VARIANCE FOR 60 RPM ROTARY PURSUIT: PCE AND DIAZEPAM

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F-RATIO	P-LEVEL
Total	342	16055.503			
Linear Day (adj.)	1	818.43684	818.43684	55.47987	<.005
Linear PCE (adj.)	1	37.45881	37.45881	2.53924	ns
Linear Diaz. (adj.)	1	129.83125	129.83125	8.80095	<.005
Linear PCE x Linear Diaz. (adj.)	1	2.45736	2.45736	.16658	ns
People Effects	8	10199.178	1274.8992		
Residual	330	4868.14844			

TABLE LVII

RESULTS OF ANALYSIS OF VARIANCE FOR
DOMINANT FREQUENCY SHIFTS FOR EACH LEAD

PCE-ETHANOL GROUP A

SUBJECT	LEAD 1	LEAD 2	LEAD 3	LEAD 4
95	NS	NS	NS	NS
117	NS	NS	NS	NS
327	NS	NS	NS	NS

PCE-DIAZEPAM GROUP B

SUBJECT	LEAD 1	LEAD 2	LEAD 3	LEAD 4
328	NS	NS	NS	NS
329	NS	NS	NS	NS
330	NS	NS	NS	NS
332	NS	NS	NS	NS
333	NS	NS	NS	NS
334	NS	NS	NS	P<.005

TABLE LVIII

RESULTS OF ANALYSIS OF VARIANCE FOR PERCENT RELATIVE ACTIVITY AT DIFFERENT TREATMENT CONDITIONS FOR FOUR FREQUENCY BANDS AND AT EACH OF FOUR LEADS

PCE-ETHANOL GROUP A

SUBJECT	BAND	LEAD 1	LEAD 2	LEAD 3	LEAD 4
95	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	P<.005	NS	NS
	β	NS	NS	NS	NS
117	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	NS	NS	NS
	β	NS	NS	NS	NS
327	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	NS	NS	NS
	β	NS	NS	NS	NS

TABLE LIX

RESULTS OF ANALYSIS OF VARIANCE FOR PERCENT RELATIVE ACTIVITY AT DIFFERENT TREATMENT CONDITIONS FOR FOUR FREQUENCY BANDS AND AT EACH OF FOUR LEADS

PCE-DIAZEPAM GROUP B

SUBJECT	BAND	LEAD 1	LEAD 2	LEAD 3	LEAD 4
328	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	NS	NS	NS
	β	P<.01	NS	NS	NS
329	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	NS	NS	NS
	β	NS	NS	NS	NS
330	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	NS	NS	NS
	β	NS	NS	NS	NS
332	δ	NS	NS	NS	NS
	θ	NS	NS	NS	P<.005
	α	NS	NS	NS	NS
	β	P<.01	P<.005	NS	P<.01
333	δ	NS	NS	NS	NS
	θ	NS	NS	NS	NS
	α	NS	NS	NS	NS
	β	P<.01	NS	NS	NS
334	δ	NS	NS	NS	NS
	θ	P<.005	NS	P<.005	NS
	α	NS	NS	NS	NS
	β	NS	NS	NS	NS

TABLE LX

TREATMENT CONDITIONS SIGNIFICANTLY DIFFERENT
FROM CONTROL FOR GROUP B SUBJECTS

SUBJECT	LEAD	ACTIVITY	TREATMENT CONDITIONS
328	1,β	↑	LO PCE - HI DIAZEPAM
	1,β	↑	HI PCE - HI DIAZEPAM
332	1,β	↑	LO PCE - LO DIAZEPAM
	1,β	↑	HI PCE - HI DIAZEPAM
	1,β	↑	HI PCE - HI DIAZEPAM
	2,β	↑	LO PCE - LO DIAZEPAM
	2,β	↑	HI PCE - HI DIAZEPAM
	4,θ	↓	LO PCE - HI DIAZEPAM
	4,β	↑	HI DIAZEPAM
	4,β	↑	HI PCE - HI DIAZEPAM
333	1,β	↑	HI DIAZEPAM
	1,β	↑	HI PCE - PLACEBO
334	1,θ	↑	LO PCE - HI DIAZEPAM
	3,θ	↓	LO PCE - HI DIAZEPAM
	3,θ	↓	HI PCE - LO DIAZEPAM
	3,θ	↓	HI PCE - HI DIAZEPAM
	4, Dom. Freq.	↓	HI PCE
	4, Dom. Freq.	↓	HI DIAZEPAM
	4, Dom. Freq.	↓	LO PCE - HI DIAZEPAM
	4, Dom. Freq.	↓	HI PCE - LO DIAZEPAM
	4, Dom. Freq.	↓	HI PCE - HI DIAZEPAM

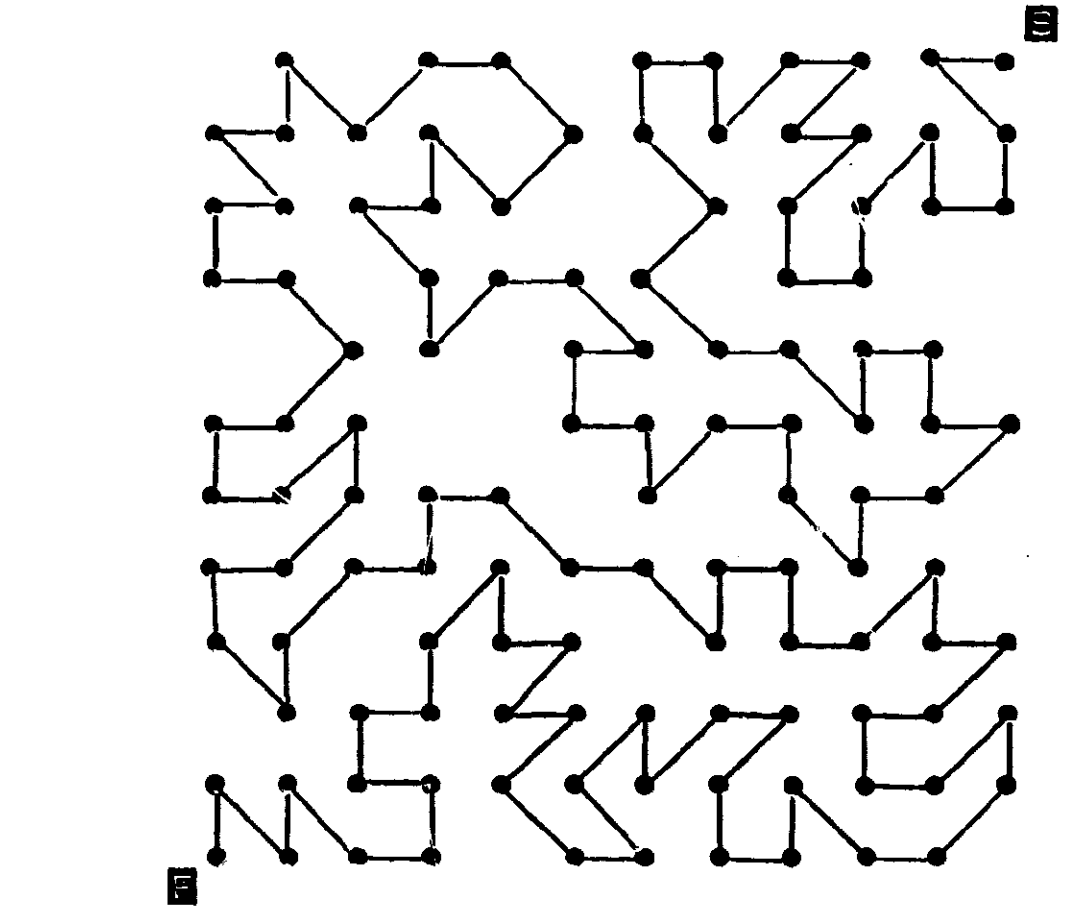
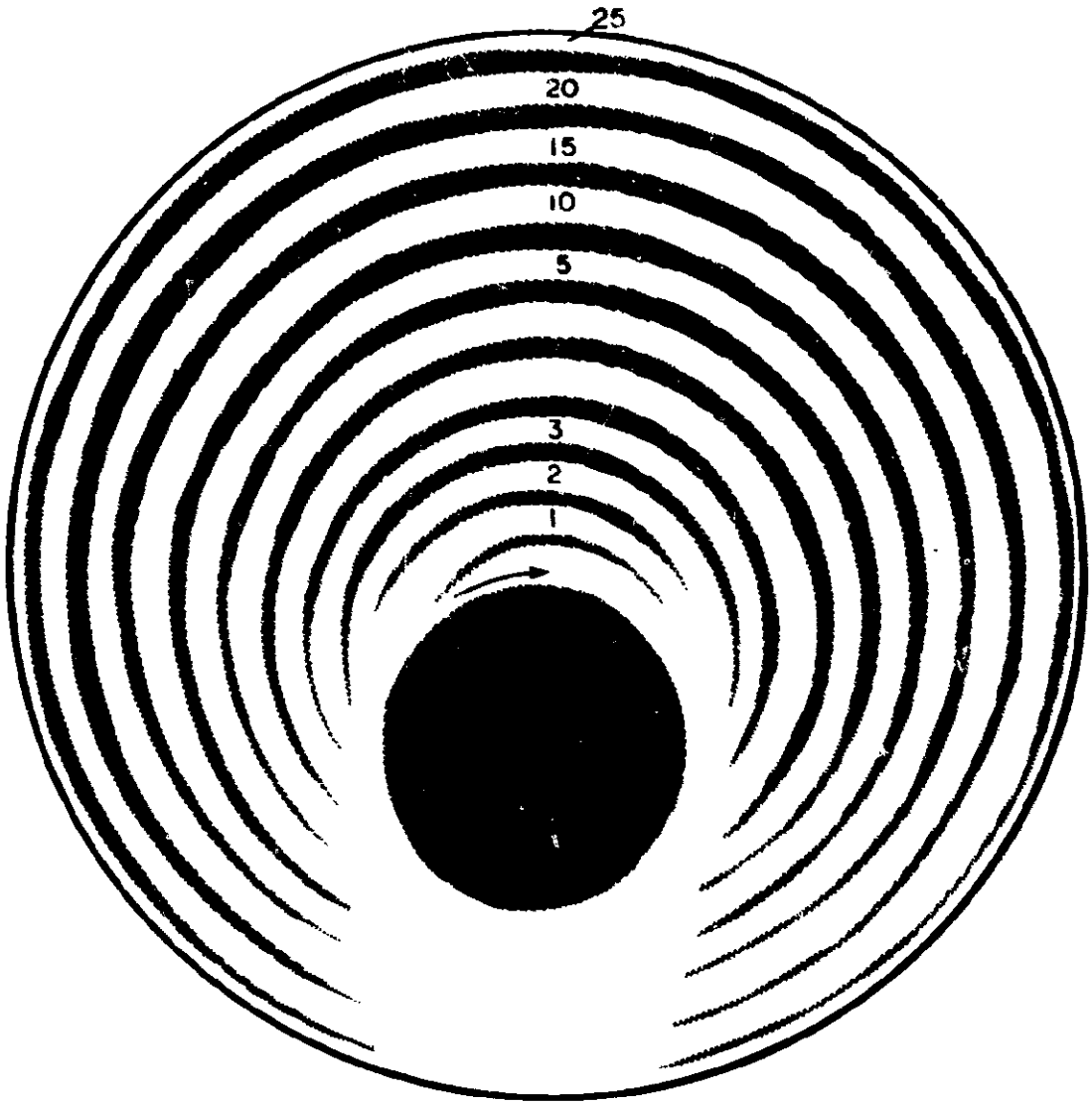
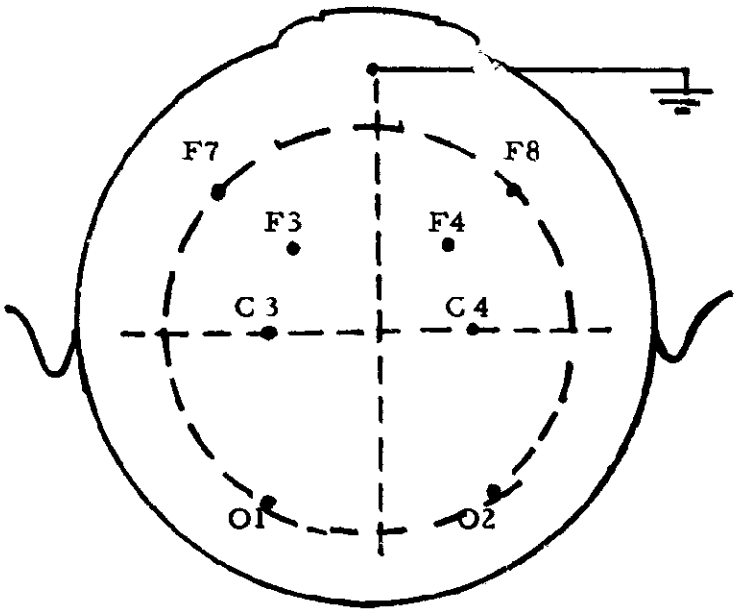


Figure 1 : MICHIGAN EYE-HAND COORDINATION TEST



TEST I

Figure 2: FLANAGAN COORDINATION TEST



Channel	Lead
1	F7-O1
2	F8-O2
3	F7-F8
4	F3-C3
5	F4-C4
6	C4-O2
7	C3-O1

Figure 3 : ELECTRODE GEOMETRY AND LEAD CONFIGURATION

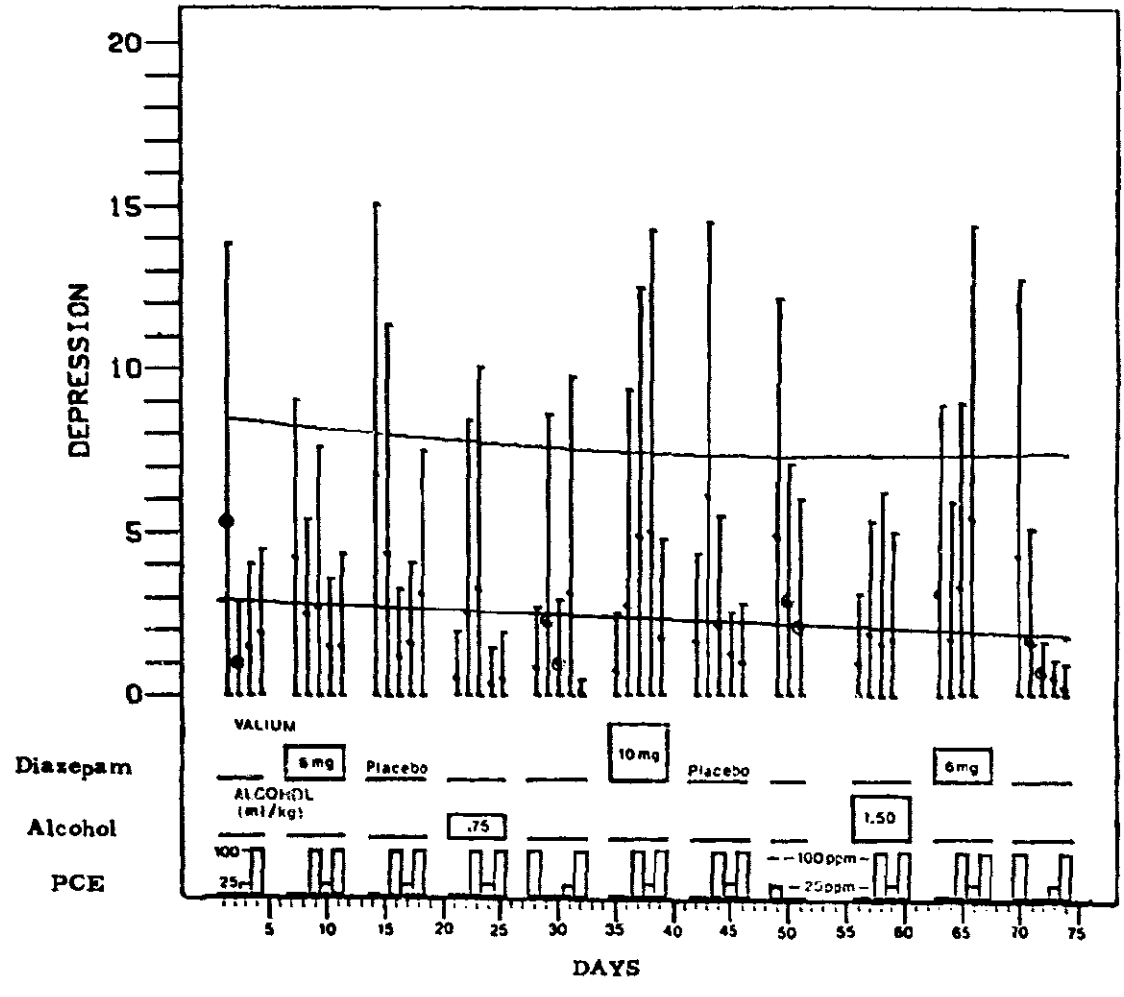


Figure 4. SUBJECTS' MOOD ASSESSMENT: DEPRESSION
Daily mean scores(± one SD). Circled dots represent zero exposure days and the straight line represents the trend of scores for these days while the outside line(s) represent the 95% confidence limits.

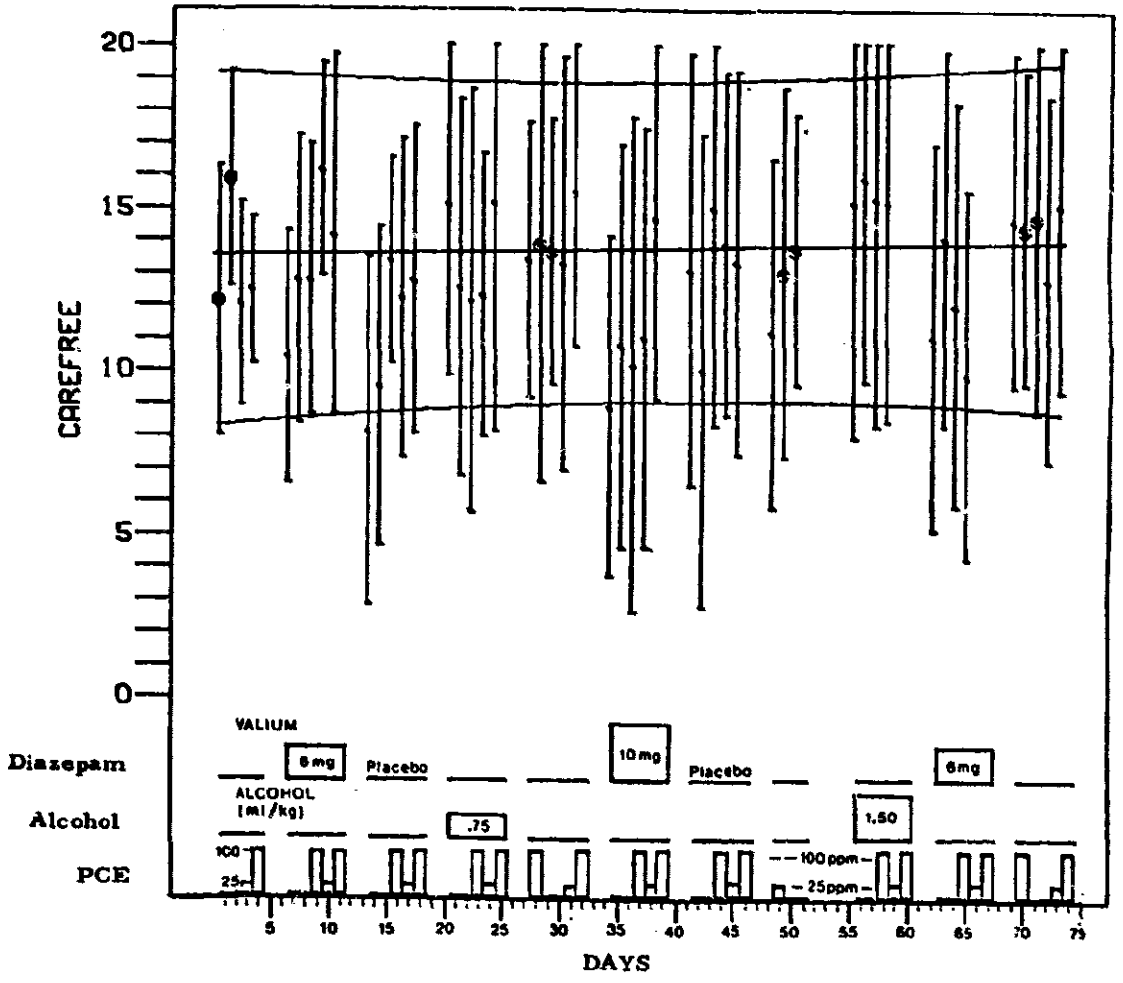


Figure 5. SUBJECTS' MOOD ASSESSMENT: CAREFREE
See Figure 4 for legend.

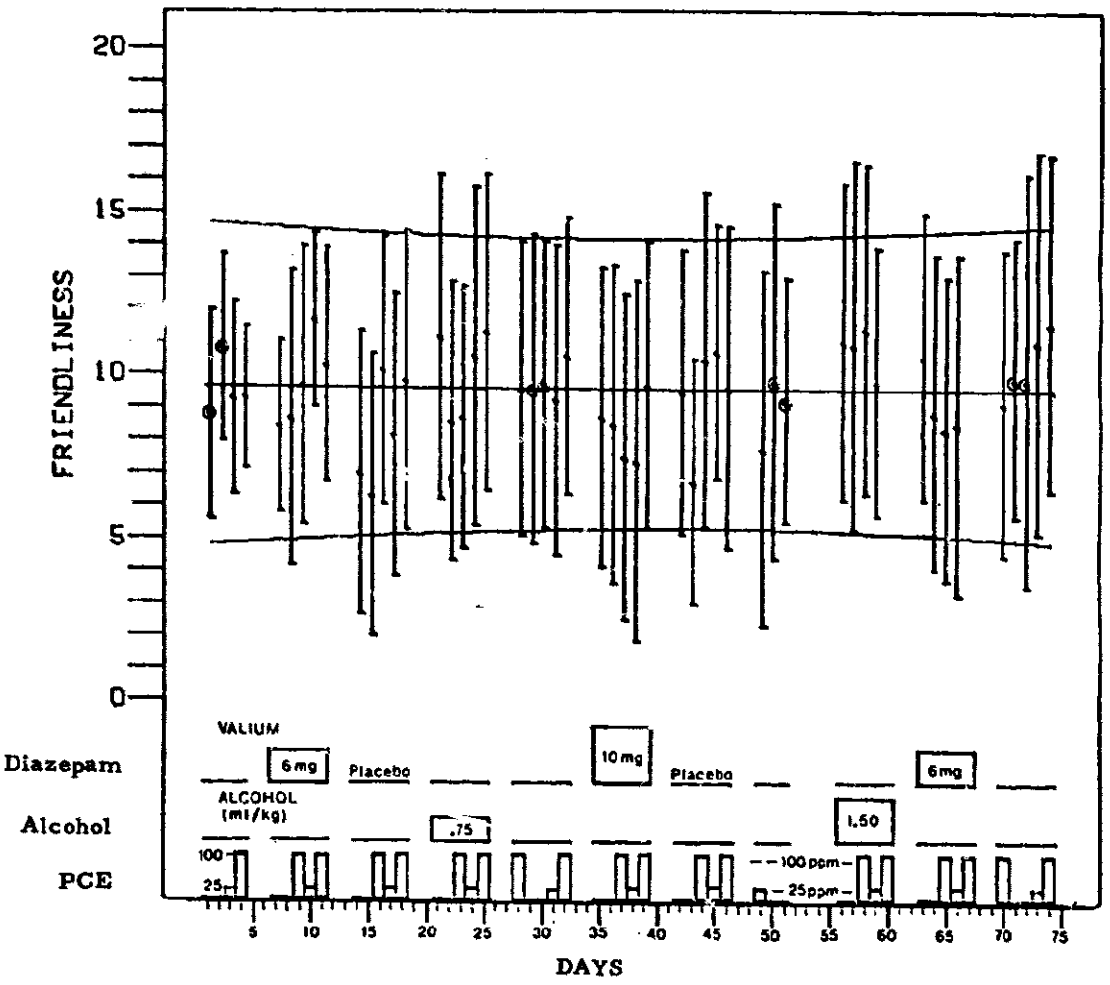


Figure 6. SUBJECTS' MOOD ASSESSMENT: FRIENDLINESS
See Figure 4 for legend.

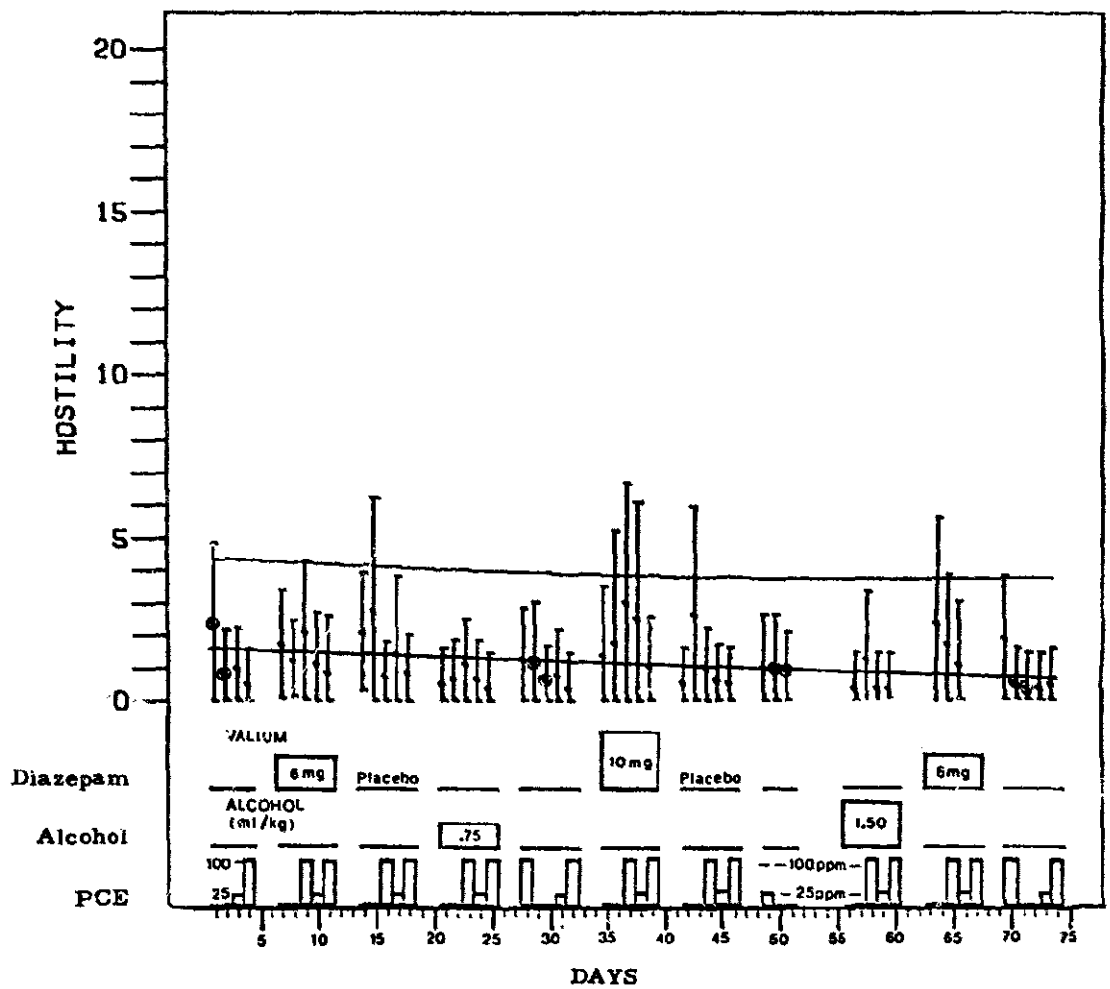


Figure 7. SUBJECTS' MOOD ASSESSMENT: HOSTILITY
See Figure 4 for legend.

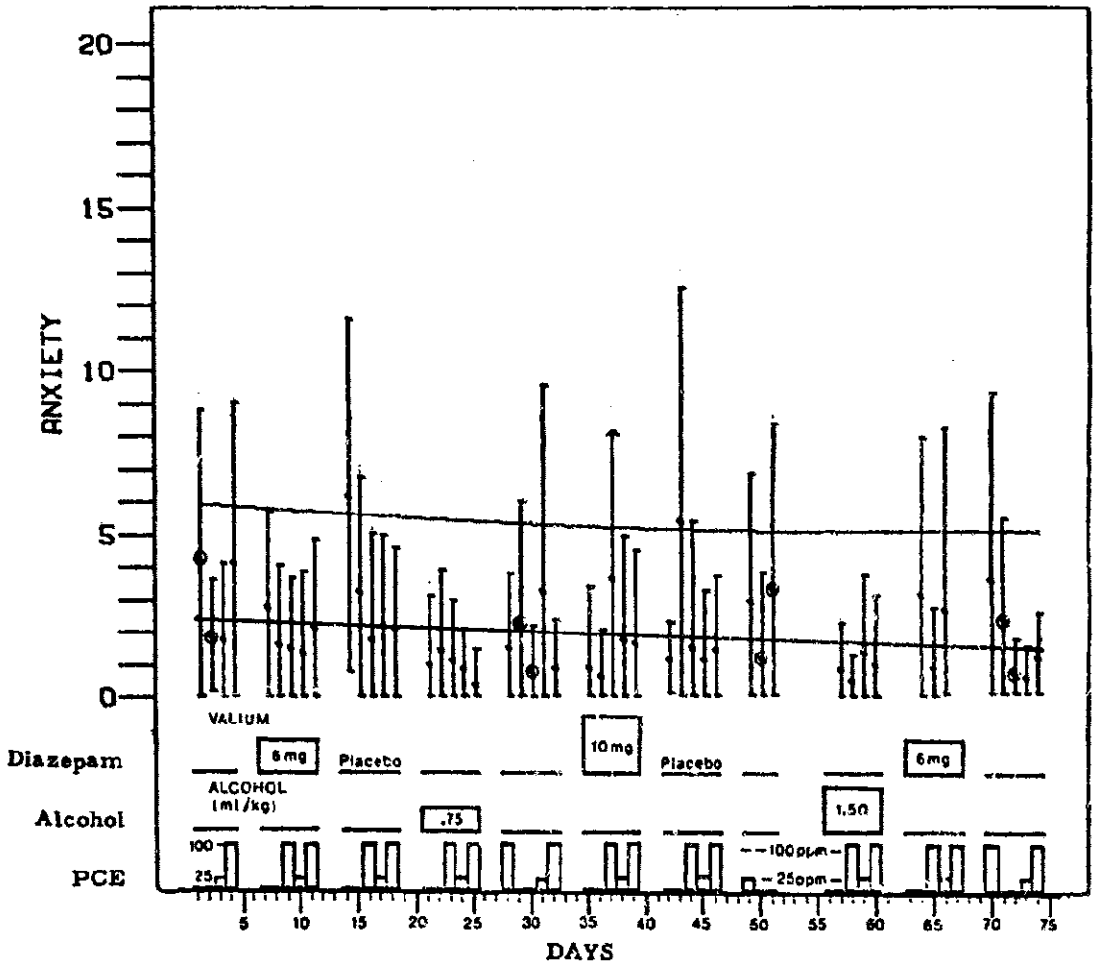


Figure 8. SUBJECTS' MOOD ASSESSMENT: ANXIETY
See Figure 4 for legend.

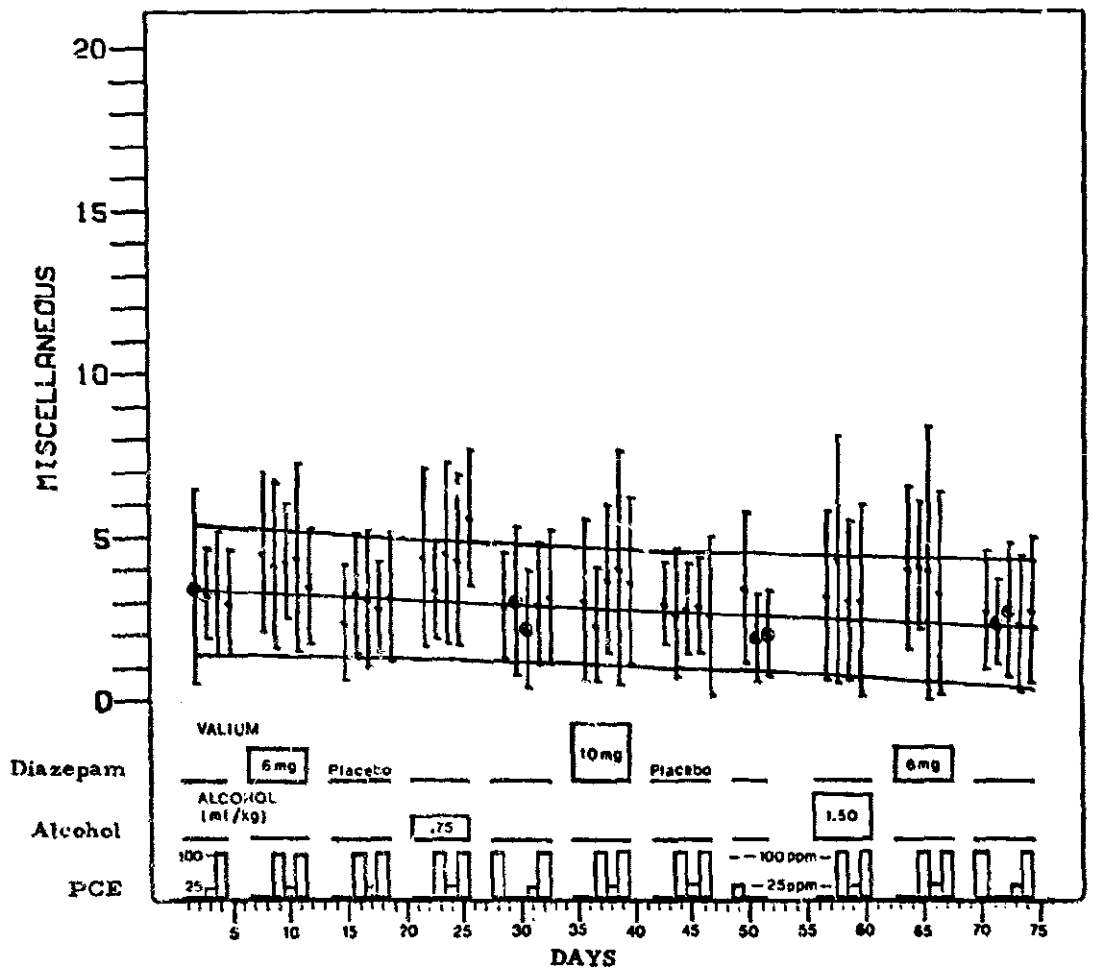


Figure 9. SUBJECTS' MOOD ASSESSMENT: MISCELLANEOUS
See Figure 4 for legend.

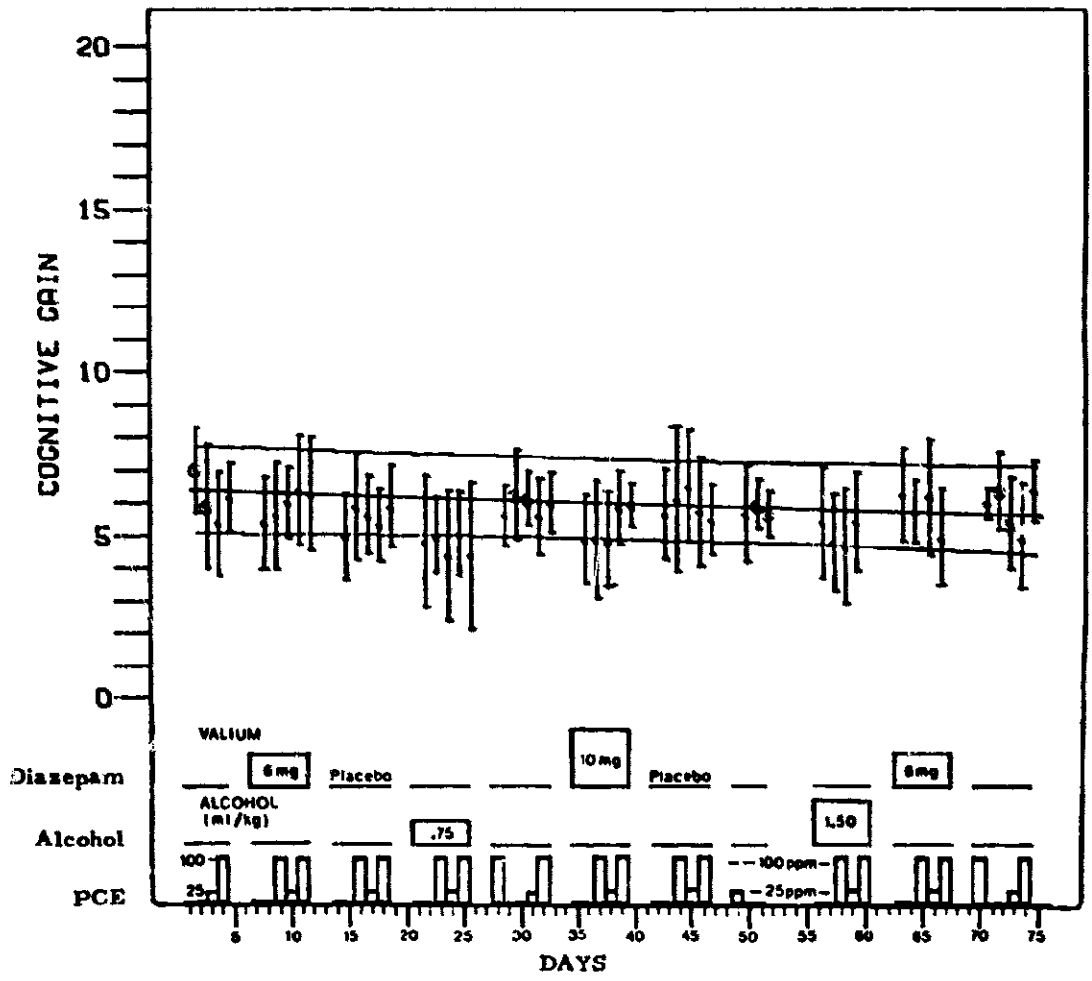


Figure 10. SUBJECTS' MOOD ASSESSMENT: COGNITIVE GAIN
See Figure 4 for legend.

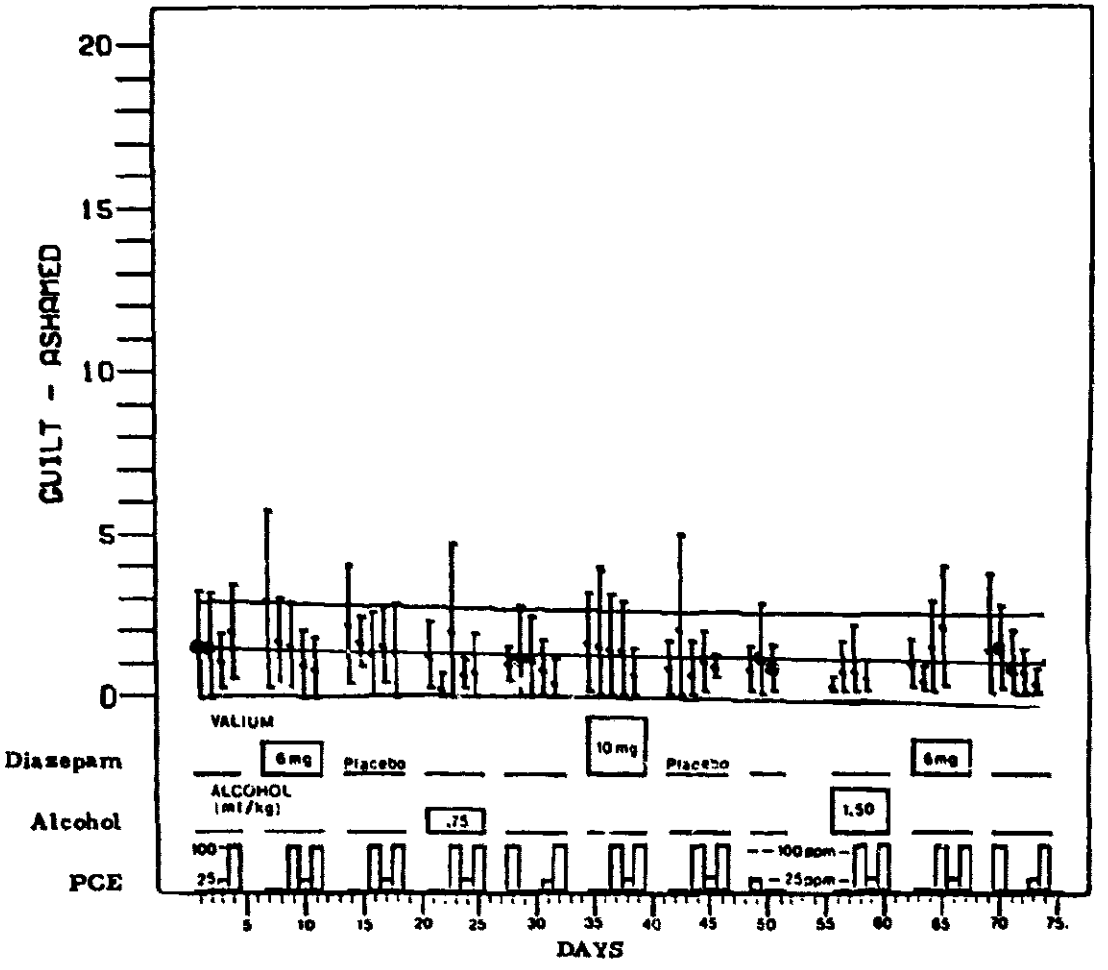


Figure 11. SUBJECTS' MOOD ASSESSMENT: GUILT-ASHAMED
SEE Figure 4 for legend.

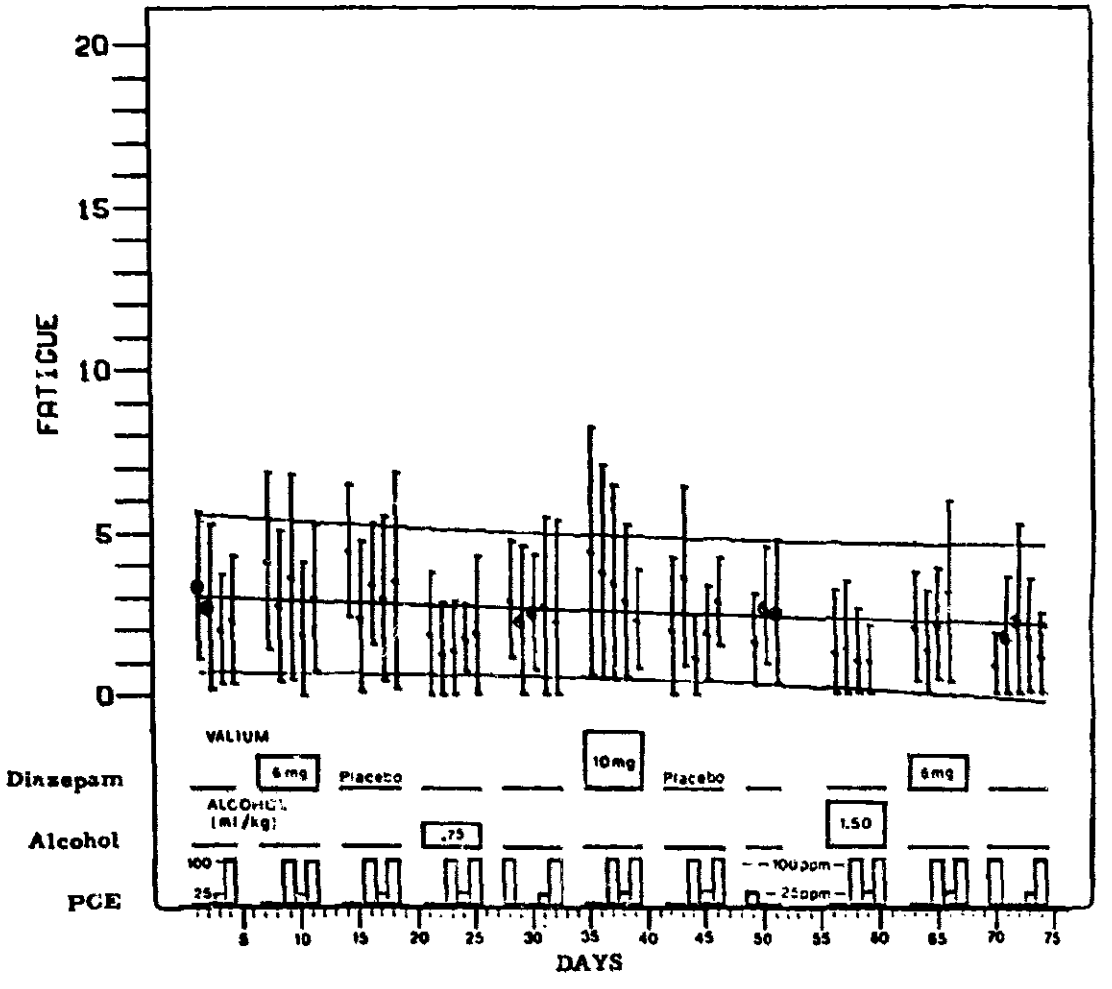


Figure 12. SUBJECTS' MOOD ASSESSMENT: FATIGUE
See Figure 4 for legend.

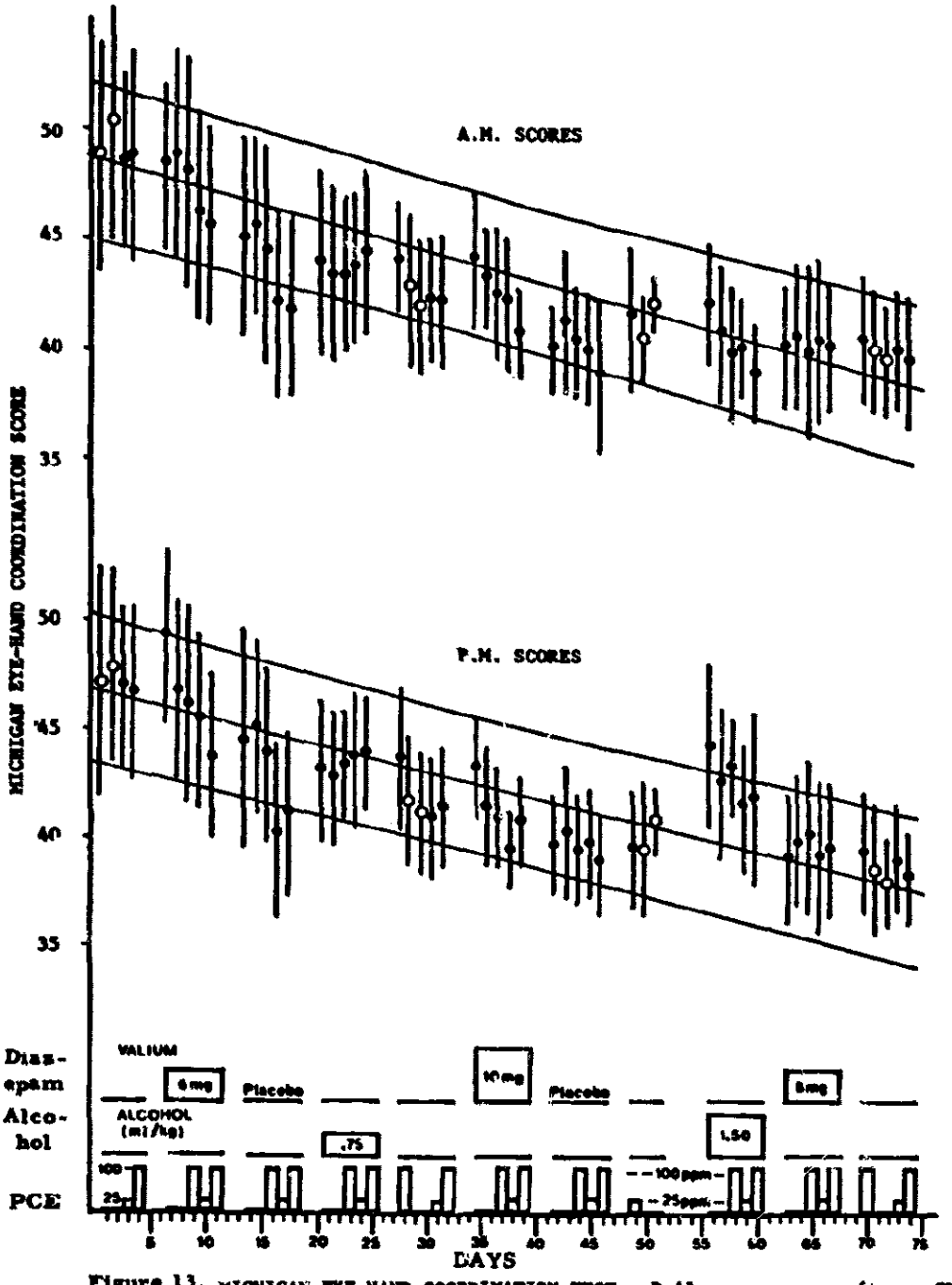


Figure 13. MICHIGAN EYE-HAND COORDINATION TEST. Daily mean scores (± one SD). Treud lines refer only to zero level exposure conditions.

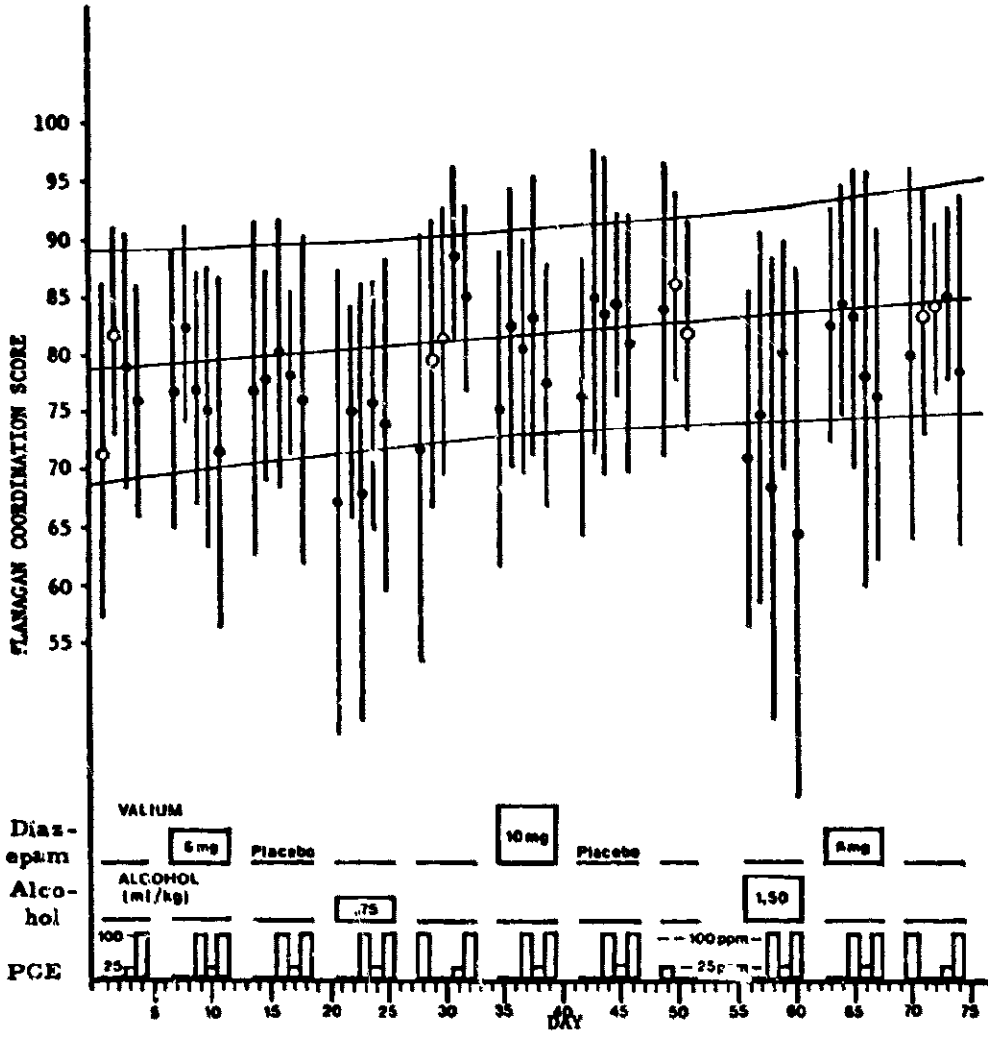


Figure 14. FLANAGAN COORDINATION TEST. Daily mean scores (± one SD) Open circles represent zero days. The straight line describes the trend of scores only for non-exposure conditions and the outer lines depict the area of expected mean scores under non-exposure conditions (with 95% confidence).

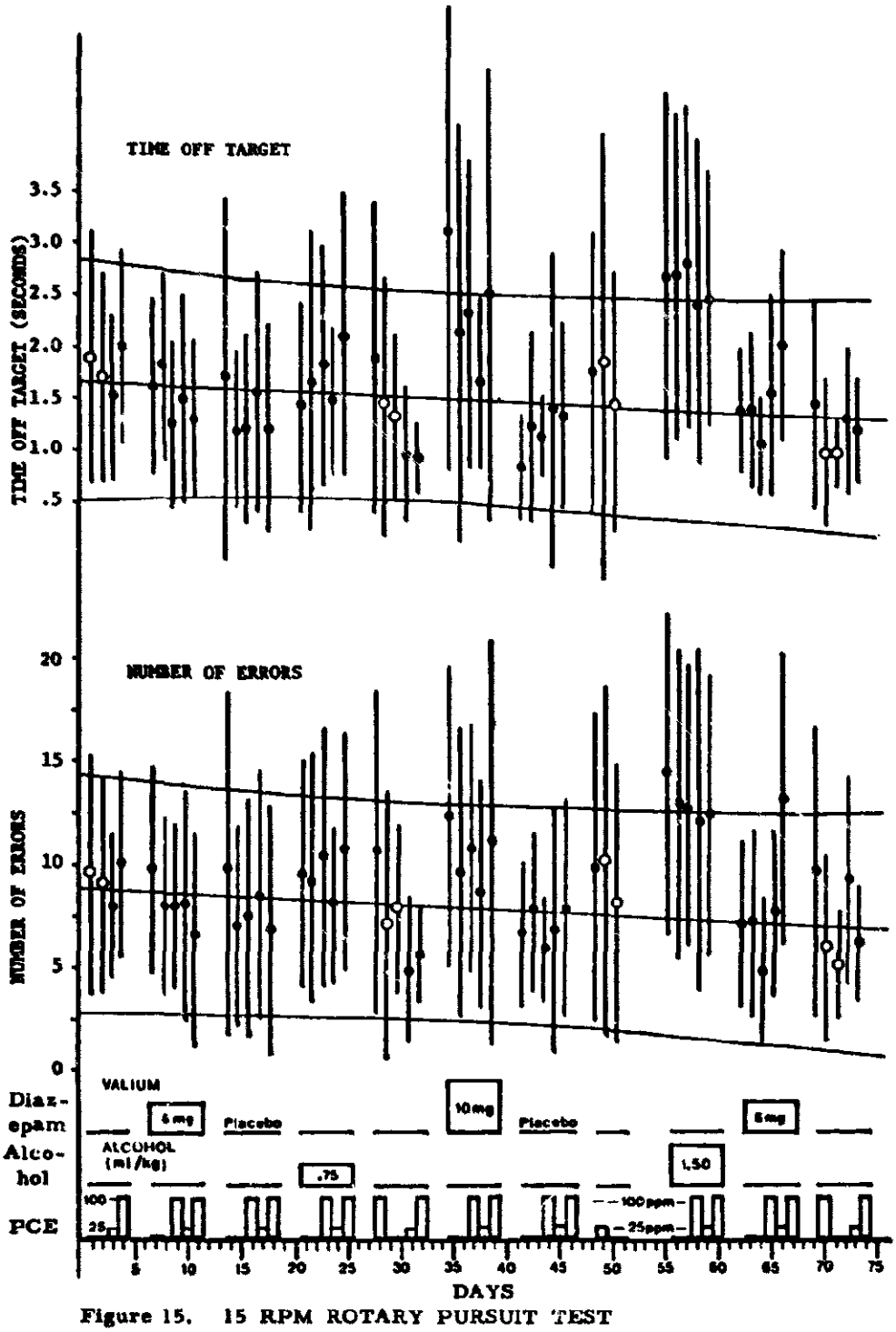


Figure 15. 15 RPM ROTARY PURSUIT TEST

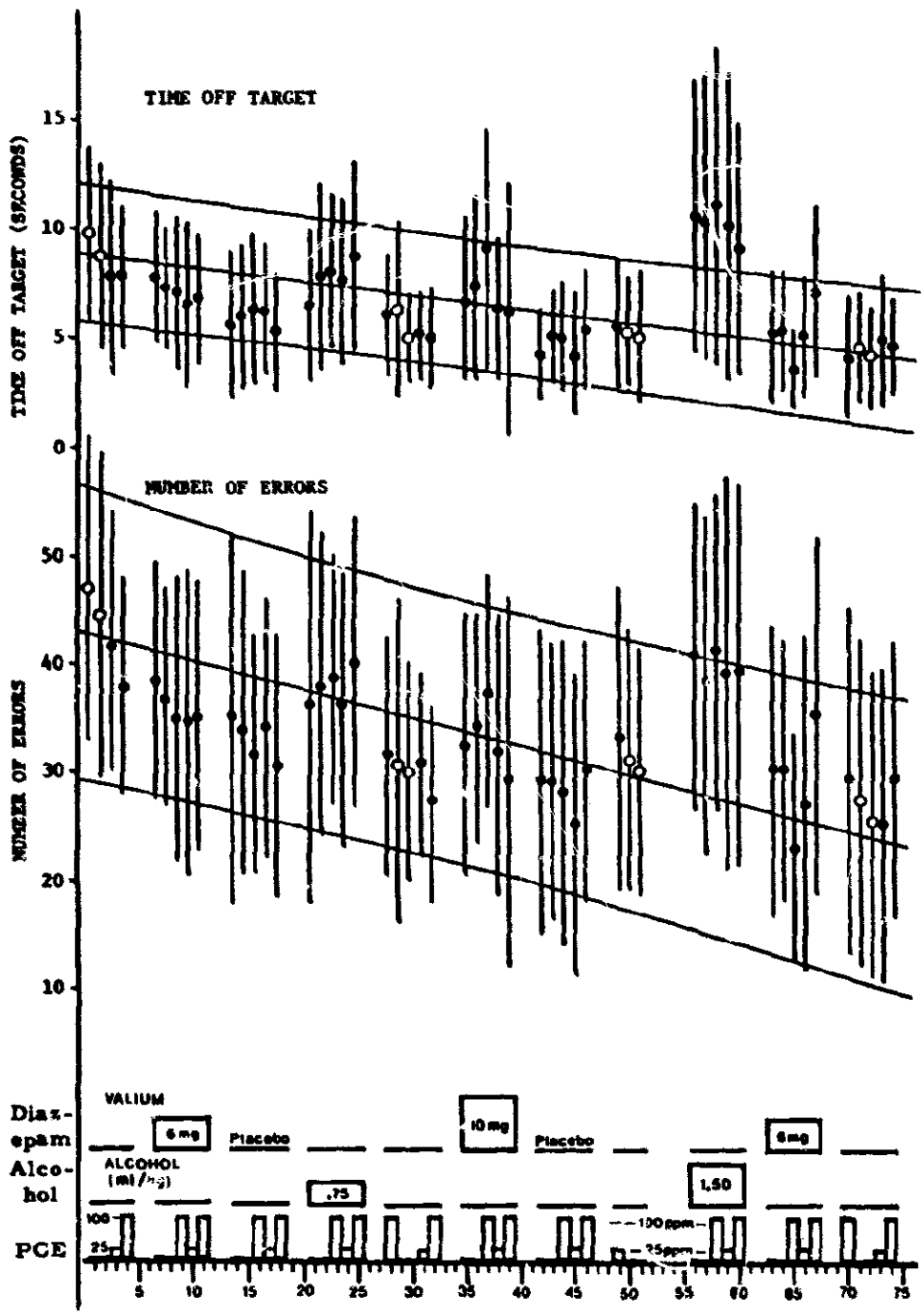


Figure 16. 30 RPM ROTARY PURSUIT TEST

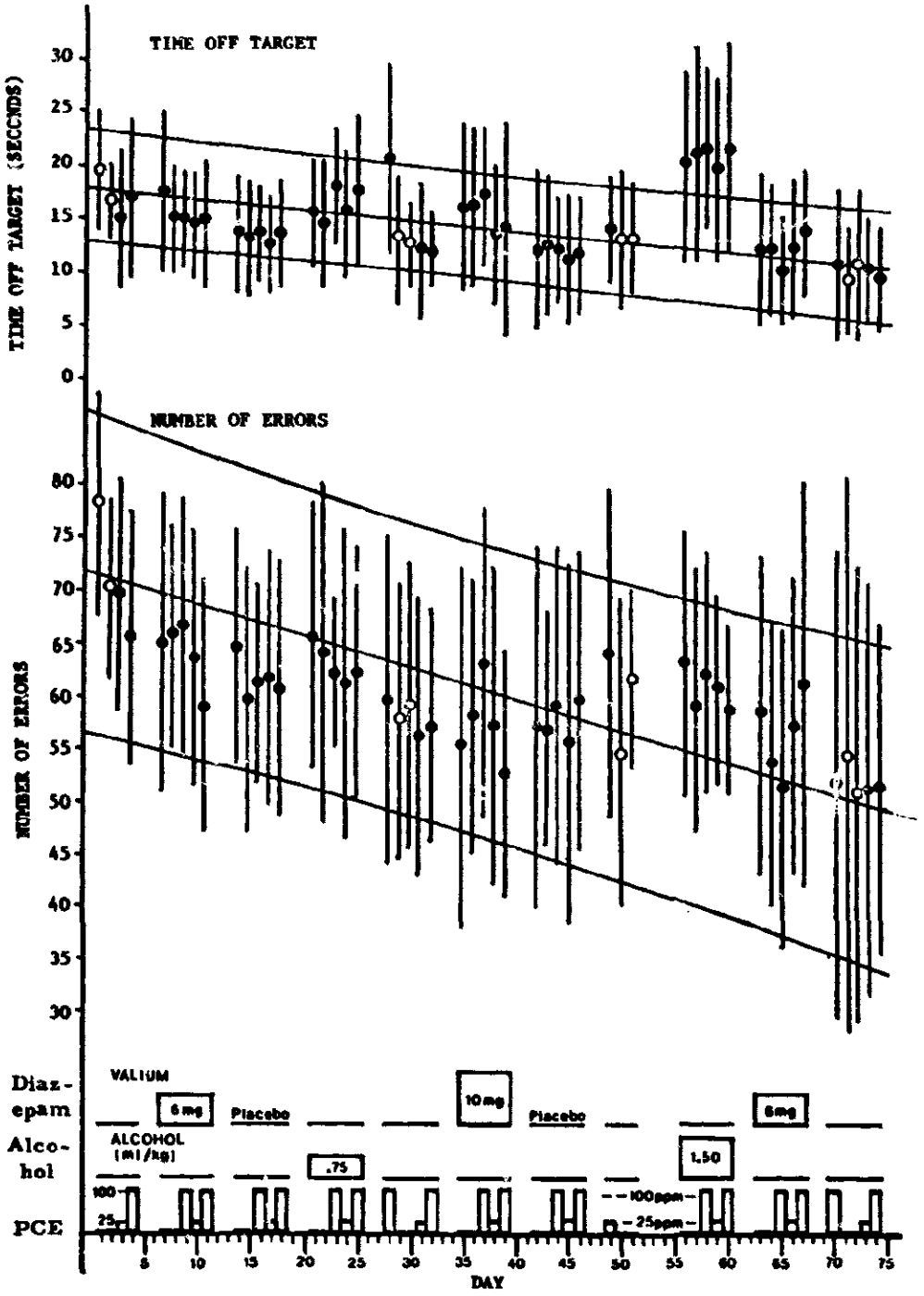


Figure 17. 45 RPM ROTARY PURSUIT TEST

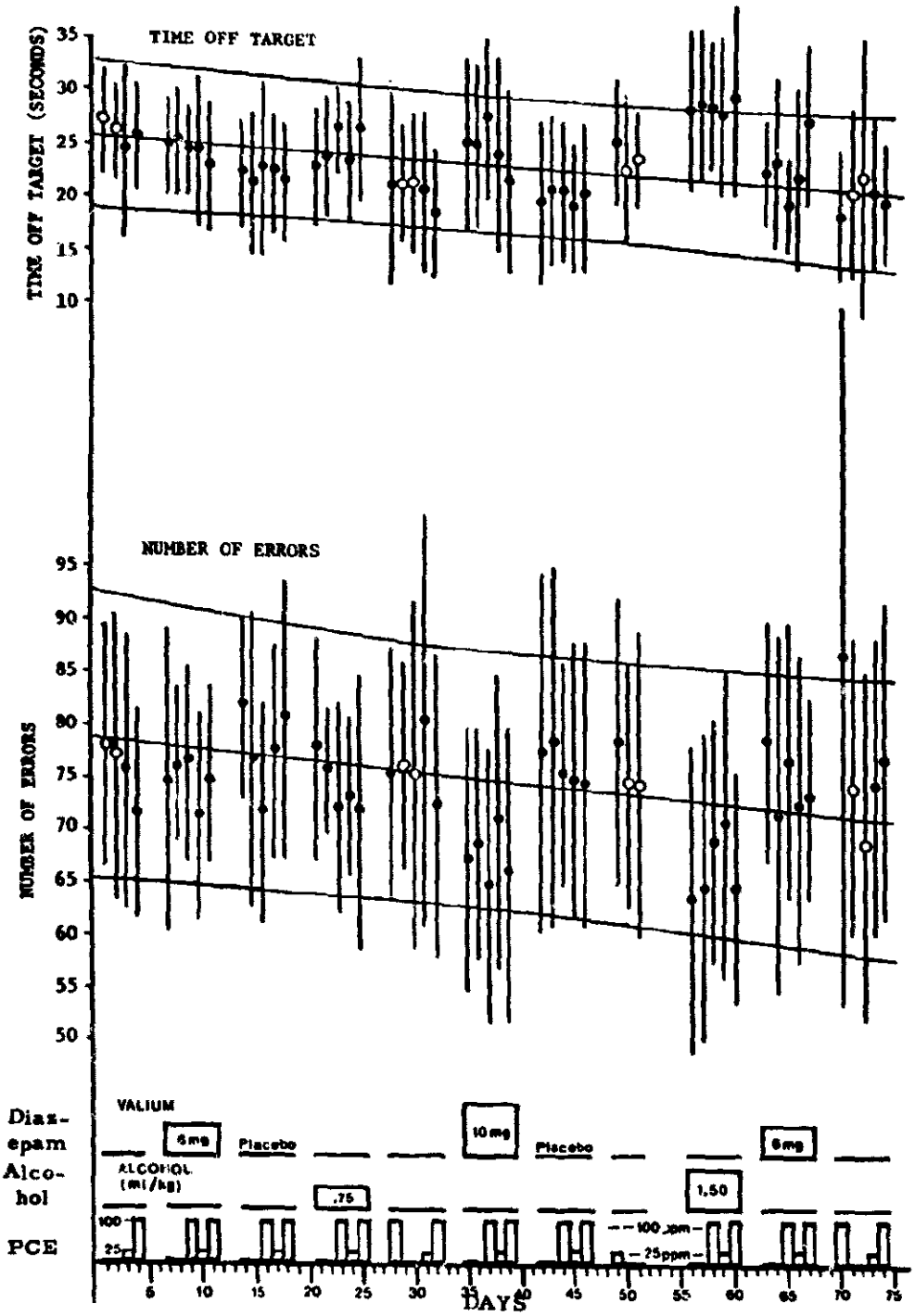


Figure 18. 60 RPM ROTARY PURSUIT TEST

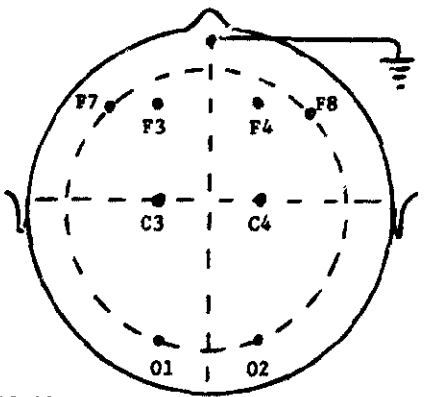
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF ETHANOL ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

LO ALCOHOL: ~0.75 ML/KG BODY WEIGHT

HI ALCOHOL: ~1.50 ML/KG BODY WEIGHT

SUBJECT: #95



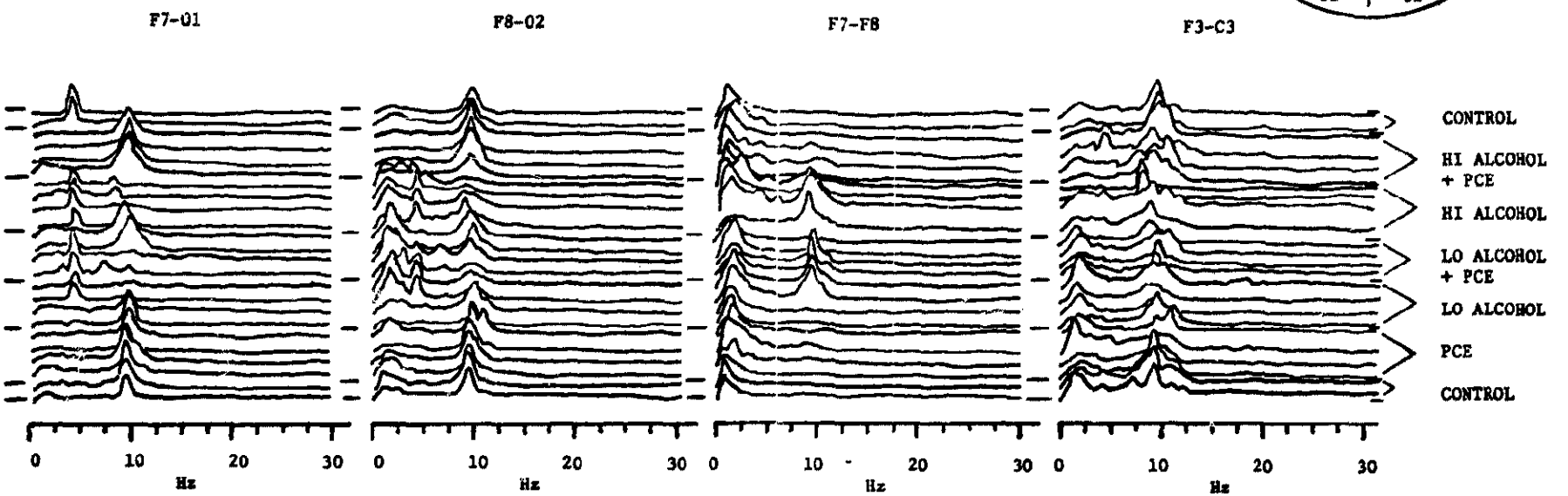


Figure 19

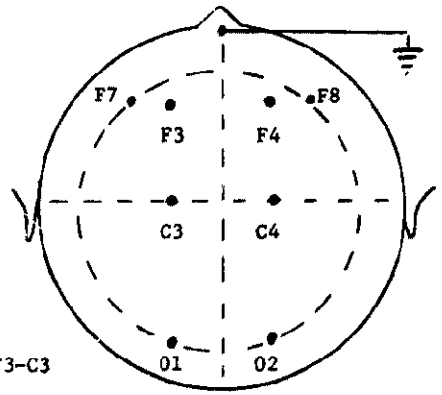
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF ETHANOL ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

LO ALCOHOL: ~0.75 ML/KG BODY WEIGHT

HI ALCOHOL: ~1.50 ML/KG BODY WEIGHT

SUBJECT: #117



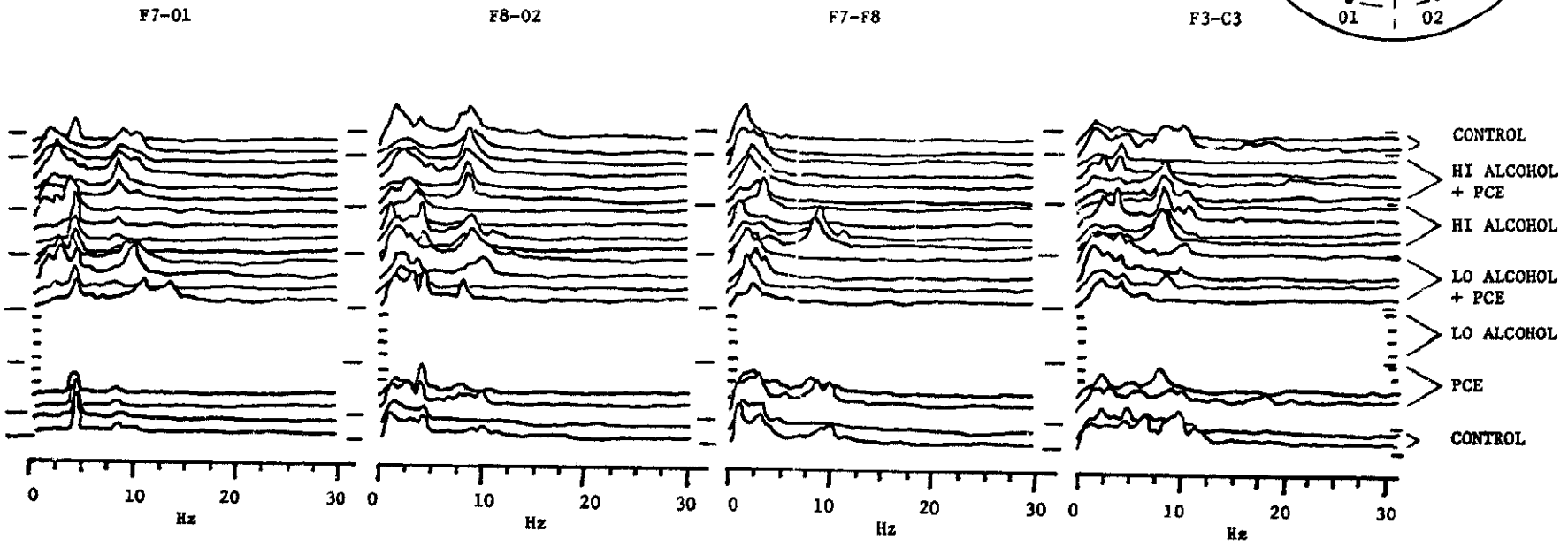


Figure 20

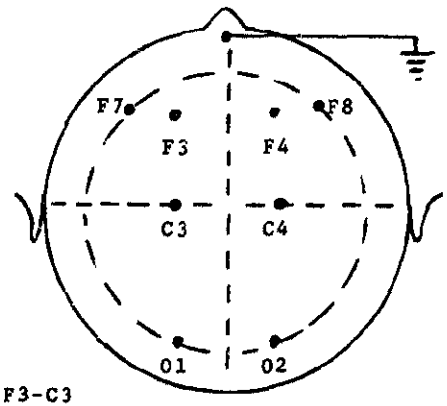
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF ETHANOL ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

LO ALCOHOL: ~0.75 ML/KG BODY WEIGHT

HI ALCOHOL: ~1.50 ML/KG BODY WEIGHT

SUBJECT: #123



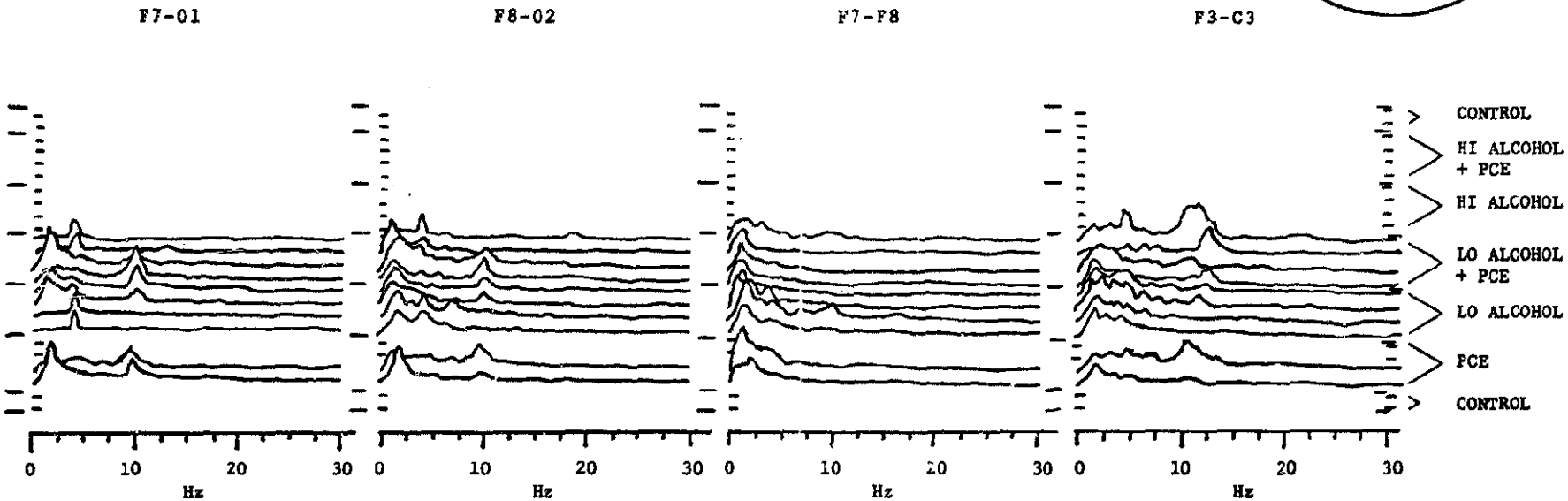


Figure 21

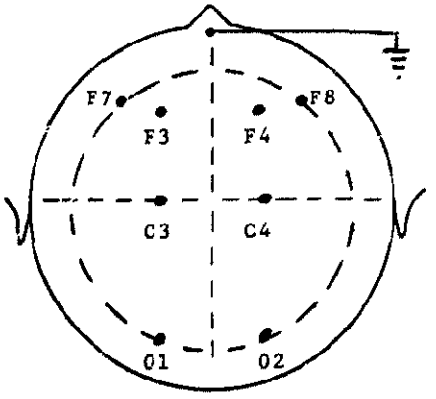
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF ETHANOL ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

LO ALCOHOL: ~0.75 ML/KG BODY WEIGHT

HI ALCOHOL: ~1.50 ML/KG BODY WEIGHT

SUBJECT: #326



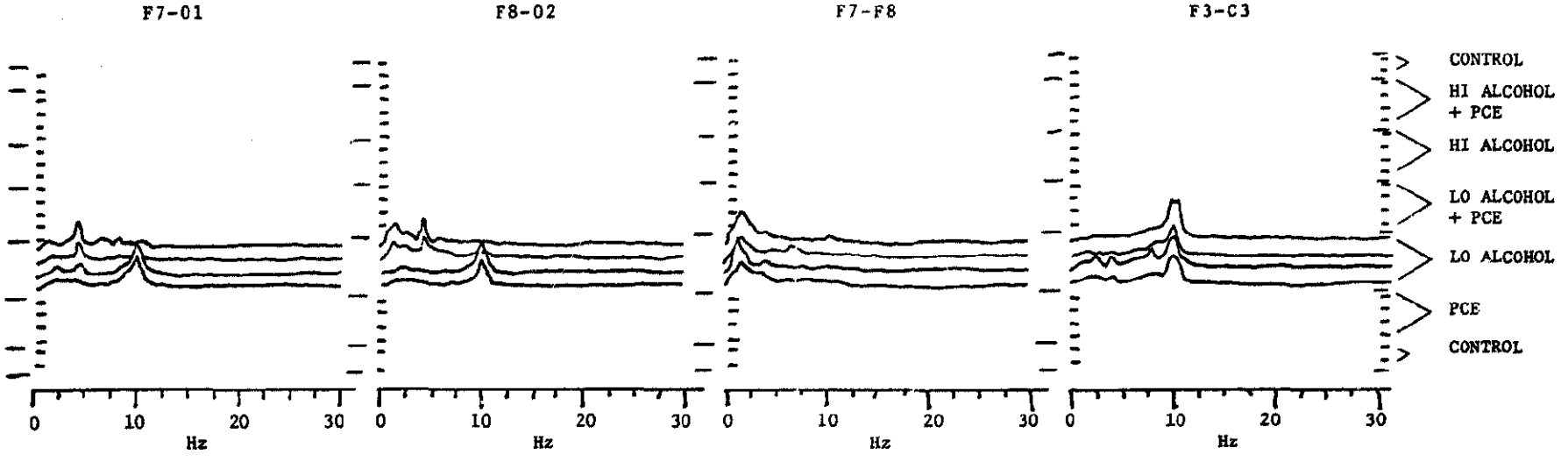


Figure 22

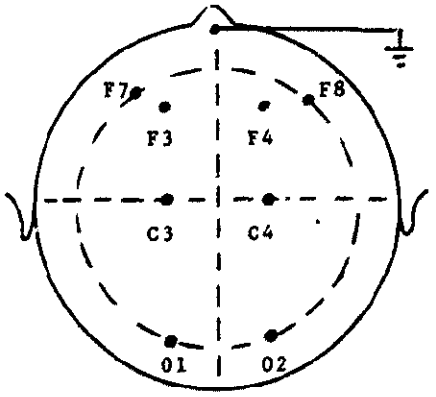
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF ETHANOL ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

LO ALCOHOL: ~0.75 ML/KG BODY WEIGHT

HI ALCOHOL: ~1.50 ML/KG BODY WEIGHT

SUBJECT: #327



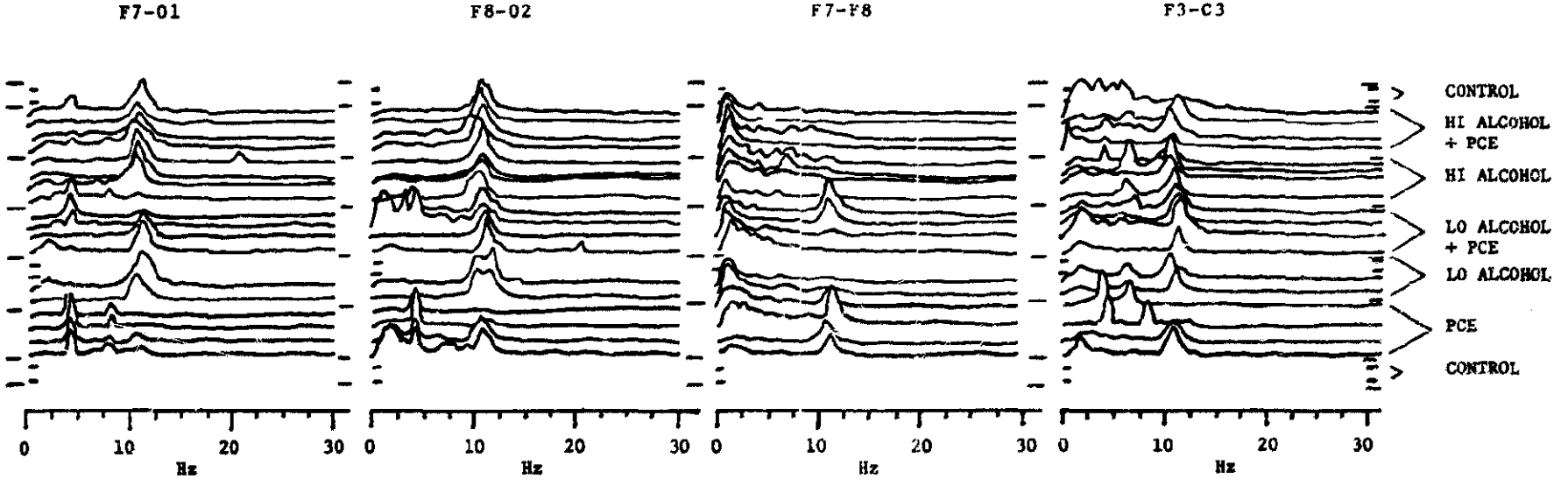


Figure 23

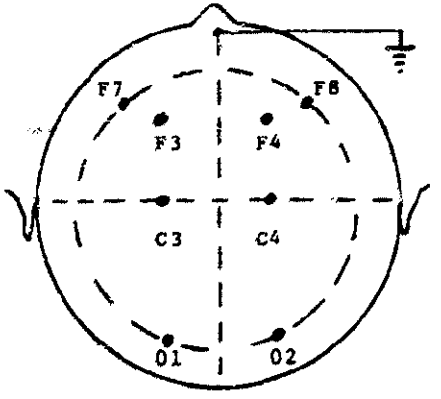
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF ETHANOL ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

LO ALCOHOL: ~0.75 ML/KG BODY WEIGHT

HI ALCOHOL: ~1.50 ML/KG BODY WEIGHT

SUBJECT: #331



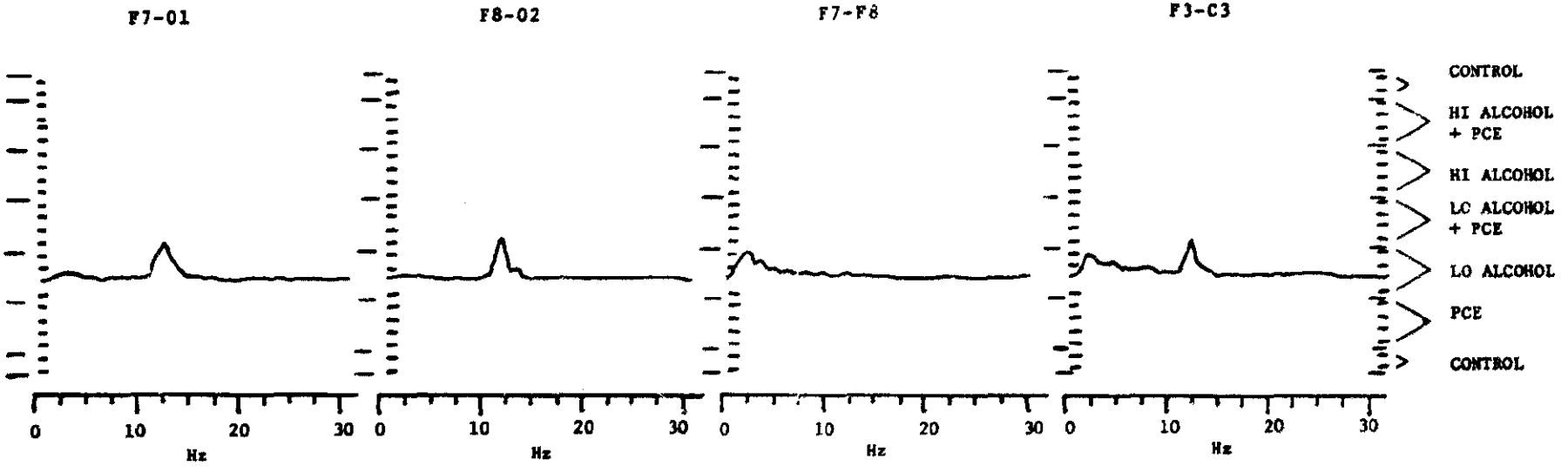


Figure 24

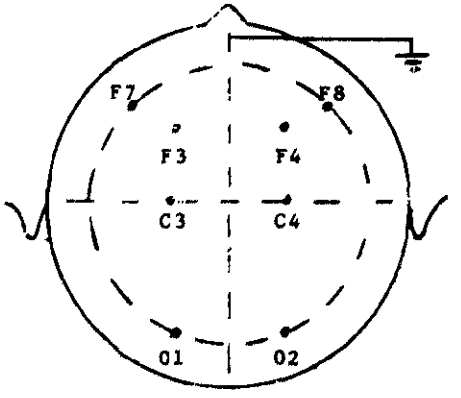
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF DIAZEPAM ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

D(6): 6 MG/DAY

D(10): 10 MG/DAY

SUBJECT: #328



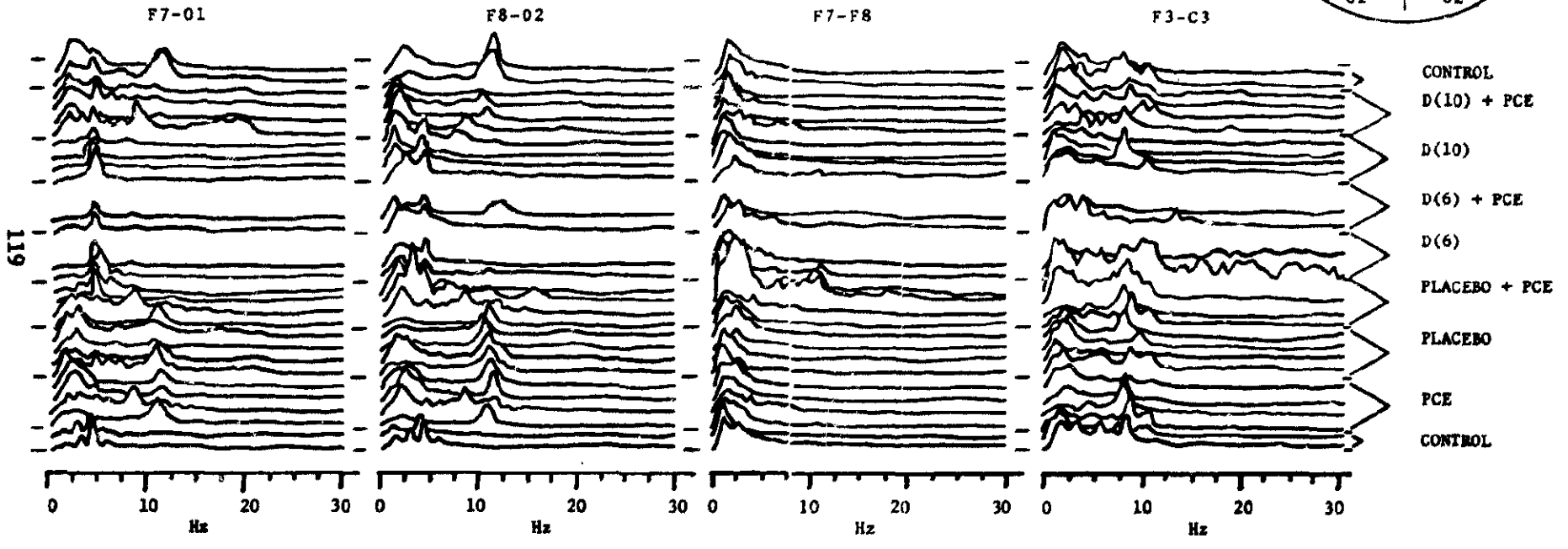


Figure 25

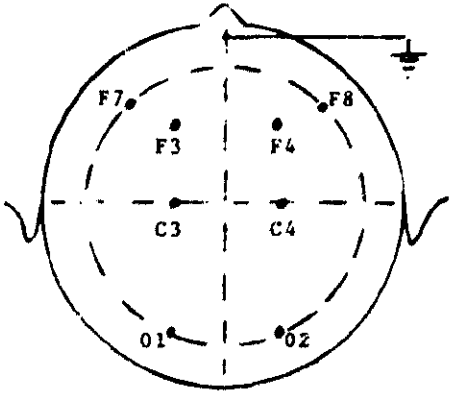
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF DIAZEPAM ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

D(6): 6 MG/DAY

D(10): 10 MG/DAY

SUBJECT: #329



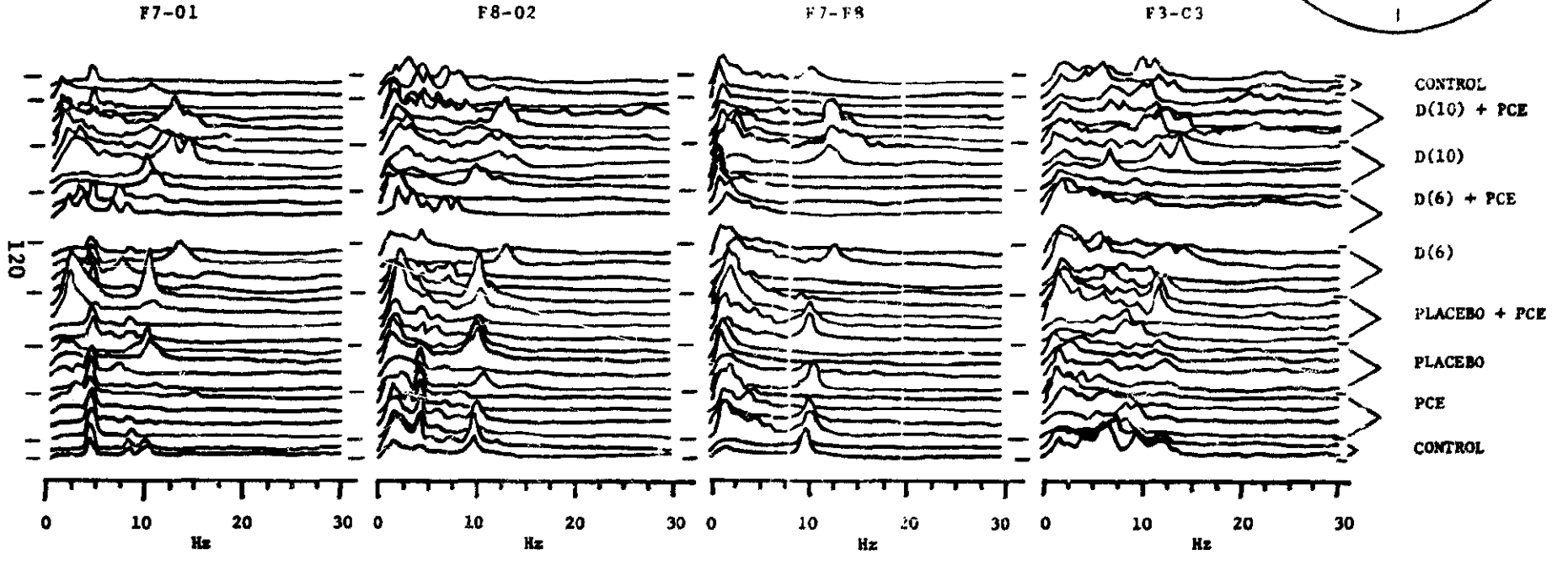


Figure 26

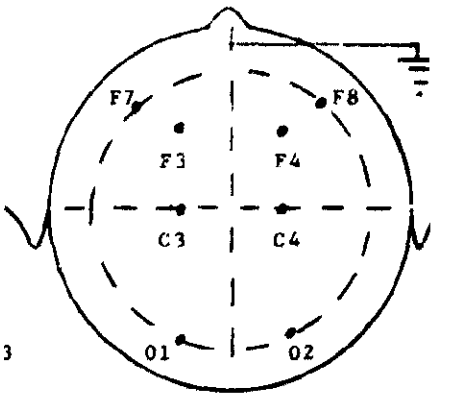
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF DIAZEPAM ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

D(6): 6 MG/DAY

D(10): 10 MG/DAY

SUBJECT: #330



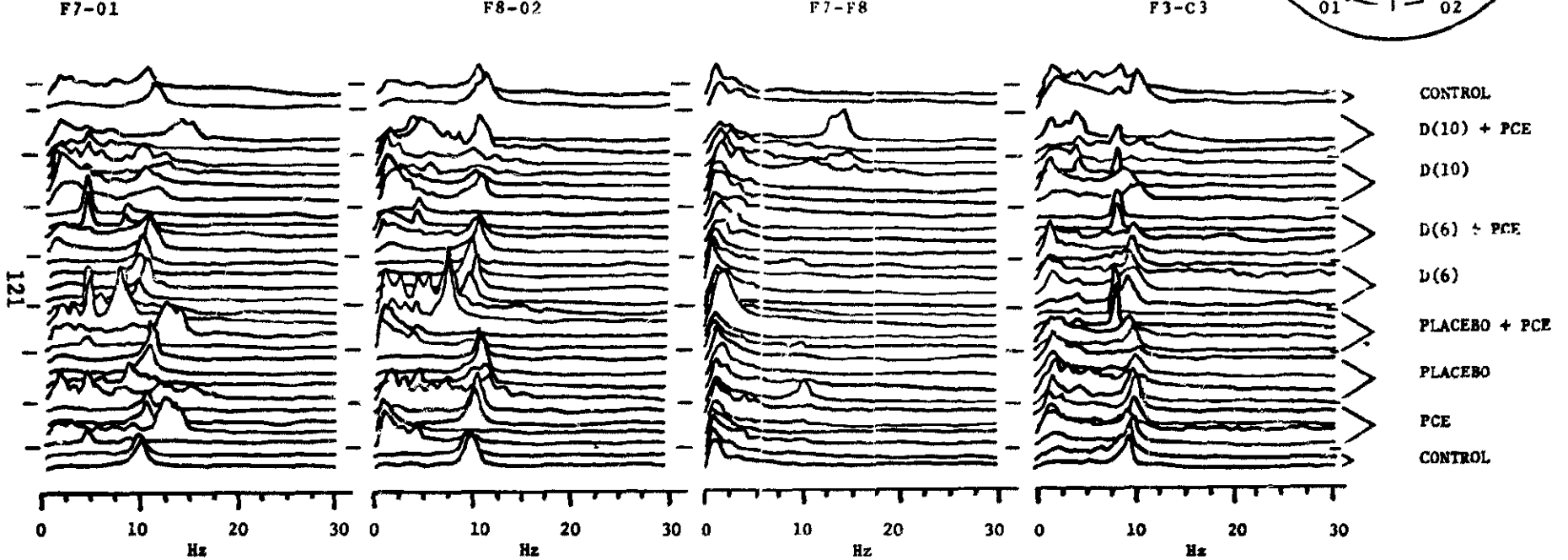


Figure 27

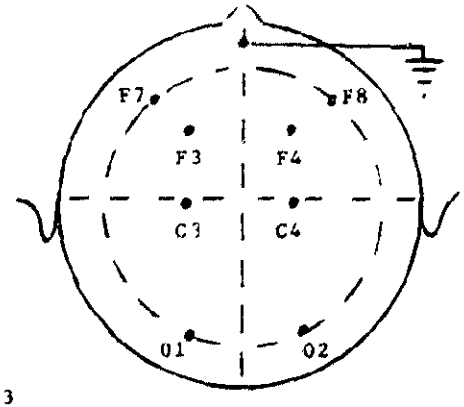
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF DIAZEPAM ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

D(6): 6 MG/DAY

D(10): 10 MG/DAY

SUBJECT: #332



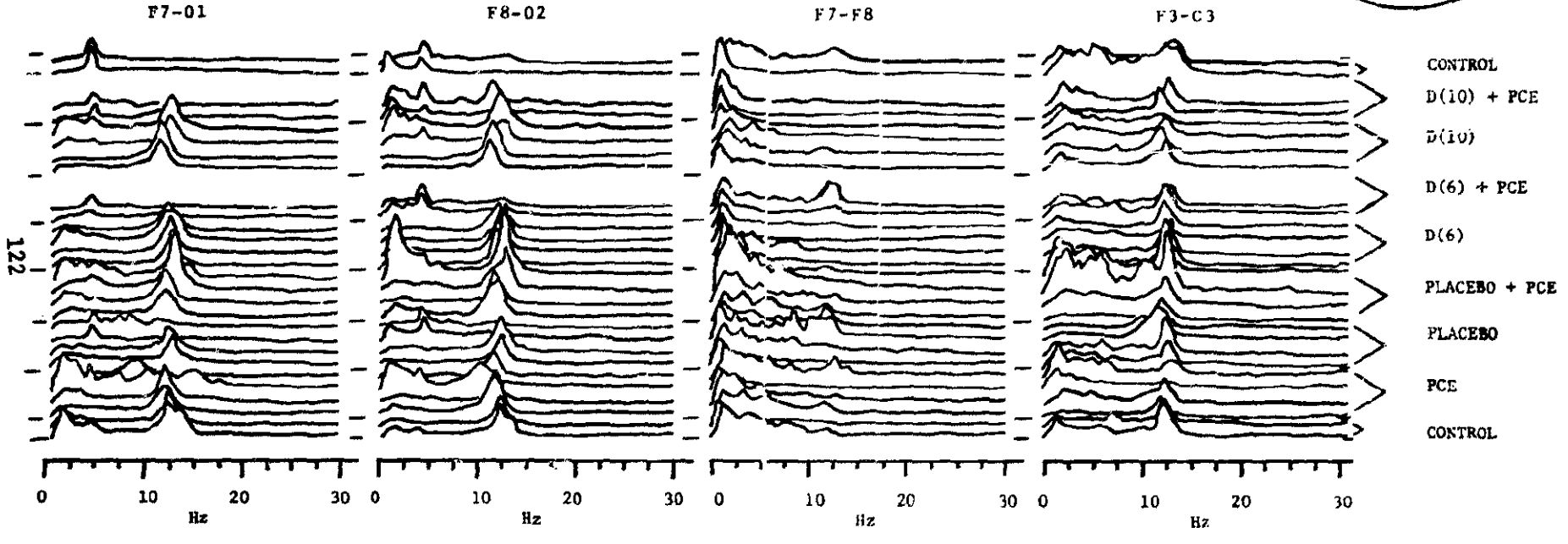


Figure 28

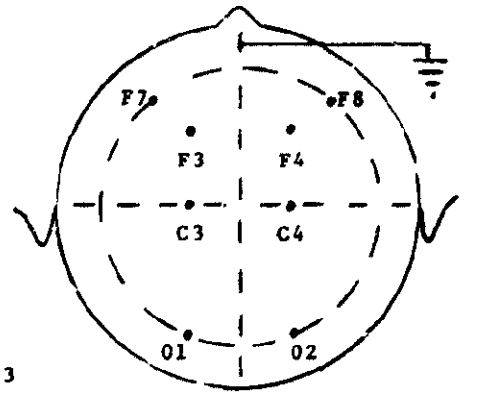
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF DIAZEPAM ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

D(6): 6 MG/DAY

D(10): 10 MG/DAY

SUBJECT: #333



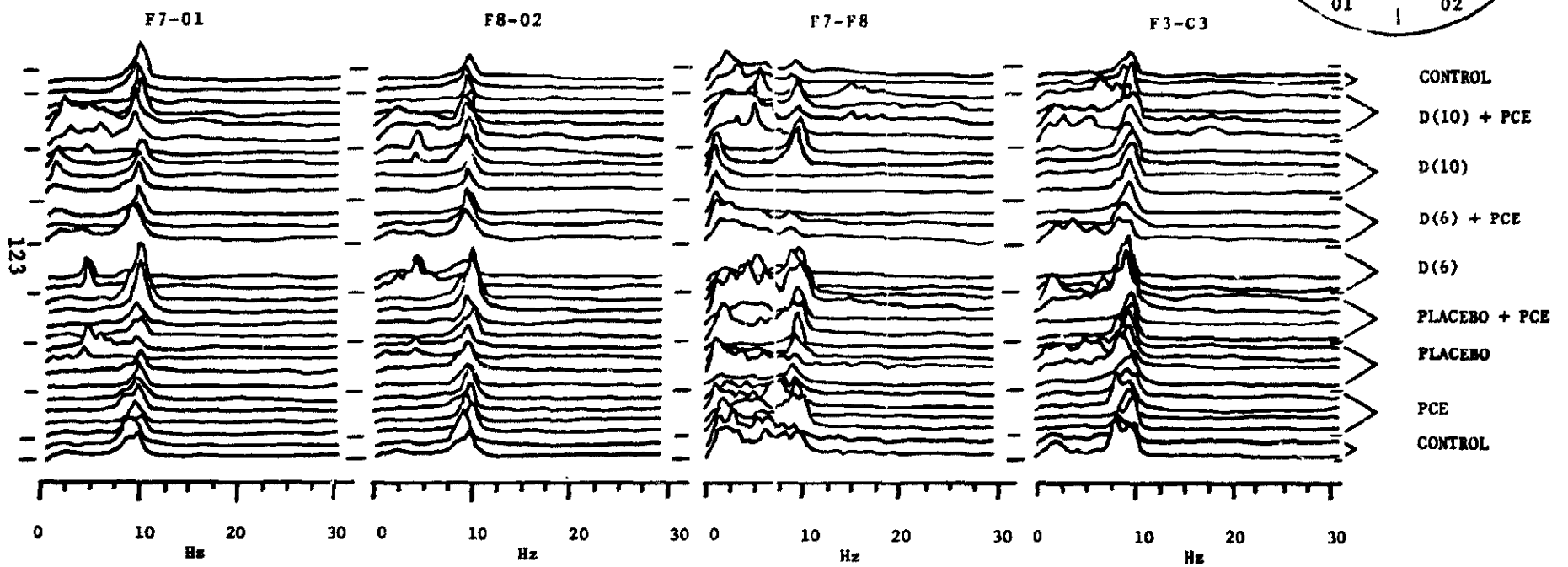


Figure 29

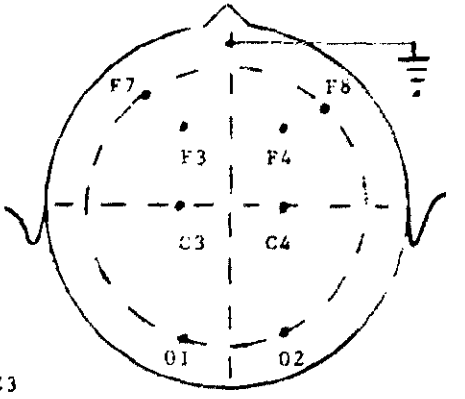
THE EFFECT OF EXPOSURE TO PERCHLOROETHYLENE AND/OR INGESTION OF DIAZEPAM ON THE ELECTROENCEPHALOGRAM

PCE: 100 PPM PERCHLOROETHYLENE

D(6): 6 MG/DAY

D(10): 10 MG/DAY

SUBJECT: #334



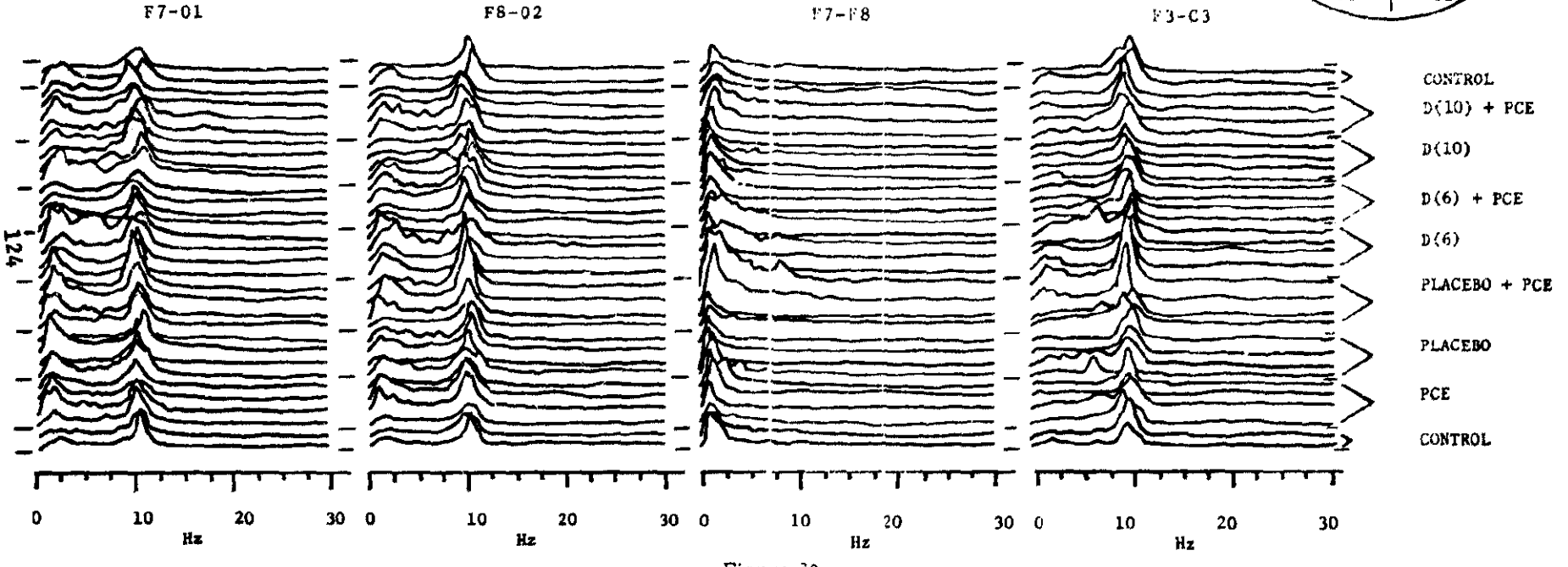


Figure 30

APPENDIX I

INFORMED CONSENT QUESTIONNAIRE

1. Do you think the investigation is based on enough information to allow the scientists to proceed safely, as explained, on human beings?

   Yes ____ No ____

2. Do you understand that you have the right to withdraw from the investigation at any time?

   Yes ____ No ____

3. Do you consider this investigation to be useful:

   - to yourself?

     Yes ____ No ____

   - to your fellow men and women?

     Yes ____ No ____

4. Do you understand that other human beings have been exposed to the same concentration of perchloroethylene for at least the same period of time without showing any harmful effect?

   Yes ____ No ____

5. Do you understand that you will be stuck with a needle a few times a day on different days of the week in order that small samples of blood can be drawn from you?

   Yes ____ No ____

6. Have the risks involved to you been adequately explained?

   Yes ____ No ____

7. Please tell us briefly why you are willing to participate in this investigation.

Date _____ Signature _____

APPENDIX II

MICHIGAN EYE-HAND COORDINATION TEST
INSTRUCTIONS-PROCEDURES

1. Determine if subject is left or right handed. Position plate accordingly.

2. Instruct subject as follows:

   a) This is an eye-hand coordination test. There are 119 holes in this maze from S to F. Your task is to insert the stylus tip into each hole according to the traced pattern. Accuracy and speed are important, and we record both. Any questions?

   b) Again, let me remind you to be accurate if you miss a hole, or deviate from the pattern, we will have to start that trial over. So accuracy is most important, and speed is second in importance but do try to go as fast and as accurate as you can.

   c) Ok - Put stylus in your right (or left hand), and place the tip in the top hole marked S for start. I will tell you when to 'start'. (Experimenter - resets clock to zero, and says 'start')

   d) Experimenter records data for trial 1. Four trials are run per session. No feed back on time values should be provided. Appropriate encouragement can be given for those subjects lacking in apparent enthusiasm. If errors are made, and you instruct subject to start over, record this under the error column on data sheet, and encourage subjects to be more accurate. If they are really slow, encourage them to work faster.

   Don't forget to date the data sheet.

APPENDIX III

INSTRUCTIONS FOR ROTARY PURSUIT

1. This is like a game. The area of white light is your target. The object of the game is to keep this pointer on the target as much of the time as possible when it goes around.

   Chase the target in a circular motion if it gets away from you. Every-time the tip of this pointer or stylus is not on the target an error is scored.

2. Do not press down on the stylus; rather, follow the target with a relaxed swinging movement of the arm. Also, relax your body to avoid becoming tired.

3. Experimenter demonstrates.

4. You will be given one trial in which to warm-up. Then, you will be given 1 trial at 15 RPMs, 1 at 30 RPMs, 1 at 45 RPMs, and 1 at 60 RPMs with a 30 second rest period between each 45 second trial.

5. Any questions?

FORM A

APPENDIX IV

SUBJECTIVE FEELING INVENTORY

1. No Names
2. Check the appropriate box - which indicates how you feel at that moment. Use your first response.
3. Some items just require you to follow directions.

1.	Useless	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
2.	Taken advantage of	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
3.	Check "not at all"	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
4.	Need a cigarette	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
5.	Check "a little"	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
6.	Sad	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
7.	Nervous	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
8.	Able to concentrate	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
9.	Carefree	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
10.	Fearful	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
11.	Warmhearted	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
12.	Cheerful	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
13.	Alert	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
14.	Restless	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
15.	Feel sexy	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
16.	Sorry for things done	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
17.	Pleasant	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
18.	Need a drink	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
19.	Check "Quite a Bit	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
20.	Efficient	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐

APPENDIX IV (cont.)

21.	Blue	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
22.	Tense	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
23.	Impatient	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
24.	Troubled	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
25.	Sarcastic	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
26.	Satisfied	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
27.	Lively	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
28.	At ease	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
29.	Suspicious	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
30.	Confused	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
31.	Unhappy	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
32.	Check "extremely"	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
33.	Headache	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
34.	Lonely	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
35.	Worn out	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
36.	Sleepy	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
37.	Weary	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
38.	Full of pep	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
39.	Goodnatured	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
40.	Considerate	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
41.	Angry	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
42.	Able to think clearly	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
43.	Stomach upset	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
44.	Annoyed	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐

APPENDIX IV (cont.)

45.	Downhearted	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
46.	Kind	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
47.	Forgetful	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
48.	Happy	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
49.	Friendly	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
50.	Jittery	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
51.	On edge	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
52.	Irritable	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
53.	Hungry	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
54.	Trouble Seeing	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
55.	Rude	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
56.	Worthless	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
57.	Tired	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
58.	Active	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
59.	Troubled by conscience	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐
60.	Depressed	Not at all ☐	a little ☐	quite a bit ☐	extremely ☐

Dr. Stewart... 782-9207

Office..... 257-6690

SUBJECTIVE RESPONSES

Subject #_____

Date_____

TIME	Immediate	1/2 hour	1 hour	2 hours	3 hours	4 hours	5 hours	1/2 hr post
HEADACHE								
NAUSEA								
DIZZINESS								
ABD. PAIN								
CHEST PAIN								
EYE, NOSE THROAT IRRITATION								
OTHER								
ODOR: MILD MODERATE STRONG								

ONLY ABNORMALITIES RECORDED

APPENDIX VI

Date:_____ Assessor:_____

Time:_____

STAFF ASSESSMENT OF THE SUBJECTS' MOOD AND BEHAVIOR IN THE CHAMBER

Directions: On the following dimensions assess the subjects' mood and behavior as observed in interactions with fellow subjects and staff. In the "comments" section describe the behavior of a particular subject if it differs appreciably from the behavior of the group in general. Mark your rating on dash (-), not on a colon (:).

(They are in touch with what is happening around them.)

ALERT :-:-:-:-:-:-:-:-:-:-:-: "OUT OF IT" (kind of in a zombie state physically but not mentally here)
+5 0 -5

CONFUSED/DISORIENTED :-:-:-:-:-:-:-:-:-:-:-: ABLE TO THINK CLEARLY/CONCENTRATE (without extreme effort)
(Aware of their environment but not able to cope with it)
-5 0 +5

HAPPY :-:-:-:-:-:-:-:-:-:-:-: DEPRESSED
+5 0 -5

ANXIOUS :-:-:-:-:-:-:-:-:-:-:-: AT EASE
-5 0 +5

FRIENDLY :-:-:-:-:-:-:-:-:-:-:-: HOSTILE
+5 0 -5

UPTIGHT :-:-:-:-:-:-:-:-:-:-:-: CAREFREE
-5 0 +5

FULL OF PEP :-:-:-:-:-:-:-:-:-:-:-: SLEEPY
+5 0 -5

SERIOUS :-:-:-:-:-:-:-:-:-:-:-: GIDDY
-5 0 +5

TALKATIVE :-:-:-:-:-:-:-:-:-:-:-: QUIET
+5 0 -5

INACTIVE :-:-:-:-:-:-:-:-:-:-:-: ACTIVE
-5 0 +5

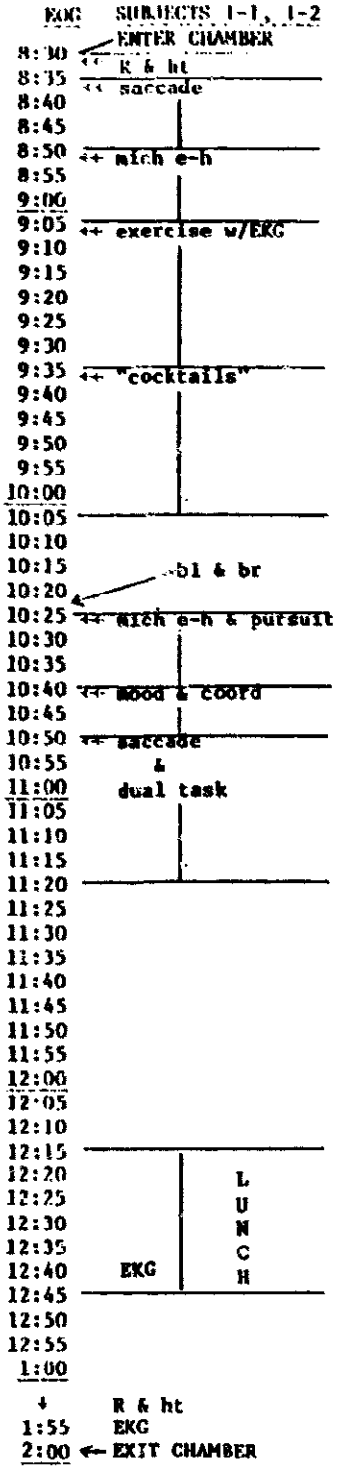
COOPERATIVE :-:-:-:-:-:-:-:-:-:-:-: UNCOOPERATIVE
+5 0 -5

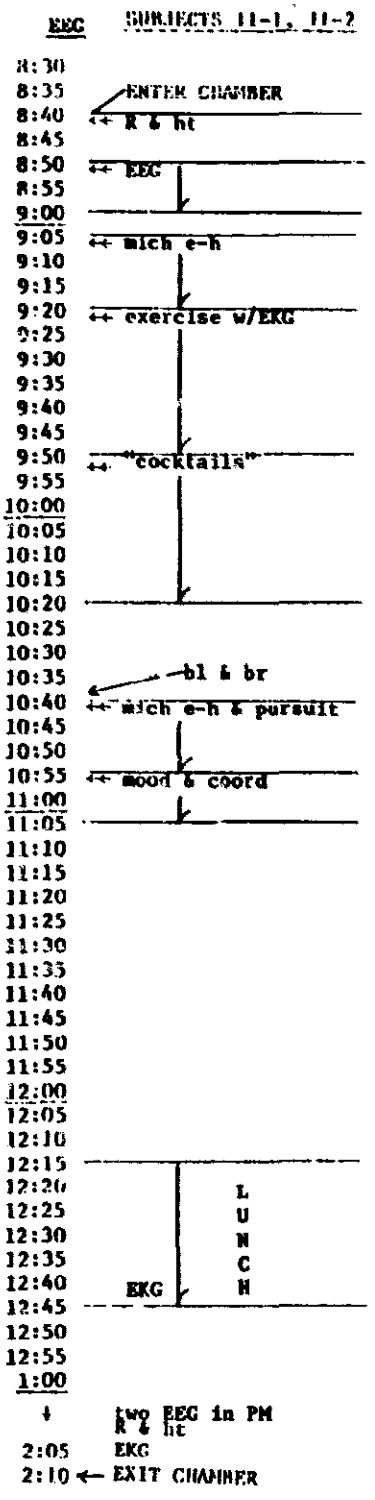
STAGGERING :-:-:-:-:-:-:-:-:-:-:-: IN BALANCE
-5 0 +5

COMMENTS:

APPENDIX VII

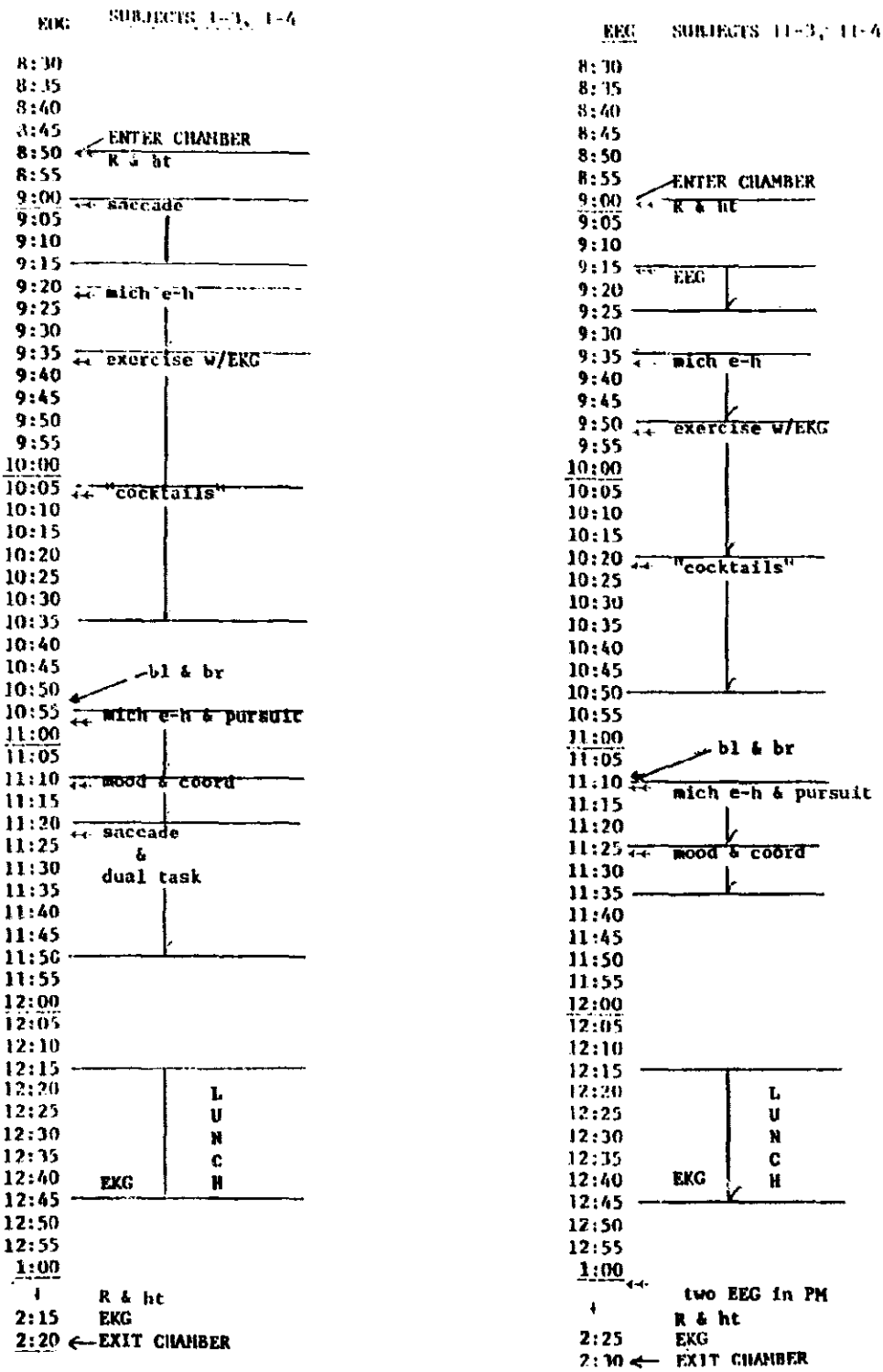
PERC/DRUG STUDY





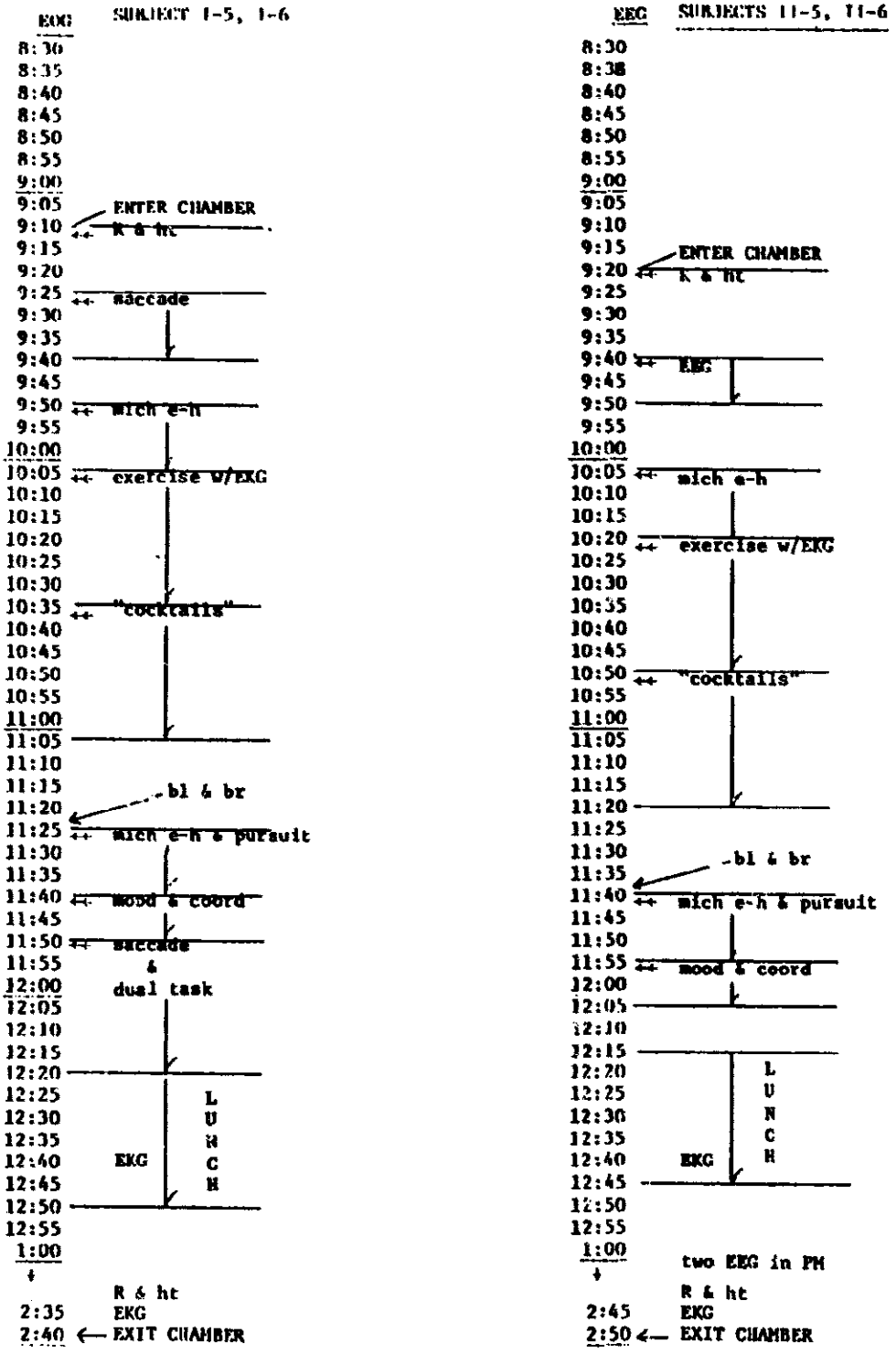
APPENDIX VII (CONT.)

PERC/PKIN. STUDY



APPENDIX VII (CONT.)

PERC/DRUG STUDY



APPENDIX VIII

NO NAME

SUMMARY† *in script*

PERC/DRUG STUDY

DEBRIEFING QUESTIONNAIRE

Prepared by S. Marlow, M.S.

1. Were you able to determine whether or not you were receiving alcohol in your juice?

never____sometimes____often 1 always 8

2. Do you believe that you received one dose, two different doses or more than two different doses of alcohol over the course of the entire study?

one 1 two 7 more than two 1

Did you answer question #2 on the basis of the way the drinks tasted, by the effects they had, or by both?

taste 2 effects 1 both 6

3. On the days you were given medication, were you able to determine whether or not you were receiving Valium rather than a drug free pill?

never 1 sometimes 6 often 2 always____

4. Before the study began you were told that you would be given two different doses of Valium. Were you able to determine on which days you were receiving the 6mg. dose and on which days you were receiving the 10mg. dose of Valium?

never 4 sometimes 4 often 1 always____

5. When under the influence of Valium, did you try to do your best on:

the Michigan--
never____sometimes____often 5 always 4

the pursuit tracking--
never____sometimes 1 often 3 always 5

the Flanagan--
never____sometimes 1 often 5 always 3

the dual task--
never____sometimes 1 often 4 always 4

6. When under the influence of alcohol, did you try to do your best on:

the Michigan--
never____sometimes 1 often 3 always 5

the pursuit tracking--
never____sometimes 1 often 3 always 5

**All nine subjects completed the questionnaire.*

the Flanagan--
never____sometimes____often__5__always__4__

the dual task--
never____sometimes__1__often__3__always__5__

7. Did Sandi fail to see errors (skipping a hole) that you made on the Michigan?

never__1__sometimes__1__often____always____

8. Did you take the mood test seriously and try to answer it honestly?

never____sometimes____often__2__always__7__

9. With "1" indicating most, "2" the next greatest, and "3" the least, please rank the following to show in your opinion the degree to which each affected your responses on the mood test:

Response	# of Ss	
1	6	things happening in my life that had nothing to do with the
2	3	chamber run...
3	0	
1	2	the chemicals (perc vapors, Valium, alcohol) I was exposed to
2	3	during the study...
3	4	
1	6	social interactions (or the lack of them) taking place in the
2	3	chamber...
3	6	

10. Did the requirement of putting a pseudonym on your mood test keep you from being honest?

never__6__sometimes__2__often__1__always____

11. If you had it to do over again would you prefer to put your real name, a pseudonym, or no name on the mood test?

real name__2__pseudonym__3__no name__4__

12. Did you have an idea of what you were scoring on the Michigan by any means other than sheer intuition?

never__7__sometimes__1__often__1__always____

13. Did you have an idea of what you were scoring on the pursuit tracking by any means other than intuition and the feedback the machine gave you (the clicks)?

never____sometimes__4__often__4__always__1__

14. Do you feel that when Rick tested you on the pursuit you performed differently than when Tom tested you?

never__2__sometimes__3__often__1__always__3__

APPENDIX VIII (cont.)

15. Do you feel that when Dr. Hake tested you on the Flanagan you performed differently than when Bert tested you?

never 5 sometimes 2 often 2 always ____

16. To what extent did the noise (conversation, laughing, joking) on the alcohol days influence your performance on the:

Michigan--
not at all 3 a little bit 3 quite a bit 2 extremely 1

pursuit tracking--
not at all 1 a little bit 4 quite a bit 2 extremely 2

Flanagan--
not at all 1 a little bit 3 quite a bit 4 extremely 1

mood test--
not at all 4 a little bit 1 quite a bit 5 extremely 1

If so, in what way for each of the above?

5Ss *stated that the noise affected their ability to concentrate.*

3Ss *stated that their own laughter made performance difficult.*

17. How frequently did lack of sleep influence your performance negatively?

never 5 sometimes 4 often ____ always ____

18. To what extent did the boredom of the day to day routine, schedule, affect your performance negatively on the behavioral tests?

not at all 4 a little bit 5 quite a bit ____ extremely ____

19. Did you fall asleep during the dual task between the tones (your signal to type)?

never 6 sometimes 2 often 1 always ____

20. On the dual task, did you make typing errors (e.g. typing four numbers, two numbers, or hitting the wrong key) while typing in the number of times you saw the white light blink?

never 2 sometimes 7 often ____ always ____

If so, explain what type of error.

4Ss stated that they hit the wrong numbers.

3Ss stated that they entered more or less than three digits.

21. Which test did you find most difficult? Rotary purs. 5; Mich. coord. 2; Dual tasks 1; Flanagan coord. 1 .

22. Which test did you find most challenging? Rotary purs. 6; Mich. coord. 1 .

23. Which test did you find most boring? Flanagan coord. 5; Mich. coord. 1; Dual tasks 1; EEG 1

24. How do you feel about behaviorally-oriented medical research after your experience at the Department of Environmental Medicine?

not worthwhile____ has some value 2 no opinion 4 worthwhile 1

very worthwhile 2

25. Did you feel exploited by any of the procedures or tests you were subjected to?

never 6 sometimes____ often 1 always____

If so, what tests or procedures made you feel this way?

The S who responded "often" stated, "treatment and attitude of some of the professionals".

Additional Comments:

"Not enough chairs or cubicles"

"It was a very pleasant experience working with both the people in the group and the Dept. staff".

APPENDIX VIII (cont.)

NO NAME

DEBRIEFING QUESTIONNAIRE (cont.)

Try to answer the following four questions as objectively and honestly as possible:

1. Were you accurate in determining when you were receiving alcohol?

   not at all____ a little bit_1_ quite a bit_1_ extremely_7_

2. Were you accurate in detecting on which days you were receiving the low dose of alcohol and on which days you were receiving doses twice as strong?

   not at all_4_ a little bit_2_ quite a bit_1_ extremely_2_

3. Were you accurate in determining when you were receiving Valium?

   not at all_3_ a little bit_1_ quite a bit_4_ extremely_1_

4. Were you accurate in detecting on which days you were receiving the 6mg. dose of Valium and on which days the 10mg. dose?

   not at all_7_ a little bit_1_ quite a bit____ extremely_1_

ADDENDUM*

DUAL-ATTENTION TASK ANALYSIS

PCE-Alcohol Combination

Response times for the dual-attention task (see page 8 of the methodology section), hereafter referred to as the peripheral light test, are shown in Figure 1 of the addendum for the different PCE-alcohol treatment combinations. Each of the nine data points in the figure represents the mean response time of five subjects for both conditions of peripheral light detection: peripheral-lights alone and peripheral-lights plus central counting. In the latter condition, only response times for those trials were included where the central count was correct or within plus or minus one value of the correct count. Inspection of Figure 1 indicates that PCE had little influence on

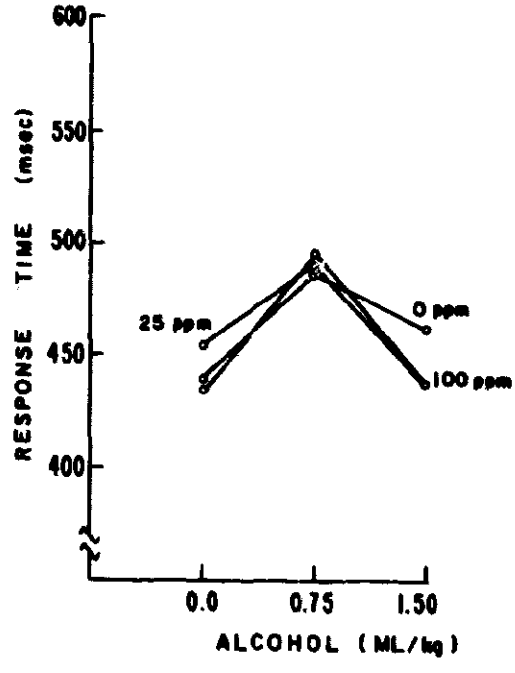


Figure 1. The effects of the three concentrations of PCE with three different levels of administered alcohol on response time of five subjects averaged over both conditions of the peripheral-light task.

*Prepared by Vernon R. Putz, Research Psychologist, Behavioral and Motivational Factors Branch, DBBS, NIOSH, Cincinnati, Ohio.

response times for peripheral lights, while alcohol, as 100-proof vodka, at the low dose of 0.75 ml/kg appeared to increase response time, only to be reduced at the higher alcohol level of 1.50 ml/kg. This observation was confirmed in the analysis of variance. No significant interactions occurred among the levels of PCE and the alcohol conditions (F (4, 16) = 0.31, p >0.01). However, a significant main effect was found with alcohol F (2, 8) = 9.65, p <0.01. The Newman-Keuls range test indicated that the control mean of 442 msec (no alcohol) was significantly different from the intermediate alcohol level, which produced a mean response time of 488 msec, p < 0.1. No further significant differences were found between the control and the high alcohol level or between the intermediate and high levels.

A main methodological interest with the peripheral light test was to determine if information loading of the subject by adding a second task of counting a central light blinking would serve to aid in the differentation of treatment effects by reducing the subject's short term compensatory capability. Analysis of variance revealed the dual-task condition was significantly different from the single activity of peripheral-light detection (F 1, 4) = 45.7, p <0.01). Mean response time for the dual-task condition was 490 msec as compared to 435 msec for the single-task condition. However, no significant differences were found in the three way interaction involving PCE, alcohol and the task conditions (F (4, 16) = 1.47, p >0.01). In other words, the dual-task condition increased general response time, but did not differentially affect the nine treatment combinations.

The above analyses were performed on the mean response times for all 30 peripheral light locations. In the subsequent analysis, the data were grouped according to the position of the peripheral lights, or angle of presentation, namely, far left, far right, and center. Center lights were those defined to be within $\pm$ 10° of the straight ahead position, while the far left and far right included the range of 30 - 70° to the left or right of center. Mean response times across all conditions averaged 429 msec for the lights positioned on the far left, 448 msec for those on the far right, and 417 msec for the lights within $\pm$ 10° center. Although the orientation of the peripheral lights did produce a significant main effect across all task and treatment conditions (F (2, 8) = 13.29, p <0.01), this variable did not interact with the PCE and alcohol treatment combinations (F (8, 32) = 0.82 p >0.01). Due in part to the high visibility of the peripheral lights, and the task procedure, misses and false positives were very infrequent, and accounted for less than 2% of the total trial data which resulted in too few responses to warrant subsequent analysis. Blink-counting during the dual-task condition was also very accurate and did not reflect any treatment effects.

PCE-Diazepam Combination

The data for the PCE-diazepam treatments averaged across the two task conditions for three subjects are shown in Figure 2 of the addendum. With zero diazepam or placebo, PCE appeared to increase the response times slightly. However, analysis of variance indicated that neither PCE nor diazepam were significant as a main effect and did not interact in any manner (F (6, 12) = 1.37, p >0.01). The only significant variable was task condition (F (1, 2) = 840, p < 0.01). Since the task conditions did not significantly interact with the PCE-diazepam treatment conditions (F (6, 12) = 1.51, p >0.01), the task

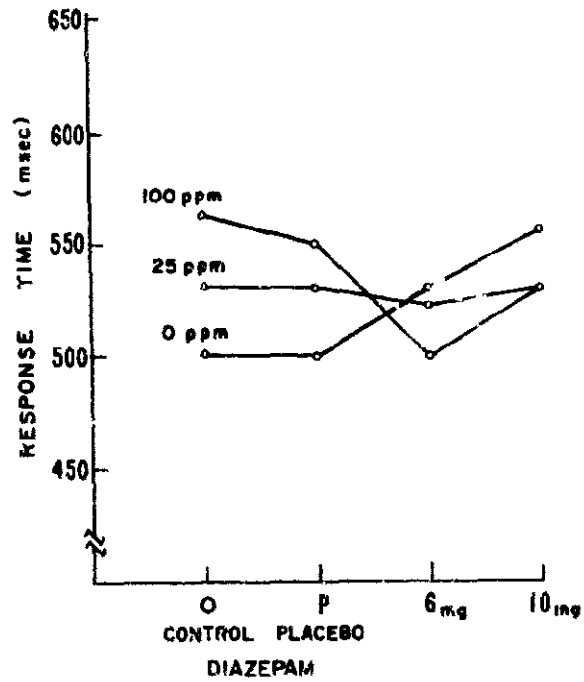


Figure 2. The effects of three concentrations of PCE at each of the four conditions of diazepam administration on response time of three subjects averaged over both conditions of the peripheral-light task.

variable did not aid in differentiating the treatment combinations or have any particular meaning in the present context.

The effect of the angle of presentation of the peripheral lights was also analyzed for the PCE-diazepam conditions. The orientation of the lights did significantly influence response times (F (2, 4) = 29.5, p <0.01). Lights located to the far left of center produced a mean response time of 492 msec, to the far right 514 msec, and 461 msec were recorded for lights in the center of the subject's visual field ($\pm 10^{o}$). Both left and right values were significantly different from the center.

A significant three-way interaction occurred with diazepam, lamp orientation, and task condition (F (6, 12) = 3.6, p <0.05). Figure 3 of the addendum shows the relationships. Three things are apparent on inspection of the figure: (a) the dual-task condition resulted in generally higher response times, (b) response times to the peripheral lights were slower than the central, and (3) no trend with regard to diazepam was evident. The expectation that the effects of the PCE and drug treatments on response time would be

ADDENDUM (cont.)

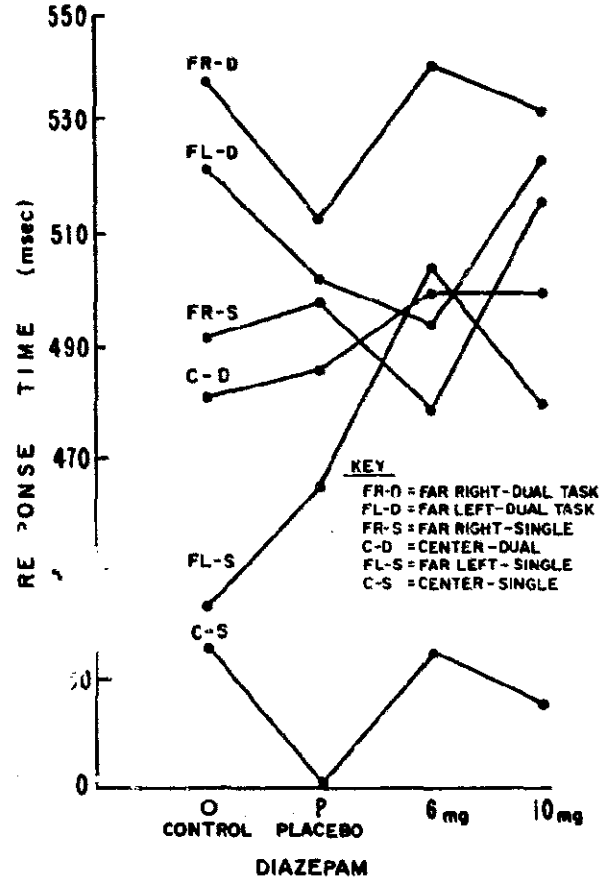


Figure 3. A three-way interaction among the four conditions of diazepam administration, the two conditions of the peripheral-light task: single and dual, and the three angles of light presentation: far right, far left, and center is indicated. Peripheral-light response times were measured to an accuracy of ± 1 msec.

more evident by the added stress of responding to peripheral lights while simultaneously counting a central blinking light received no support in this study with three subjects. Variations in the data with regard to misses, false positives, and central light blinking accuracy were extremely small and did not warrant analysis.

The general conclusion from this behavioral test was that the peripheral-light test, as applied, provided little insight into possible PCE-diazepam and PCE-alcohol interactions. Furthermore, the test did not reveal any significant or consistent trend with regard to the main effects of PCE, alcohol, or diazepam.

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