U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES ■ Public Health Service
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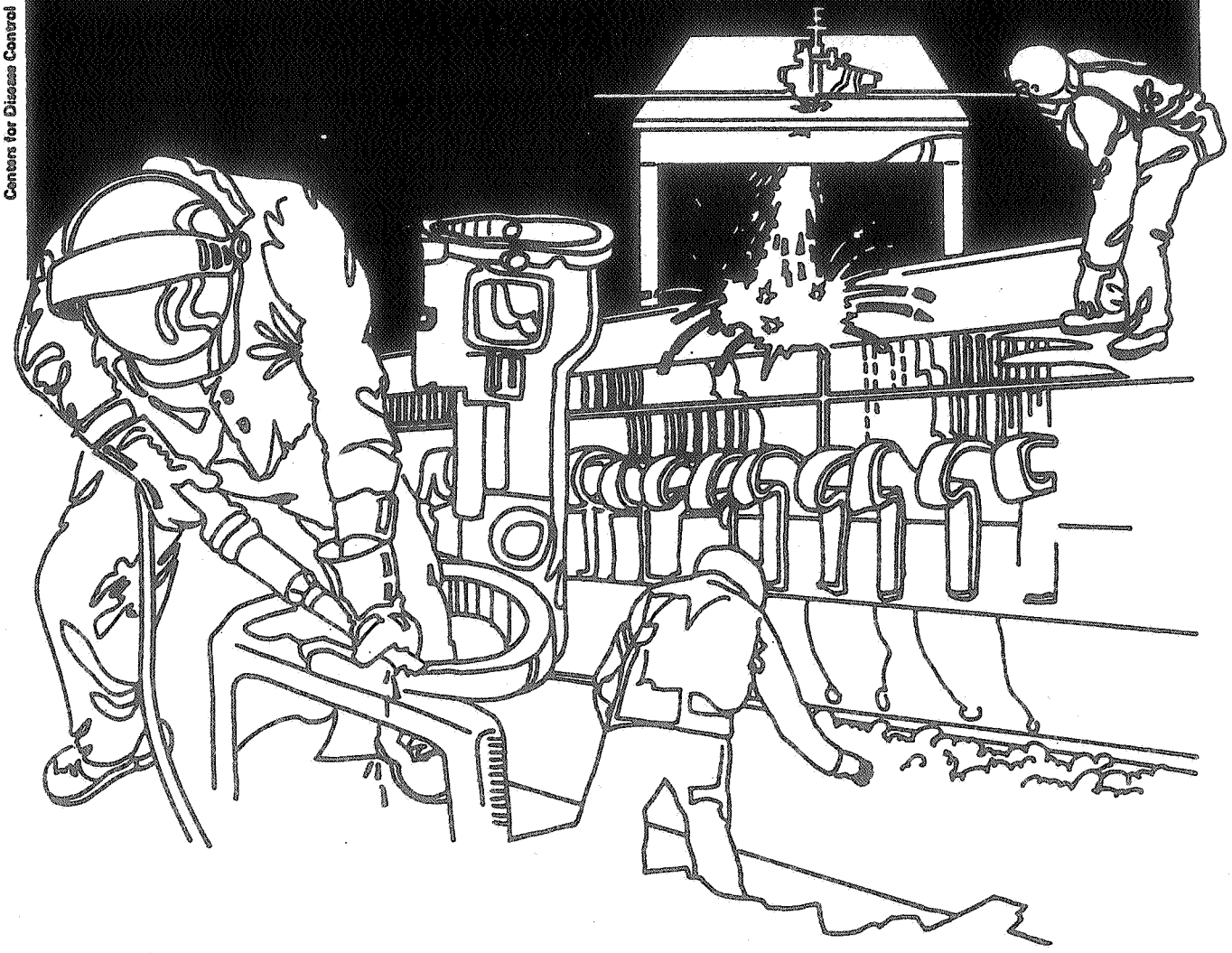

Health Hazard Evaluation Report

HHE 80-137-1145
SHELL CHEMICAL COMPANY
DENVER, COLORADO

PREFACE

The Hazard Evaluations and Technical Assistance Branch of NIOSH conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The Hazard Evaluations and Technical Assistance Branch also provides, upon request, medical, nursing, and industrial nygiene technical and consultative assistance (TA) to Federal, state, and local agencies; labor; industry and other groups or individuals to control occupational health hazards and to prevent related trauma and disease.

Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

SHELL CHEMICAL COMPANY
DENVER, COLORADO
JULY 1982

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I. SUMMARY

In April 1980 the National Institute for Occupational Safety and Health (NIOSH) received a request for a health hazard evaluation at Shell Chemical Company, Denver, Colorado The request originated from concerns for the potential health effects--both short and long term--to approximately 175 workers at the plant. The chemicals of concern were chloroform, trimethyl phosphite (TMP), trimethyl phosphate (TMPO), acetone, sodium hydroxide, hexane, methyl isobutyl ketone (MIBK), methyl isocyanate (MIC), methylthioacetoldoxime (MSAO), Nudrin®, Vapona®, and Azodrin®. Concern was also expressed as to the adequacy of the medical screening program in general and the cholinesterase monitoring program in particular.

To evaluate these problems, NIOSH conducted an industrial hygiene and medical evaluation. Personal and area environmental samples, as well as wipe and bulk samples, were obtained and the Company's personal protective program and plant ventilation systems were reviewed. The medical evaluation consisted of a detailed study of Shell's 1979-80 cholinesterase data, a screening review of laboratory work, and interviews with 43 individual workers at the Denver plant.

The environmental evaluation determined that personal and area air samples for chloroform, TMP, TMPO, acetone, sodium hydroxide, hexane, MIBK, MIC, MSAO, Nudrin®, Vapona®, and Azodrin® did not exceed the criteria established for this survey, i.e., 9.8 mg/M^3, 10 mg/M^3, 590 mg/M^3, 2.0 mg/M^3, 90 mg/M^3, 200 mg/M^3, 0.05 mg/M^3, 2.5 mg/M^3, 1.0 mg/M^3, and 0.25 mg/M^3 respectively. Trimethyl phosphite (TMP) and methylthioacetoldoxime (MSAO) do not have a criterion and/or a standard. The wipe samples did indicate the potential for skin contamination from Azodrin®. Nudrin® contamination was also found on wipe samples taken on two lunch tables.

Review of the cholinesterase monitoring data covering 2717 tests on 288 individuals showed only four depressions requiring follow-up in the previous 23 months. None were low enough to require removal. Only two appeared to have been followed up promptly. Although the laboratory methods and calculations used appeared to work well except when only small numbers of tests were done on a given day, use of a method with an external standard should work better.

Review of laboratory work on 202 workers failed to establish any job related trends towards abnormal results. Individual interviews showed follow-up of medical screening to be generally good. There were a few instances of accidents or overexposures causing problems, but these appeared to be individual instances, but do illustrate the continuing need for attention to functioning engineering controls, good work practices, and worker education.

Based on the data obtained in this investigation, NIOSH determined that a health hazard did not exist to those employees evaluated at Shell Chemical Company, Denver, Colorado, from the chemicals evaluated. Finally, the personal protective program, employee education program regarding safe work practices and pesticides handling, as well as the engineering/exhaust ventilation system evaluated, were considered sufficient for the operations surveyed. Some work practices, personal hygiene, and medical methods/monitoring concerns were noted during the investigation and recommendations are included in Section VIII of this report to assist in resolving these problems.

KEYWORDS: SIC 2879 (Pesticides and Agricultural Chemicals), pesticides, herbicides, cholinesterase, chloroform, trimethyl phosphate, trimethyl phosphite, acetone, sodium hydroxide, hexane, methyl isobutyl ketone, methyl isocyanate, methylthioacetoldoxime, Nudrin®, Vapona®, Azodrin®.

II. INTRODUCTION

On May 12, 1980, an authorized representative of the employees at Shell Chemical Company, Denver, Colorado, submitted a health hazard evaluation request. The request stated that in a previous NIOSH Health Hazard Evaluation (HHE 77-126-646) the environmental and medical emphasis was directed towards the potential health risk, both past and present, to dibromochloropropane (DBCP) and failed to adequately address the environmental and medical concerns related to various other chemicals processed at the Denver facility. These concerns included the need for an objective characterization of the potential exposures to approximately 175 employees from chloroform, trimethyl phosphite (TMP), and Vapona®. It was also felt by the requestor that Shell's medical screening/monitoring program in general and cholinesterase monitoring program in particular was not adequate and, therefore, should be evaluated to determine its overall effectiveness in safeguarding the health of the employees at Shell's Denver facility. An environmental survey was conducted during June and November 1980, and the chemicals evaluated during these surveys included chloroform, trimethyl phosphite (TMP), and Vapona® as described in the union request. It was also felt by the project officer that trimethyl phosphate (TMPO), acetone, sodium hydroxide, hexane, methyl isobutyl ketone (MIBK), methyl isocyanate (MIC), methylthioacetoldoxine (MSAO), Nudrin®, and Azodrin® should be included in the survey. The medical evaluation was performed on November 14 and 19, 1980, and follow-up interviews with the workers on July 22 and 29, 1981. After each evaluation, concerns and recommendations were given to union and management officials during each closing conference. These concerns and recommendations are included in this report.

Besides the NIOSH study of DBCP workers (HHE 77-126-646) and the current study, the workers at this plant have been a part of a mortality study of pesticide manufacturers/formulators done under contract (210-76-0173) for Industry Wide Studies Branch, Division of Surveillance, Hazard Evaluation, and Field Studies (DSHEFS), NIOSH. Those workers who were exposed to DBCP are being followed as part of NIOSH's DBCP register (Project 625, Surveillance Branch, DSHEFS).

III. BACKGROUND

Shell Chemical Company, Denver, Colorado, a producer of various pesticide products, is located at the Rocky Mountain Arsenal outside of Denver. The Company leases several buildings on a 60 acre plot for the pesticide manufacturing, formulation, and storage of their products. There are approximately 300 full-time employees at the facility, about 140 of whom are administrative. The plant operates seven days per week with employees working an 8-10 hour day, 40 hour week with rotating shift schedules.

A. Process Description

The various insecticide and herbicide pesticides that are manufactured and/or formulated at the facility are processed in closed reaction systems and drummed under local exhaust ventilation and enclosed engineering control systems. A brief description of each process will be presented below by building number but specifics of the operations are not detailed, due to trade secrets.

1. Building 471

This building has three floors with open central bays. This unit produces Vapona® and, basically, the raw materials used in this product are

distilled in closed column systems and then reacted in closed looped reactor systems. The products can then be drummed at central drumming (Building 451), or at a small drumming station within Department 471 or can be pumped directly into tank cars. All processes contain local exhaust ventilation. The process sampling ports are also under engineering controls. There are one to two operators for each shift in this building. A lunch room is provided which is under positive pressure.

2. Building 451 - Central Drumming

This building is solely used to drum the various products, label, and prepare shipments. The drumming stations are enclosed and locally exhausted. Two lines fill 30 or 55 gallon drums and a third line fills 5-gallon cans. During the NIOSH survey, formulated Azodrin® was being drummed. There are normally 3-4 drummers who work here and this process is performed one day per week for approximately 5-8 hours. The drumming is performed in closed exhaust chambers.

3. Buildings 525 and 515 East

Nudrin®, a carbamate insecticide, is produced in Buildings 525 and 515 East. Each building contains three floor levels with the operator's control room/lunchroom on the second floor. The control rooms are air conditioned and under positive pressure.

Building 525 contains closed reactors for reaction steps 1 and 2 and the extraction process. The material proceeds outside to a dehydration process and then to Building 515 for reaction step 3 (toxification), recrystallization, centrifugation/drying, and drumming. The process is basically a batch operation producing about 25 to 30 drums per batch.

4. Buildings 514/516

Azodrin® is produced in these buildings. Building 516 contains closed reactors for reactions 1 through 3, neutralization, and extraction. The material is then pumped to building 514 for reaction (toxification) and purification. At this point the Technical Azodrin® can be drummed into 5-gallon quads in an enclosed exhaust ventilated drumming station or it can be blended with solvent to form formulated Azodrin® which is drummed in Building 451. Each building has four floor levels for process equipment. Building 514 contains the operator's lunch area which is air conditioned and under positive pressure.

In general each building has a number of safety features; that is, each stage of the process in each building contains engineering controls to prevent toxic emission, electrical lockout procedures, safety alarms, and local exhaust ventilation at those drumming stations.

All of the buildings described contain eye wash fountains, emergency showers, gas mask cannisters, supplied air respirator hose connections, gas alarms, and fire extinguishers on each floor in several easily accessible strategic locations. Where it is possible, the processes contain solvent recovery systems for recycling of the solvents to the processes. The various tank farms also have emergency equipment and gas alarms. Maintenance at the facility is divided into assigned zones. Most of the support personnel are based from a central maintenance shop which also has showers and lunch areas.

B. Employees at Risk

The employees most likely exposed (at highest risk) to the chemicals evaluated in this survey were considered to be all of the employees who work directly with the production of the various pesticides produced. That is, each of the employees in buildings 471, 451, 514, 515, 516, and 525. These include reaction/chlorine operators, column operators, reaction/stripper operators, centrifuge operators, crystal recovery operators, utility operators, filter change operators, sampling operators, toxification operators, reduction and neutralization operators, drummers, pipefitters, and electric operators. Another group of employees considered to be at risk are those who work in the laboratories where the various chemical intermediates and final products are tested for their quality. These employees, as well as others besides those listed above, were included in the evaluation for the medical concerns addressed in the request. Only the production/process operators were sampled for environmental contaminants.

C. Engineering Controls

During the evaluation it was determined that Shell has developed a very thorough, extensive local exhaust ventilation system in each of those buildings evaluated, i.e., buildings 471, 451, 514, 515, 516, and 525. These include local exhaust systems at each of the sampling stations, at locations where routine maintenance is performed, and at the drum/bottle filling stations. The exhaust systems are primarily elephant trunk-type portable exhaust for maintenance operations, semi or completely enclosed exhaust ventilation chambers for drum/bottle filling, and chamber type exhaust systems for all of the sampling stations.

D. Personal Protective Equipment

Shell Chemical has a very complete personal protective program for all of its employees who work at the Denver plant. For those operations evaluated the mandatory clothing included coveralls which were worn at work only, hard hats, impervious boots, and safety glasses. Individuals involved in drum filling also wore impervious gloves throughout the operation. Some operators wore face shields, gauntlets, and impervious aprons during the drum filling operation but this was not consistent throughout.

The respiratory protection program developed by Shell is also very thorough and includes: (1) Policies and Responsibilities; (2) Types and Use; (3) Location of Respirators Used; (4) Operating Instructions; (5) Training Requirements; (6) Maintenance and Repair; (7) Cleaning and Sanitizing, and (8) Breathing Air Systems.

E. Safety/Health and Procedures-Training

Another program provided to each of the Shell employees is a health and safety program which includes guidelines and procedures and training for each of the workers. Basically, all new employees received training in respiratory protection, fire fighting, emergency reporting, specific safety rules for the Denver plant, hazard of toxic chemicals, proper handling of drums, and forklift operations. Annual training is provided which includes respiratory protection and fire fighting. Supervisors and selected personnel also receive annual training in first aid, CPR, the Heimlich maneuver, and ambulance training. Shell also provides specialized training which includes

industrial fire fighting, industrial hygiene, laboratory safety, new equipment and processes, and monthly "Tailgate Meetings". The tailgate meetings are routinely scheduled for both maintenance and operations personnel and may include topics such as proper asbestos handling, chloroform handling, update on drum handling, emergency shower requirements, food/drink contamination, updates on respiratory equipment, and new information on hot/cold work permits.

F. Environmental Sampling Program

The Denver plant has developed a routine sampling and analytical evaluation program for all of its raw/intermittent chemicals, as well as its final products. The majority of these sampling and analytical techniques follow NIOSH's recommended procedures. The remaining Shell methods have not been developed and/or evaluated by NIOSH to date and therefore NIOSH recommended methods may not exist as of this writing.

G. Medical Concerns

The Company has had a medical program since 1951. Cholinesterase test data, which is a primary concern in this evaluation, has been available for a considerable period of time, as is physical examination data. In the last couple of years all medical data back to 1974 has been or is being computerized in the Corporate Medical offices in Houston. At the time of the November 1980 visit approximately half of the data had been entered, each worker's data being sent when they came up for their routine examination. Cholinesterase data was not, however, included as it was maintained in a separate consolidated file.

The union expressed concern that significant portions of the work force would not be followed as a part of NIOSH ongoing studies because interest had been narrowed to DBCP exposed workers. Discussion with the project officer within NIOSH responsible for the mortality study (Project 625, Surveillance Branch, DSHEFS) on workers included in the DBCP register revealed that no one was excluded when the focus was narrowed down from earlier studies at the plant to DBCP in particular.

IV. EVALUATION DESIGN AND METHODS

A. Environmental

A variety of sampling techniques were used to evaluate the suspected contaminants. Personal and area samples were taken on a portion of the population from each of the areas of concern. The following is a description of sampling techniques used.

1. Azodrin®

Personal and area air samples for Azodrin® were taken using chromosorb tubes. The air was pulled through the media with low flow sampling pumps. The flow rates were set at 200 cubic centimeters per minute (cc/minute). These samples were analyzed by gas chromatograph (GC) and flame photometric detector. Prior to analysis each sample was desorbed for acetonitrile for ten hours.

Wipe samples for Azodrin® contamination were also analyzed using the technique described above. These samples were obtained using dry wipes and collected on the worker's hands, neck and forehead.

2. Trimethyl Phosphite and Trimethyl Phosphate (TMP and TMPO)

Personal and area air samples for TMP and TMPO were taken using chromosorb tubes. The air was pulled through the media at 200 cc/minute with low flow sampling pumps. These samples were analyzed by GC and mass spectrometer.

3. Vapona®

Personal and area air samples for Vapona® were taken using chromosorb tubes. The air was pulled through the media at 200 cc/minute with low flow sampling pumps. These samples were analyzed by GC and electron capture detector. The samples were desorbed for 16 hours in toluene prior to analysis.

Wipe samples for Vapona® contamination were also analyzed using the technique described above.

4. Acetone and Chloroform

Personal and area air samples for acetone and chloroform were taken using charcoal tubes. The air was pulled through the media at 50 and 200 cc/minute with low flow sampling pumps. NIOSH modified Methods S-1 and S-351 were used in the analysis of these samples.

5. Nudrin® and Methylthioacetoldoxine

Personal and area air samples for Nudrin® and Methylthioacetoldoxine (MSAO) were taken using chromosorb tubes in conjunction with AA 13 millimeter filters. The air was pulled through the media at 200 cc/minutes with low flow sampling pumps. The samples were analyzed using the Shell Development Company recommended method (refer to Appendix A).

6. Sodium Hydroxide

Personal and area air samples for sodium hydroxide were taken using 37 millimeter AA cellulose membrane filters. The air was pulled through the media at 1.5 liters per minute (lpm) with high flow pumps. These samples were analyzed by atomic emission spectroscopy.

7. Hexane and Methyl Isobutyl Ketone (MIBK)

Personal and area air samples for hexane and MIBK were taken using charcoal tubes. The air was pulled through the media at 50 and 200 cc/minute using low flow pumps. The samples were analyzed using a modified NIOSH Method P&CAM No. 127.

8. Methyl Isocyanate (MIC)

Personal and area air samples for MIC were taken using impinger solution. The air was drawn through the media at 1.5 lpm using high flow pumps. The samples were analyzed using a modified NIOSH Method P&CAM N-240.

B. Medical

The mortality study performed by NIOSH was designed to identify any long term health effects in the worker population. Other studies had looked at more current effects and, therefore, this study limited itself to (1) a detailed study of the 1979 and 1980 cholinesterase test results and (2) a screening review of laboratory work. After these reviews, (3) a number of workers were individually interviewed to find out what was the outcome of the test results. Tables I and I-A give a breakdown by pay account of the various sample sizes.

1. Cholinesterase Test Results

Data was obtained by individual for 1979 and the first eleven months of 1980. Each individual's results were screened for clinically significant lowering of cholinesterase activity. Group means and standard deviations were obtained. (Groups are listed in Table I.) The data were then realigned by date, the correction factor for each individual calculated, outliers checked for accuracy, and if remaining unreconciled with the bulk of the day's data, eliminated from calculations. The outliers, of which there were three or less on any one day, differed from the bulk of the day's results by many orders of magnitude. This realigning by date was done for all 1979 data (a year when the cholinesterase program was said to have been running well) and for the months of July, August, and September 1980. There were reportedly problems in standardizing the tests in August 1980. For thirty days in 1979 and twenty days in 1980 (all except those with only one determination) baseline data was also calculated.

In evaluating the 1979-80 cholinesterase data the following concerns were addressed:

a. How frequently were low values observed and what was done about them?

In this section the first half of the question was addressed by count. The second half was determined by interview.

b. How well did the Company's method of standardizing the tests work?

Variation in any individual result could be due to:

(1) The day's variation in the lab test (due to temperature variations, solution age, line voltage fluctuations, etc.);

(2) The individual's baseline level;

(3) The individual's day to day variation;

(4) The individual's exposure to substances lowering cholinesterase.

By using the average value for the day, both the variations in the individual baseline (2) and the individual's day to day variation (3) should have been nearly eliminated. If only rarely was a cholinesterase significantly depressed, this should not have significantly affected the average. Thus the day-to-day variation inherent in the laboratory method should have been controlled by correcting the day's average to the preset

average of 81 S.U. A corollary of this method of correction would be that the average of individual percentages of baseline should have been 100%. Also the correction factor should have related to the average of the raw data, but not to the average of the individual's baselines nor to the area of the plant from which they came. This last point was examined both by the groups shown in Table I and by a grouping of high, moderate, and low exposure as judged by the frequency of cholinesterase determinations (7.5 or more determinations per year, at least three but less than 7.5 determinations per year, less than three determinations per year).

2. Other Laboratory Work

Laboratory work for 202 individuals was supplied by the corporate medical department as computer printouts. All were identified by job and all but nine by name. Also supplied was a list of "normal" values used by the corporate medical department. These are in line with published normals and so were used in the evaluation. Numbers of specific white blood cells were calculated from the total white count and percentage on differential count and compared to published normals.[1,2] Number of tests by year and study group are tabulated in Table II. Abnormally high and abnormally low values were counted and compared to total tests. After a preliminary review of abnormal results, individuals were interviewed to evaluate what follow-up had been done or what medical conditions might account for the findings.

3. Worker Interviews

The breakdown of 43 workers interviewed is given in Table I. Workers were chosen so as to meet two criteria: (1) either their cholinesterases left some question (usually a value low enough to approach clinical significance, although in two cases it was the extremely large number of determinations) or their more recent laboratory work suggested that they might have been followed up; and (2) at least some workers should be interviewed from all sections of the plant. Those with questions on their cholinesterase were all interviewed; of the rest about two-thirds were seen, a number judged sufficient to assess how follow-up was accomplished.

V. EVALUATION CRITERIA AND TOXICOLOGY

A. Environmental

In this study numerous sources of criteria and existing research data were used to assess the worker's exposure to the suspected chemicals evaluated in the workplace at Shell Chemical Company, Denver, Colorado.

The exposure limits to toxic chemicals are derived from existing human and animal data, as well as industrial experience, to which it is believed that nearly all workers may be exposed for an 8-10 hour day, 40-hour work week, over a working lifetime with no adverse effects. However, due to variations in individual susceptibility, a small percentage of workers may experience effects at levels at or below the recommended exposure limit; a smaller percentage may be more seriously affected by aggravation of a pre-existing condition or by development of an occupational illness.

Three sources of criteria are generally used to assess the workroom concentrations of air contaminants: (1) NIOSH criteria for a recommended standards; (2) recommended Threshold Limit Values (TLVs) and their supporting documentation as set forth by the American Conference of Governmental Industrial Hygienists (ACGIH), 1981; and (3) Occupational Safety and Health Administration (OSHA) standards (29 CFR 1910.1000), July 1980.

	Permissible Exposure Limits 8-Hour Time-Weighted Exposure Basis mg/M^3		
Substance	NIOSH	OSHA	TLV
Chloroform	(C)9.8	50	(S)240
Trimethyl phosphate (TMPO)	None	None	None
Trimethyl phosphite (TMP)	None	None	10
Acetone	590	2400	1800
Sodium hydroxide	(C)2.0	2.0	2.0
Hexane	350	1800	90
Methyl isobutyl ketone	200	410	205
Methyl isocyanate	None	0.05	(S)0.05
Methylthioacetoldoxime	None	None	None
Nudrin®	None	None	2.5
Vapona®	None	1.0	1.0
Azodrin®	None	None	None

mg/M^3 = milligrams of substance per cubic meter of air.
C = ceiling level which cannot be exceeded beyond a 15 minute period.
S = potential contribution to exposure by the cutaneous route.

B. Medical/Toxicology

1. Cholinesterase Inhibitors[3]

Both organophosphate pesticides and carbamate pesticides exert their primary toxic effects on humans by inhibiting the enzyme cholinesterase. Cholinesterase is necessary to "reset" nerves after they have carried an impulse. Chronic low level exposure to cholinesterase inhibitors can lead to progressive depression of cholinesterase until a level is reached where symptoms occur. Symptoms can include respiratory tightness, sweating, nausea, vomiting, abdominal cramps, constriction of the pupils of the eyes, muscular fatigue and weakness, twitching, muscle cramps, anxiety, headache, emotional instability, confusion, unsteady gait, slurred speech, convulsions and, in the extreme case, circulatory and respiratory depression and death.

Organophosphates usually permanently inhibit the cholinesterase, requiring the body to produce a new supply. Carbamates usually cause only temporary inhibition allowing a much more rapid recovery. Some organophosphates also cause a delayed toxic effect on the peripheral nervous system.

Besides being found in conjunction with nerves, cholinesterase is found in blood plasma and in red blood cells. Cholinesterase can be measured in either plasma, or red cells, or a combination of both (whole blood). The red cell cholinesterase is a relatively stable measurement and is the

test recommended by NIOSH for monitoring organophosphate exposure. Carbamates cause a rapid reduction in plasma cholinesterase as well as red cell cholinesterase. As the inhibition is rapidly reversed, particularly in plasma, it is important that blood be obtained promptly after exposure and the test be done promptly after the blood is drawn.

Three pesticides were identified in this study as being present at detectable levels. All are included in Group I of the NIOSH Criteria Document indicating they are toxic enough to require the more stringent attention to exposure, work practices, and medical monitoring. They are: Azodrin® (Monocrotophos) - an organophosphate; Nudrin® (Methomyl) - a carbamate; Vapona® (Dichlorvos) - an organophosphate.

2. Sodium Hydroxide (Lye)

The toxic effects of sodium hydroxide are due solely to its caustic nature. Strong solutions can penetrate most body tissues destroying them in the process. Burns due to exposure to excessive concentrations of sodium hydroxide tend to be deep. More dilute solutions will feel soapy and can cause dermatitis on chronic exposure. Dry solid sodium hydroxide will probably not affect dry skin, but will readily dissolve in any moisture giving off considerable heat and quite possibly will yield a strongly caustic solution. Solid sodium hydroxide will readily absorb moisture from the air and dissolve in it.

If necessary to wash off sodium hydroxide plenty of water should be used to dissipate the heat of solution and assure the sodium hydroxide is rapidly diluted to a safe level.

VI. RESULTS AND DISCUSSION

A. Environmental

Employee exposure to suspected airborne concentrations of chloroform, trimethyl phosphate, trimethyl phosphite, acetone, sodium hydroxide, hexane, methyl isobutyl ketone, methyl isocyanate, methylthioacetoldoxime, Nudrin®, Vapona®, and Azodrin® were evaluated. An evaluation of the exhaust ventilation, as well as the Company's personal protection program was also assessed during the survey periods. The following are the results and discussion of NIOSH's environmental evaluation.

1. Chloroform and Acetone

A total of 15 personal air samples and 5 area type air samples were taken during the survey periods for chloroform and acetone. Each of these showed non-detectable levels. The employees sampled included inside and outside utility operators, chlorination and toxification operators, and reduction and neutralization operators.

2. Trimethyl Phosphate and Trimethyl Phosphite

A total of 6 personal air samples were taken on the operators during the survey period for trimethyl phosphate and phosphite evaluation. Each of these samples showed levels below the detectable level of anaylsis.

3. Sodium Hydroxide

A total of three personal air samples were taken during the survey for sodium hydroxide (refer to Table III). The exposure levels were approximately one-tenth (range 0.01-0.02 mg/M^3) of the OSHA standard of 2.0 mg/M^3. Therefore, the results of this evaluation would not indicate a health hazard.

4. Hexane and Methyl Isobutyl Ketone

A total of 12 personal air samples and 10 area type air samples were taken for hexane and methyl isobutyl ketone. All of the sample results for both compounds were below the analytical detection methods used on these. These samples were taken on the outside and inside utility operators, column operators, reaction and stripper operators, crystal recovery operators, and drummers.

5. Methyl Isocyanate

A total of 16 personal air samples were taken for methyl isocyanate and all of these results were below the level of detection. These samples were taken on the crystal recovery operators, outside utility operators, toxification and reaction operators, centrifuge operators, and drummers in Building 515.

6. Nudrin® and Methylthioacetoldoxime

A total of 12 personal air samples and 12 area type air samples were taken for Nudrin® and methylthioacetoldoxime and each of these samples was below the level of analytical detection. However, wipe samples taken for Nudrin® in the lunchroom (2) and control room (1) of Building 515 did show levels from 0.77 to 20.0 micrograms per samples (refer to Table IV). These samples cannot be compared to a criteria or standard and therefore only indicate the presence of these contaminants.

7. Vapona®

A total 16 personal air samples were taken for Vapona® and five of these showed levels from 0.04 to 0.88 mg/M^3. The OSHA standard and ACGIH criteria for Vapona® is 1.0 mg/M^3 and therefore these levels did not indicate a health hazard during the survey period (refer to Table V).

8. Azodrin®

A total of 30 personal air samples and 30 area type air samples were taken for Azodrin®. Each of these samples showed nondetectable levels. The wipe samples taken for Azodrin® did, however, indicate the presence of this contaminant. This was found on the Azodrin® drummer's neck, forehead, and chin and the same areas of the Azodrin® drummer's assistant (refer to Table VI). Again, there is no standard or criteria for such exposures although it does indicate the need for good personal protection, as well as personal hygiene after this type of activity.

9. Engineering Controls

Due to the various closed chemical systems used by Shell at the Denver facility it was determined that the majority of potential exposures were reduced because of these types of systems.

The exhaust ventilation systems used in the buildings evaluated all operated at or above the design specifications. That is, the following are the face velocity results received at each of the drumming/bottle filling stations:

a. Building 471 - Vapona®: 100-125 feet per minute (fpm) at the entrance (west side) of the filling hood and 100-125 fpm at the exit or east side of the filling hood.

b. Building 514 - Azodrin®: 175-200 fpm at the drumming hood in the southwest room.

c. Building 515 - Nudrin®: 225-250 fpm with and without drums inside the chamber.

Other ventilation measurements were taken at the various elephant trunk type ventilation locations in each of the buildings and these ranged from 800-1000 fpm. The various sampling boxes in each of the buildings have face velocities from 200-700 fpm.

10. Personal Protective Equipment

The basic personal protective equipment worn by the employees included impervious boots, hard hats, safety glasses, and coveralls. This was sufficient for normal work activities in the various operations evaluated. However, based on the wipe results, it was determined that during the drum filling operations that all the employees, especially those workers directly involved in drum filling, were not wearing the additional clothing that should have been worn. This included impervious aprons, gloves, and face shields.

B. Medical

1. Cholinesterase Testing

a. Current Status

The method the Company was using to determine cholinesterase activity (Ellman Colorimetric Method) is given in Appendix B. This is a whole blood method depending on the plasma and, to a lesser extent, the red cell cholinesterase activity. The frequency of testing by major job groups and jobs within groups is given in Appendix C. The Company preferred this method as it was readily run at the plant and reflected depressions due to both organo-phosphorous compounds (red cell cholinesterase) and carbamates (plasma cholinesterase). Although the Company nurse is glad to tell workers of their individual results, policy dictates that only those with clinically significant depressions of their cholinesterase be notified. Experience has shown very few such depressions over the years.

The Ellman Method gives relative results. Although the Appendix to Appendix B gives a procedure for obtaining results in International Units, the Company has relied on using the average of the day's determinations as a basis for correcting the data for the day-to-day variation in the test. This allowed a ready comparison with previous data. In this report the corrected results will be referred to as Shell Units (S.U.). The correction factor was found by dividing 81 by the day's average, and then multiplying each individual's result by that factor.

NIOSH[3] recommends use of red cell cholinesterase as being quite stable. Plasma cholinesterase inhibition readily reverses both in the individual and in the blood sample waiting to be analyzed. However, red cell cholinesterase is not a particularly good indicator of carbamate activity. Since the Company runs the samples on site quite promptly, specimen stability should not be a serious problem. Although the Company did not routinely compare individuals to their own baselines, as analyzed later in this report the screening levels utilized appear adequate. Under the circumstances of past use at this plant, the Ellman method appears reasonable.

b. Low Cholinesterase

Over the one year, eleven month period there were only seven cholinesterase determinations in which the raw value was less than 70% of the individual's raw baseline. When converted to Shell Units, only four were below the 0.55 suggested by the Shell laboratory method as requiring follow-up; three also being below 70% of their baseline in Shell units (the level at which NIOSH recommends follow-up investigation[3]). None were below 60% of their baseline. Values below 60% would cause medical concern; those below 70% would indicate the need for follow-up. Excessively low cholinesterases were not found.

c. Standardization Method - Overall Analysis

Table VII gives group means for base cholinesterase (S.U.), raw data, adjusted data (S.U.), percent base and correction factor (adjusted data/raw data). Table VII-A gives an analysis of variance for this data, Table VII-B gives confidence limits, and Table VII-C gives correlation coefficients. The difference in mean base was not significantly different between the groups, however there were statistically significant differences in the other means (Table VII-A). In no case was there a statistically significant difference between any one group and the remainder of the groups (Table VII-B). The correlation coefficients (Table VII-C) were then used to suggest where the significance might lie.

The positive correlations between baseline and raw data and between baseline and adjusted data are expected. If the differences in baseline were adequately corrected by the correction method used there should be no correlation between baseline and % baseline and between baseline and correction factor. Table VII-C shows a significant negative correlation for the latter and a weak negative correlation (not statistically significant) for the former. The strong negative correlation between the raw data and the correction factor is expected. Although a positive correlation between the raw data and the

adjusted data is expected, it should not be so strong. Also the negative correlation between adjusted data and correction factor should be less strong.

Tables VIII, VIII-A, VIII-B, and VIII-C repeat the information in Tables VII through VII-C correcting for the differences in mean baseline between groups. Table VIII-A shows there are still statistically significant differences between group means. Table VIII-B shows that the Purchasing workers show a significantly lower raw data mean than the rest of the groups and a significantly higher correction factor (explaining why the adjusted data and % base are not significantly different from the rest). However, Table VIII-C shows that the anticipated correlations, or lack thereof, have been achieved. Thus it appears that the method of adjustment used obscured a statistically significantly lower mean cholinesterase level among workers in the Purchasing Department (undoubtably stock handlers or warehousemen rather than desk workers). Also using an arbitrary figure of 81 for correction purposes gave a poorer correction than using the mean base for the day would have done.

d. Standardization Method - Day-by-Day Analysis

Looking at the spread of individual correction factors calculated from the recorded raw and adjusted data for each individual proved a very reliable method of checking for consistency of the day's results. Total "reliable" determinations for any one day ranged from 1 to 46. On several occasions it was evident that two batches with significantly different correction factors were involved. One case was found where there were two batches with correction factors sufficiently close to cause an overlap. There were also a few cases where there were many determinations done during the day with slight inconsistencies at the very largest values suggesting two batches with nearly identical correction factors. It also became apparent that the rounding procedures used in the calculations changed during this study period.

Examination of the 1980 months studied showed that besides some relatively large correction factors, there were a number of days with relatively few tests and there was one day in which the correction factor from the previous day was inappropriately used.

Table IX correlates the mean raw data with the proportion of workers with a high, medium, or low frequency of cholinesterase determinations. It is assumed this should be a reasonable measure of anticipated exposure. Each day was corrected to a mean base of 81.316 to eliminate that variable. For the total days studied there was a statistically significantly positive correlation between proportion of high frequency workers and the mean of raw data, and statistically significant negative correlation between the proportion of medium frequency workers and the raw data. When only those days where there were 20 or more tests done were examined there were no correlations. When only those days where there were less than 15 tests done (excluding days with only one or two tests) were examined the negative correlation between proportion of medium frequency workers and raw data became stronger.

From this it appears that there most likely was a slight depression of cholinesterase in the medium frequency group which affected the adjustment process, most noticeably when only small numbers of tests were run. The tendency to run the smaller departments in batches could explain why the Purchasing Department workers showed a statistically significantly larger correction factor when corrected for mean base than other groups, allowing masking of differences in other means.

The switch to a cholinesterase determination method using external standards should eliminate the problem of properly adjusting the raw data. To correlate the new data with past data the mean base for the past data could be calculated for several days in which at least twenty tests are run. This figure could be related to the mean data using the new method.

2. Other Laboratory Work

Laboratory tests included a complete blood count (CBC), including red cell indices, and differential, and the following chemistries: glucose, BUN (blood urea nitrogen), creatinine, uric acid, total protein, albumin, globulin, A/G ratio (albumen/globulin ratio), calcium, phosphate, cholesterol, triglycerides, alkaline phosphatase, SGOT (serum glutamic-oxaloacetic transaminase), SGPT (serum glutamic-pyruvic transaminase), LDH (lactate dehydrogenases), total bilirubin, direct bilirubin, GGTP (gamma glutamyl transpepsidase). Not all chemistries were run every year tests were run. This decrease in total tests is noted in Table X-A.

Laboratory "normals" are determined so that 95% of healthy people will test within the normal range. Thus 5% of healthy people will have "abnormal" results. With this built-in source of "abnormal" results, the small numbers involved, and the fact that individual workers varied in the number of tests they had run, it was felt that only those instances where there were 10% or more abnormal results warranted more careful study.

The CBC and differential results are given by study group in Table X-B and the chemistries in Table X-A. Eleven percent (11%) of the white blood counts (WBC) were below normal, and 17% and 37% of the mean corpuscular volumes (MCV) and mean corpuscular hemoglobins (MCH) respectively were above normal. On differential 11% of results for the Engineering and Safety workers showed less monocytes than expected. Twenty-five percent (25%) of the globulins were low resulting in 15% of the A/G ratios being elevated. Twenty percent (20%) of the phosphates and 88% of the direct bilirubins were also low. High values constituted 20% of the triglycerides, 10% of the SGPTs, and 25% of the GGTPs. Additionally, 11% of the creatinine levels for Engineering and Safety workers were elevated, and 14% of the uric acid levels for Engineering and Safety workers and 11% for Maintenance workers were elevated.

The low monocytes on differential count and the low direct bilirubins were not further studied because no clinical significance could be attached to any statistical relationships which might have been found. As it is not that unusual to fail to find monocytes on the

standard differential count, reliable monocyte counts require counting many more than the usual 100 cells with allowances made for biases introduced by the technique used to make the blood smear in which the cells are counted[4]. Direct bilirubins were not further studied both because the number reported were too small to make comparisons meaningful and because no clinical significance could be assigned to a low direct bilirubin when the total bilirubin was normal.

For the other tests with at least one group or the total showing 10% or more abnormals, or the distribution of results gave a statistically significant X^2, the results were weighted so that each individual's results totaled to one (1). Thus if an individual had only one test, it counted for 1. If the individual had 5 tests, each one counted only 1/5th. Possibly 1/5th would be below normal, 3/5th would be normal and 1/5th would be above normal for a total of 5/5th--or 1. When weighted results were used there were no statistically significant differences between groups, although before weighting the WBCs, MCVs, BUNs, uric acids, globulins, phosphates, and SGPTs showed statistically significant differences. (Chi-squares were, respectively, 30.105 (8 d.f.), 20.993 (8 d.f.), 11.428 (4 d.f., 1 sided), 13.547 (4 d.f., 1 sided), 11.548 (4 d.f., 1 sided), 18.063 (8 d.f.), 13.633 (4 d.f., 1 sided), 9.743 (4 d.f., 1 sided). NOTE: Weighted results are available as a supplement (Tables 1-12) which can be requested from the National Technical Information Service (NTIS).

With no significant differences between groups, it is unlikely that specific work exposures would account for any general increases or decreases in laboratory findings. The decreased white blood counts (WBC), decreased globulins and increased A/G ratios might suggest an increased suceptibility to infection as the white cells fight germs and the antibodies are contained in the globulin. However no such tendency was noted during employee interviews. The increases in mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) probably represent an adaption to the slightly decreased oxygen content of air at Denver's elevation. The elevated triglycerides probably reflect the national problem of too much saturated fat in the diet, too much body fat, and not enough exercise. The significance of the decreased phosphate levels is not immediately apparent, but may reflect the fact that serum phosphate level varies by time of day and by the nature of recent meals (a heavy carbohydrate meal tends to decrease serum phosphate)[5]. The serum glutamic-pyruvic transaminase (SGPT) and gamma glutamyl transpepsidase (GGTP) levels both suggest some slight liver toxicity. Without any significant differences between groups one might suspect that alcoholic intake was a significant factor.

3. Individual Interviews

a. Overall Assessment of Follow-Up

Follow-up appeared generally to be good. The two workers with the most cholinesterase determinations had obtained more than required by their work exposures for personal interest. Laboratory results taken in conjunction with the periodic physical examinations were discussed

with each worker individually by the plant physician. For findings deemed to require follow-up the worker was given appropriate reports and counseled to see his own physician. Not all did. Regarding discussion of specific tests, it seemed that a worker's failure to mention it in response to a more general question was more likely to be due to his having forgotten than to it not having been done.

b. Low Cholinesterases Prior to 1979

Twelve (12) of the 43 interviewed had had a total of 15 episodes of low cholinesterase determinations prior to 1979. Follow-up varied from a repeat determination which proved within the acceptable range to removal from that job for a period of time. Six (6) episodes involved persons in operations (two with Vapona® specifically mentioned). Two episodes involved pipefitters, one a shipper, one a laboratory technician, two a process manager, one Phosdrin® drumming, one a Phosdrin® spill, and one a Vapona® trailer clean-out.

c. Low Cholinesterases 1979 to 1980

Four (4) operators, two laboratory technicians, and one pipefitter were interviewed because they had shown a low cholinesterase during the study period. This represents all the low cholinesterases found using any unadjusted value of less than 70% of the unadjusted base as the selection criteria. Of these seven (7), four (4) were lower than the 0.55 S.U. specified by the company as requiring follow-up. (None were below 0.40 S.U. requiring restriction.) Of the four, two remembered being retested with the repeat test in the acceptable range. The records confirmed this. Two, however, did not remember being recalled for a retest, nor did the record show a retest. In both cases the next subsequent test was within the acceptable range.

Of the seven with low cholinesterases, the pipefitter's low value involved only the unadjusted value so probably represented laboratory variation rather than a true depression of cholinesterase. Both laboratory technicians identified that they had been working with cholinesterase inhibitors at the time, one specifying Azodrin®. Of the four in Operations, three indicated that they were working with Azodrin® at the time and the other with Nudrin®.

d. Other Health Complaints

Although there were cases of high blood pressure, arthritis, allergies, and a variety of other health complaints, 17 of the 43 interviewed had no health complaints which could especially be considered work related. Eight (8) of the 21 workers in operations were included in this group.

Three (3) workers in operations and three others indicated that they had skin and/or upper respiratory irritative or allergic symptoms to specific exposures. The substances were: Bladex®, rubber gloves, fiberous glass (at first), "Monochlor", "MMCAA" (an Azodrin® intermediate), Pydrin®. One worker in operations and one other had medical conditions which were sometimes aggravated by exposures in the plant. Two workers in operations and one other had hearing losses (one definitely related to a high pressure air line accident). Two

workers in operations had been overexposed to chlorine in the past, but gave no particular persistent problems due to the episode. Two workers mentioned headaches and fatigue from solvent exposures, one also noting a gradual change in mood of his fellow workers (to grouchiness) when working with Nudrin®. One worker had been a part of the DBCP study and was found to be sterile although he had been fertile in the past. Three workers had diverse medical problems which could possibly be related to work, but the relationship is unclear. The mortality study should shed some light on the situation if there is a significant problem in these areas.

The opinion was expressed that replacement operators for equipment cleanout were not given proper training for the job. Although this study cannot establish the soundness of this opinion, certainly all workers, including replacement operators, need to be properly trained to avoid running into problems with exposure to the chemicals found in this plant.

VII. CONCLUSIONS

It is felt by the environmental and medical officers that those employees evaluated at Shell's Denver facility are not and were not being overexposed on a continuous basis to the contaminants evaluated in this study. Occasionally an employee might through accidental or maintenance operations be exposed for a short period; however, under normal conditions it is not felt by NIOSH that the employees are exposed. Specially, the following conclusions were determined:

A. Environmental

It was concluded, based on all those environmental air samples taken during NIOSH's survey periods, that no employee was exposed to airborne levels that exceeded established criteria and/or standards. It was felt, however, that those employees involved in the Vapona®, Nudrin®, and Azodrin® drum filling processes were exposed via skin absorption to these materials. This conclusion is based on the wipe samples taken. Therefore, it is felt that the recommendations made in the next section should be incorporated into Shell's present health protection policies and procedures program.

B. Medical

The cholinesterase test program evaluated indicated that there were no medically significant cholinesterase depressions although over the 1-11/12 years studied there were four cholinesterases which should have been followed up. The method of adjusting the raw data to Shell Units worked acceptably well when at least 20 tests were run but was somewhat less satisfactory when only a few tests were run. It would have been better to correct to the mean base for the individuals being run for the day rather than the standard 81. The switch in method to one utilizing an external standard is a very satisfactory correction for all the problems.

Due to the small number of determinations requiring follow-up and the desire to maintain confidentially, the current policy of only notifying workers requiring follow-up appears to be the most practical method of notification as long as individuals are able to obtain their own results without undue difficulty.

Regarding the other laboratory work evaluated, it is concluded that although there are some values which appear to lie outside of normal limits on some basis other than the method of establishing laboratory normals, they do not appear to relate to workplace exposure on any general basis.

Based on employee interviews, it was concluded that for the most part Shell's follow-up program has been good. There is a question of how well two out of the four low cholinesterase levels were followed up. Further, although the company criterion of follow-up of values below 0.55 S.U. appears to give results comparable to the NIOSH recommendation[1] of below 70% of baseline, there could be some discrepancies in actual use. Specific complaints were scattered and not surprising considering the chemicals to be found in this plant. They emphasize the need for continued attention to properly functioning engineering controls, good work practices, and worker education.

VIII. RECOMMENDATIONS

In view of the NIOSH's environmental and medical study, the following recommendations are made to ameliorate potential health hazards and to provide a better work environment for the employees covered by this determination.

A. Environmental

Whenever possible, engineering controls are the preferred method for decreasing potential exposures to toxic substances for the protection of the employees' health. However, given the results found and the conditions and/or processes in which these levels were determined, it is almost impossible to engineer such concerns out of the operation. Therefore, the following environmental recommendations are made:

1. When drum filling is being performed, all objects such as empty drums should be kept away from the filling area itself. This will reduce and/or eliminate impedance for the necessary make-up air which is required to effectively operate the exhaust ventilation system used in the drum fill processes.

2. Based on the contaminants found on the skin in a portion of the employees who work in the drum filling operations, it is recommended that all employees directly involved with this operation wear all the personal protective gear provided. This would include impervious gloves, aprons, and boots, as well as face shields.

3. All employees should observe strict personal hygiene, and based on those results found on the wipe samples, those employees who perform drum filling should be given time to shower before going to their next assignment or home. Drinking, eating, and smoking should not be done outside the designated areas and only after washing of hands.

4. All employees and supervisors who work with drum filling should maintain good work practices in order to keep their exposures to a minimum.

5. Based on the results found on the lunch tables and control room, it is recommended that these surfaces be cleaned at the end of each work shift. This procedure would also assist in reducing or eliminating skin exposures.

6. Management is encouraged to continue development and refinement of its health and safety programs, particularly an employee educational awareness programs. This will help in developing better understanding and alleviation of fears and/or uncertainty about health and safety matters, especially those about what is the "stuff:, what can it do, what isn't known about it, and what is being done to protect "our" health.

7. A strict routine maintenance program should be continuously reviewed and revised as experience is gathered. Employee input is critical because they become more familiar with daily operations than do the engineers that design and upgrade processes.

B. Medical

1. The cholinesterases should be run using a method with an objective standard. The Company reports that they are now doing so.

2. To allow comparison of current cholinesterase values with values obtained in the past, a conversion factor should be calculated to relate the objective units now being obtained with the adjusted values (Shell Units) previously obtained. This should be done by calculating the average baseline value for all the workers tested on a given day (when at least twenty [20] are included in the run) and relating that to the average of the day's results in the new units. Doing this for several days should give a reliable conversion factor.

3. To assure adequate follow-up of low cholinesterases, notification of workers requiring follow-up should be documented in a way that will call attention to those workers who do not come back for the retests.

4. For practicality a set figure can continue to be used to spark follow-up procedures. However, individuals whose baselines are high enough to allow them to drop below 70% of their baseline without triggering follow-up procedures should be identified so that the 70% - 60% criteria recommended by NIOSH[1] can be used in their individual cases.

5. By use of more powerful computers and a considerably more detailed job breakdown it would be possible to, over time, identify more subtle health problems relating to specific jobs if they should exist. The corporate medical department indicates that they are developing such a system.

IX. REFERENCES

1. Rubenstein, E. & Federman, D.D. (Eds.), Scientific American Medicine. Scientific American, Inc., New York. 1981. Section 5, Chapter VII, p. 6.

2. Henry, J.B. (Ed.), Todd-Sanford-Davidsohn - Clinical Diagnosis and Management by Laboratory Methods, 16th Edition. W.B. Saunders Company, Philadelphia. 1979. p. 902.

3. Criteria for a Recommended Standard...Occupational Exposure During the Manufacture and Formulation of Pesticides. DHEW (NIOSH) Publication No. 78-174, 1978.

4. op.cit., Henry, J.B., p. 1047.

5. Ibid., p. 279.

ADDITIONAL BIBLIOGRAPHY

Frank Patty (editor), Industrial Hygiene and Toxicology, second edition, Interscience Publishers, 1967, Vol. II.

Hamilton and Hardy, Industrial Toxicology, third edition, Publishing Service Group, Inc., 1974.

"Threshold Limit Values for Chemical Substances in Workman Air", America Conference of Governmental Industrial Hygienists, 1981.

Encyclopedia of Occupational Health and Safety, International Labor Office, McGraw-Hill Book Company, New York.

Occupational Diseases, A Guide to Their Recognition, U.S. Department of Health, Education, and Welfare, Public Health Service Publication (NIOSH) No. 77-181.

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XI. DISTRIBUTION AND AVAILABILITY

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Information Resources and Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days the report will be available through the National Technical Information Service (NTIS), Springfield, Virginia. Information regarding its availability through NTIS can be obtained from NIOSH, Publications Office, at the Cincinnati address.

Copies of this report have been sent to:

1. Shell Chemical Company.
2. Oil, Chemical and Atomic Workers International Union.
3. Oil, Chemical and Atomic Workers Local Union 2-477.
4. U.S. Department of Labor/OSHA - Region VIII.
5. NIOSH - Region VIII.
6. Colorado State Department of Health.
7. State Designated Agency.

For the purpose of informing the affected employees, a copy of this report shall be posted in a prominent place accessible to the employees for a period of 30 calendar days.

TABLE I

Characterization of Study Group

Shell Chemical Company
Denver, Colorado

Group	Identification Status*	Pay Account Numbers	Number on Current List	Cholinesterase Studies				Laboratory Work	Questionnaires
				Total Cases	Frequency Group High	Medium	Low		
Operations#	With ID	1000	113	109	18	89	2	98	21
	Without ID			(32)**	(2)	(18)	(12)	(2)	
Laboratory#	With ID	1300,1400,1500 1600	32	28	8	12	8	22	5
	Without ID			(16)	(0)	(5)	(11)	(1)	
Engineering and Safety#	With ID	5500,5700,5800	24	24	10	6	8	22	6
	Without ID			(6)	(1)	(3)	(2)	(3)	
Pipefitters	With ID	2700	16	16	11	5	0	14	3
	Without ID			(1)	(1)	(0)	(0)	(0)	
Instrumentmen and Electricians#	With ID	1900,2200	10	9	5	4	0	9	3
	Without ID			(8)	(1)	(5)	(2)	(1)	
Other Maintenance#	With ID	2600,2800,2900 3000,3200	11	9	6	3	0	8	1
	Without ID			(2)	(0)	(2)	(0)	(1)	
Powerhouse Operators#	With ID	2000	17	9	0	0	9	6	1
	Without ID			(1)	(0)	(0)	(1)	(0)	
Purchasing#	With ID	600	15	12	0	4	8	8	2
	Without ID			(0)	(0)	(0)	(0)	(1)	
Shipping#	With ID	900	4	4	1	1	2	3	1
	Without ID			(0)	(0)	(0)	(0)	(0)	
Other#	With ID	100,300,400	18	1	0	0	1	3	0
	Without ID			(1)	(0)	(0)	(1)	(0)	
Total	With ID		260	221	59	124	38	193	43
	Without ID			(67)	(5)	(33)	(29)	(9)	

\# Partial breakdown of job titles given in Table IA.
* With Identifier, i.e., name.
** Because 1-11/12 years of cholinesterase results were studied, and it was not possible to link unidentified individual's results for the two years, the actual number of individuals involved is only slightly over one half this figure.

TABLE I-A

Partial Breakdown of Study Groups

Shell Chemical Company
Denver, Colorado

Group	Total in Group With ID	List of Jobs with Few Representatives Included & Number	
Operations	113	Shift Foremen	7
		Shift Supervisors	5
		Process Managers	2
Laboratory	32	Engineers	4
		Chemists	2
		Manager	1
Engineering and Safety	24	Maintenance Foremen	9
		Engineers	4
		Engineering Inspectors	3
		Safety Inspectors	2
		Managers	2
		Maintenance Supervisor	1
		Nurse	1
Maintenance			
Pipefitters	16		
Instrumentmen & Electricians	10	Electricians	2
Other Maintenance	11	Machinists	4
		Welders	4
		Painter	1
		Carpenter	1
		Heavy Equipment Operator	1
Others			
Powerhouse Operators	17	Engineer	1
		Foreman	1
		Supervisor	1
Purchasing	15	Stock Handlers	5
		Salvageman	1
		Supervisor	1
Shipping	4	Loading Foremen	2
		Supervisor	1
Other	18	Finance	10
		Employee Relations	6
		Administration	2

TABLE II

Number of Laboratory Tests by Year and Group

Shell Chemical Company
Denver, Colorado

		1974	1975	1976	1977	1978	1979	1980	Total
Total Blood Counts	Number	16	85	54	70	109	163	128	625
Operations		5	41*	32	33	60**	82	72##	325
Laboratory		1	5	5	4	9	19	12	55
Engineering & Safety		1	11	4	8	10	19	11	64
Pipefitters		3	11	4	10	10	11	10	59
Instrumentmen & Electricians		3	3	4	5	7	9	8	39
Other Maintenance		2	4	3	5	5	8	6	33
Powerhouse Operators		0	2	0	1	2	5	2	12
Purchasing		1	4	2	2	4	8	4	25
Shipping		0	2	0	1	1	2	1	7
Other		0	2	0	1	1	0	2	6
Total Chemistries	Number	16	85	56	71	111	163	128	630
Operations		5	41*	33	34	61#	82	72##	328
Laboratory		1	5	5	4	9	19	12	55
Engineering & Safety		1	11	4	8	11	19	11	65
Pipefitters		3	11	4	11	10	11	10	60
Instrumentmen & Electricians		3	3	5	5	7	9	8	40
Other Maintenance		2	4	3	5	5	8	6	33
Powerhouse Operators		0	2	0	1	2	5	2	12
Purchasing		1	4	2	2	4	8	4	25
Shipping		0	2	0	1	1	2	1	7
Other		0	2	0	0	1	0	2	5

* 42 individuals
** 59 individuals - one seen twice in same year
\# 60 individuals - one seen twice in same year
71 individuals - one seen twice in same year

Shell Chemical Company
Denver, Colorado

TABLE III

Summary of Area Air Samples for Sodium Hydroxide (N_aOH)

Sample Date	Job/Area Description	Sample Time (minutes)	N_aOH mg/M^3
11/19/80	Nudrin® - 2nd Floor Reactor	300	0.02
11/19/80	Nudrin® - 2nd Floor Reactor	300	0.02
11/19/80	Nudrin® - 2nd Floor Reactor	300	0.01
EVALUATION CRITERIA		OSHA/NIOSH	2.0 mg/M^3
LIMIT OF DETECTION			0.003 mg

mg/M^3 = milligrams of substance per cubic meter of air
mg = milligrams per filter

TABLE IV

Summary of Wipe Samples for Nudrin®

Sample Date	Job/Area Description	Nudrin®* (ug/sample)
11/20/80	Lunch Room - Building 515	20.0
11/20/80	Lunch Room Table - Building 515	8.3
11/20/80	Control Room	0.77

* = These samples were obtained by wiping the surface areas in the lunch and control rooms.
ug/sample = micrograms per sample - indicates presence of contaminant only which cannot be compared to any criterion or standard.

TABLE V

Summary of Personal Air Samples for Vapona®

Shell Chemical Company
Denver, Colorado

November 1980

Sample Date	Job/Area Description	Sample Time (minutes)	Vapona® mg/M^3
11/18/80	Column Operator	420	ND
11/18/80	Outside Utility	420	ND
11/18/80	Reaction/Substitution	420	0.06
11/18/80	Recovery	420	ND
11/18/80	Centrifuge	420	0.88
11/18/80	Drumming	420	ND
11/18/80	Column	420	ND
11/18/80	Outside Utility	420	ND
11/19/80	Drumming	420	ND
11/19/80	Column	420	0.01
11/19/80	Outside Utility	420	ND
11/19/80	Reaction/Substitution	420	0.04
11/19/80	Centrifuge	420	ND
11/19/80	Column	420	ND
11/19/80	Outside Utility	420	ND
11/19/80	Drumming	420	0.31
EVALUATION CRITERIA		OSHA/ACGIH	1.0 mg/M^3
LIMIT OF DETECTION			0.001 mg/ sample

ND = Nondetectable (below level of analytical detection)
mg/M^3 = milligrams of substance per cubic meter of air

TABLE VI

Summary of Wipe Samples for Azodrin®

Shell Chemical Company
Denver, Colorado

June 1980

Sample Date	Job/Area Description	Azodrin® (ug/sample)
6/25/80	Operator - Building 471	ND
6/25/80	Operator - Building 471	ND
6/25/80	Drummer/Labels	ND
6/25/80	Drummer	1.8*
6/25/80	Spoutman	ND
6/25/80	Lunch Table	ND
6/25/80	Drummer-Assistant	0.3*
6/25/80	Forklift	ND
LIMIT OF DETECTION		0.1 ug

ND = Nondetectable (below level of analytical detection)
ug/sample = micrograms per sample - indicates presence of contaminant only which cannot be compared to any criterion or standard.
* = These samples were obtained by wiping the worker's neck, forehead, and hand areas.

TABLE VII

Group Means of Base Cholinesterase Level, Raw Cholinesterase Level, Adjusted Cholinesterase Level, % of Adjusted Base, and Correction Factor (Adjusted Level/Raw Level)

Shell Chemical Company
Denver, Colorado

	Operations	Laboratory	Engineering & Safety	Pipe-fitters	Instrument-men & Electricians	Other Maintenance	Powerhouse Operators	Purchasing	Shipping	Other	Total
Base Cholinesterase Shell Units (S.U.)											
Number	141	44	30	17	17	11	10	12	4	2	288
Mean	81.76	79.16	82.43	80.76	79.24	82.45	84.80	81.17	79.25	84.50	81.32
Standard Deviation	5.30	5.13	5.56	6.40	3.98	4.55	12.15	8.48	4.99	26.16	6.04
Total Data 1979 & 1980											
Number	1325	409	276	270	166	156	20	57	36	2	2717
Raw Data											
Mean	66.73	64.81	67.39	67.41	64.27	68.65	69.35	62.81	64.53	75.00	66.45
Standard Deviation	8.17	7.61	7.52	8.33	6.50	6.99	10.13	9.74	8.42	28.28	8.05
Adjusted Data, S.U.											
Mean	81.84	79.45	81.95	81.97	79.58	83.04	83.45	77.63	79.56	84.50	81.33
Standard Deviation	8.72	8.65	8.34	8.99	7.61	8.11	10.39	11.26	9.46	26.16	8.77
% Base											
Mean	99.90	100.41	99.29	100.89	101.23	101.85	95.69	100.46	99.84	100	100.19
Standard Deviation	9.37	9.11	8.01	9.96	8.64	8.90	15.24	8.12	9.04	0	9.23
Correction Factor											
Mean	1.230	1.229	1.219	1.220	1.240	1.212	1.208	1.239	1.236	1.142	1.227
Standard Deviation	0.069	0.065	0.060	0.072	0.044	0.063	0.061	0.058	0.055	0.082	0.066

TABLE VII-A

Analysis of Variance of Group Means, Table VII

Shell Chemical Company
Denver, Colorado

	Sum of Squares	Degrees of Freedom	Mean Square	F Ratio
n=288				$F_{.95}(9,278)=1.915$
Base				
Category Means	521.83	9	57.9812	
Within	9952.42	278	35.8001	F = 1.620
Total	10474.25	287		Not Significant
n=2717				$F_{.95}(9,2707)=1.884$
Raw Data				
Category Means	4448.43	9	494.270	F = 7.806
Within	171400.84	2707	63.318	
Total	175849.27	2716		Statistically Significant
Adjusted Data				
Category Means	3966.82	9	440.758	F = 5.825
Within	204818.01	2707	75.662	
Total	208784.84	2716		Statistically Significant
% Base				
Category Means	1505.05	9	167.228	F = 1.967
Within	230084.32	2707	84.996	
Total	231589.37	2716		Statistically Significant
Correction Factor				
Category Means	0.13828	9	0.0153645	F = 3.544
Within	11.73624	2707	0.0043355	
Total	11.87452	2716		Statistically Significant

TABLE VII-B

L Values for Group Means, Table VII - Group vs. Rest

Shell Chemical Company
Denver, Colorado

	Raw Data		Adjusted Data		% Adjusted Base		Correction Factor	
	Group Mean - Rest	L	Group Mean - Rest	L	Group Mean - Rest	L	Group Mean - Rest $\times 10^{-2}$	L $\times 10^{-2}$
Operations	0.55	±3.00	0.99	±3.28	-0.56	±3.47	0.50	±2.48
Laboratory	-2.54	±3.28	-2.21	±3.59	0.26	±3.80	0.20	±2.72
Engineering & Safety	0.33	±3.47	0.69	±3.79	-0.99	±4.02	-0.93	±2.87
Pipefitters	1.07	±3.48	0.71	±3.81	0.78	±4.03	-0.80	±2.88
Instrumentmen & Electricians	-2.32	±3.82	-1.86	±4.17	1.11	±4.42	1.33	±3.16
Other Maintenance	2.33	±3.87	1.81	±4.23	1.18	±4.49	-1.62	±3.20
Powerhouse Operators	2.92	±7.82	2.14	±8.55	-4.53	±9.06	-1.92	±6.47
Purchasing	3.72	±5.18	-3.78	±5.66	0.27	±6.00	1.23	±4.28
Shipping	-1.95	±6.14	-1.80	±6.71	-0.36	±7.11	0.90	±5.08
Other	8.55	±23.20	3.17	±25.36	-0.19	±26.88	8.50	±19.20

No statistically significant differences.

TABLE VII-C

Correlation Coefficients using Group Means

Shell Chemical Company
Denver, Colorado

Mean	Mean Raw Data	Mean Adjusted Data	Mean % Base	Mean Correction Factor
Base Cholinesterase	0.802*	0.801*	-0.559	-0.727*
Raw Data		0.925*	-0.242	-0.958*
Adjusted Data			-0.315	-0.778*
% Base				0.160

TABLE VIII

Group Means Corrected to a Base of 81.316 S.U.

Shell Chemical Company
Denver, Colorado

	Operations	Laboratory	Engineering & Safety	Pipe-fitters	Instrument-men & Electricians	Other Maintenance	Powerhouse Operators	Purchasing	Shipping	Other	Total
Total Data, Corrected Number	1325	409	276	270	166	156	20	57	36	2	2717
Raw Data											
Mean	66.37	66.58	66.48	67.88	65.96	67.71	66.50	62.92	66.21	72.17	66.55
Standard Deviation	8.13	7.82	7.42	8.39	6.67	6.90	9.72	9.76	8.64	27.22	6.70
Adjusted Data, S.U.											
Mean	81.39	81.62	80.84	82.53	81.67	81.89	80.02	77.77	81.63	81.32	81.45
Standard Deviation	8.67	8.88	8.24	9.05	7.81	8.00	9.97	11.28	9.70	25.18	7.24
% Base											
Mean	100.10	100.37	99.41	101.49	100.43	100.71	98.41	95.64	100.39	100	100.16
Standard Deviation	9.37	9.11	8.01	9.96	8.64	8.90	15.24	8.12	9.04	0	9.24
Correction Factor											
Mean	1.225	1.221	1.223	1.198	1.233	1.201	1.223	1.292	1.228	1.127	1.222
Standard Deviation	0.069	0.065	0.060	0.072	0.044	0.063	0.061	0.058	0.055	0.082	0.067

TABLE VIII-A

Analysis of Variance for Corrected Means, Table VIII

Shell Chemical Company
Denver, Colorado

	Sum of Squares	Degrees of Freedom	Mean Square	F Ratio
n=2717				$F_{.95}(9,2707)=1.884$
Raw Data				
Category Means	1601.52	9	177.947	F = 4.006
Within	120240.94	2707	44.419	
Total	121842.46	2716		Statistically Significant
Adjusted Data				
Category Means	1299.03	9	144.337	F = 2.767
Within	141183.96	2707	52.155	
Total	142482.99	2716		Statistically Significant
% Base				
Category Means	1941.97	9	215.775	F = 2.539
Within	230084.69	2707	84.996	
Total	232026.66	2716		Statistically Significant
Correction Factor				
Category Means	0.55925	9	0.0621383	F = 14.335
Within	11.73412	2707	0.0043347	
Total	12.29337	2716		Statistically Significant

TABLE VIII-B

L Values for Group Means Corrected to a Base of 81.316 S.U. - Group vs. Rest

Shell Chemical Company
Denver, Colorado

	Raw Data		Adjusted Data		% Adjusted Base		Correction Factor	
	Group Mean - Rest	L	Group Mean - Rest	L	Group Mean - Rest	L	Group Mean - Rest $\times 10^{-2}$	L $\times 10^{-2}$
Operations	-0.56	±2.51	0.36	±2.72	0.45	±3.47	0.89	±2.48
Laboratory	-0.33	±2.75	0.61	±2.98	0.75	±3.80	0.47	±2.72
Engineering & Safety	-0.44	±2.91	-0.26	±3.15	-0.31	±4.02	0.67	±2.87
Pipefitters	1.11	±2.92	1.62	±3.16	2.00	±4.03	-2.13	±2.88
Instrumentmen & Electricians	-1.02	±3.20	0.67	±3.47	0.82	±4.42	1.74	±3.16
Other Maintenance	0.92	±3.24	0.92	±3.51	1.13	±4.49	-1.79	±3.20
Powerhouse Operators	-0.42	±6.55	-1.16	±7.10	-1.43	±9.06	0.63	±6.47
Purchasing	-4.40*	±4.33	-3.66	±4.70	-4.50	±6.00	8.35*	±4.28
Shipping	-0.74	±5.14	0.62	±5.57	0.77	±7.11	1.22	±5.08
Other	5.88	±19.43	0.28	±21.06	0.34	±26.88	10.05	±19.20

*Statistically significant at a = 0.05.

TABLE VIII-C

Correlation Coefficients using Group Means with Corrected Base

Shell Chemical Company
Denver, Colorado

Mean	Mean Adjusted Data	Mean % Base	Mean Correction Factor
Raw Data	0.572	-0.572	-0.998*
Adjusted Data		1.000*	-0.610
% Base			-0.610

* Correlations where r lies outside the range -0.632 to +0.632 are statistically significant at the 95% confidence level.

TABLE IX

Correlation of Corrected Raw Data Means and Proportion of Workers with Low, Medium, or High Frequency of Cholinesterase Determinations

Shell Chemical Company
Denver, Colorado

		Mean	Standard Deviation	Correlation Coefficient
All days studied	n=48			
Raw Data, Corrected to a Mean Base of 81.316		65.95	4.29	
Proportion:				
Low Frequency of Tests*		0.051	0.081	0.146
Medium Frequency*		0.554	0.167	-0.391#
High Frequency*		0.396	0.182	0.293#

Correlations outside the range -0.286 to +0.286 are statistically significant at the 95% confidence level.

Days with 20 or more tests	n=31			
Raw Data, Corrected		66.97	3.69	
Proportion:				
Low Frequency		0.054	0.065	0.064
Medium Frequency		0.539	0.126	-0.235
High Frequency		0.408	0.126	0.201

Non-significance range -0.356 to +0.356.

Days with less than 15 test	n=11			
Raw Data, Corrected		64.10	5.77	
Proportion:				
Low Frequency		0.065	0.127	0.226
Medium Frequency		0.653	0.173	-0.700#
High Frequency		0.283	0.208	0.443

Non-significance range -0.602 to +0.602.

*Low Frequency is less than 3 visits per year.
Medium Frequency is 3 to less than 7.5 visits per year.
High Frequency is 7.5 or more visits per year.

#Statistically significant at a = 0.05.

TABLE X-A

Blood Chemistry Results by Group, 1974-1980

Shell Chemical Company
Denver, Colorado

Group	Operations						Laboratory						Engineering and Safety						Maintenance						Other						Total					
Total Individuals	(100)						(23)						(25)						(33)						(20)						(201)					
Total Tests	328						55						65						133						49						630					
	Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal	
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
Glucose	12	4	308	94	8	2	1	2	51	93	3	5	0	0	64	98	1	2	4	3	123	92	6	5	0	0	46	94	3	6	17	3	592	94	21	3
BUN* **	9	3	319	97	0	0	5	9	50	91	0	0	0	0	62 **	97	2	3	7	5	126	95	0	0	0	0	49	100	0	0	21	3	606 **	96	2	#
Creatinine**	2	1	313 **	97	9	3	0	0	55	100	0	0	0	0	58	89	7	11	0	0	129	97	4	3	1	2	46 **	96	1	2	3	#	601 **	96	21	3
Uric Acid	0	0	300	91	28	9	0	0	55	100	0	0	0	0	56	86	9	14	0	0	118	89	15	11	0	0	48	98	1	2	0	0	577	92	53	8
Total Protein	0	0	322	98	6	2	0	0	55	100	0	0	0	0	65	100	0	0	0	0	133	100	0	0	0	0	49	100	0	0	0	0	624	99	6	1
Albumen	1	#	324	99	3	1	0	0	55	100	0	0	0	0	65	100	0	0	1	1	132	99	0	0	0	0	49	100	0	0	2	#	625	99	3	#
Globulin**	65	20	233 **	73	21	7	12	22	38	69	5	9	22	34	37 **	58	5	8	37	28	90 **	68	5	4	19	40	28 **	60	0	0	155	25	426 **	69	36	6
A/G Ratio* **	0	0	275 **	86	44	14	0	0	51	93	4	7	0	0	53 **	83	11	17	0	0	112 **	85	20	15	0	0	34 **	72	13	28	0	0	525 **	85	92	15
Calcium**	2	1	322 **	99	2	1	0	0	55	100	0	0	1	2	64	98	0	0	0	0	132	99	1	1	0	0	49	100	0	0	3	#	622 **	99	3	#
Phosphate**	67	20	261	80	0	0	11	20	44	80	0	0	3	5	61 **	95	0	0	36	27	97	73	0	0	9	18	40	82	0	0	126	20	503 **	80	0	0
Cholesterol	7	2	316	96	5	2	0	0	55	100	0	0	0	0	62	95	3	5	0	0	129	97	4	3	0	0	47	96	2	4	7	1	609	97	14	2
Triglycerides**	0	0	178 **	79	48	21	0	0	33 **	87	5	13	0	0	31 **	74	11	26	0	0	61 **	81	14	19	0	0	27 **	82	6	18	0	0	330 **	80	84	20
Alkaline Phosphatase	3	1	319	97	6	2	0	0	53	96	2	4	0	0	65	100	0	0	0	0	128	96	5	4	0	0	48	98	1	2	3	#	613	97	14	2

TABLE X-A (Continued)

Blood Chemistry Results by Group, 1974-1980

Shell Chemical Company
Denver, Colorado

Group	Operations			Laboratory			Engineering and Safety			Maintenance			Other			Total		
Total Individuals	(100)			(23)			(25)			(33)			(20)			(201)		
Total Tests	328			55			65			133			49			630		
	Below Normal	Normal Range	Above Normal	Below Normal	Normal Range	Above Normal	Below Normal	Normal Range	Above Normal	Below Normal	Normal Range	Above Normal	Below Normal	Normal Range	Above Normal	Below Normal	Normal Range	Above Normal
	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %	# %
SGOT* **	0 0	312 ** 96	14 4	0 0	55 100	0 0	0 0	61 ** 95	3 5	0 0	126 95	7 5	0 0	46 ** 96	2 4	0 0	600 ** 96	26 4
SGPT* **	1 #	213 ** 88	27 11	2 5	33 ** 87	3 8	0 0	40 ** 80	10 20	2 2	82 ** 92	5 6	0 0	33 ** 97	1 3	5 1	401 ** 89	46 10
LDH*	0 0	307 94	21 6	0 0	50 91	5 9	0 0	61 94	4 6	0 0	124 93	9 7	0 0	46 94	3 6	0 0	591 94	39 6
Total Bilirubin	0 0	325 99	3 1	0 0	55 100	0 0	0 0	64 98	1 2	0 0	133 100	0 0	0 0	47 96	2 4	0 0	624 99	6 1
Direct Bilirubin**	9 100	0 ** 0	0 0	1 100	0 ** 0	0 0	2 100	0 ** 0	0 0	6 100	0 ** 0	0 0	3 50	3 ** 50	0 0	21 88	3 ** 12	0 0
GGTP* **	2 7	19 ** 68	7 25	1 100	0 ** 0	0 0	0 0	13 ** 76	4 24	1 5	13 ** 65	6 30	0 0	1 ** 100	0 0	4 6	46 ** 69	17 25

* Respectively: Blood Urea Nitrogen, Albumin/Globulin Ratio, Serum Glutamic-Oxaloacetic Transaminase, Serum Glutamic-Pyruvic Transaminase, Lactate Dehydroenase, Gamma Glutamyl Transpepsidase.

**Note reduced number of total tests.

Less than 0.5%.

TABLE X-B

Complete Blood Count (CBC) Results by Group, 1974-1980

Shell Chemical Company
Denver, Colorado

Group	Operations						Laboratory						Engineering and Safety						Maintenance						Other						Total					
Total Individuals	(100)						(23)						(25)						(33)						(21)						(202)					
Total Tests	325						55						64						131						50						625					
	Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal		Below Normal		Normal Range		Above Normal	
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
White Blood Count (WBC)	28	9	291	90	6	2	5	9	50	91	0	0	19	30	44	69	1	2	13	10	113	86	5	4	4	8	46	92	0	0	69	11	544	87	12	2
Red Blood Count (RBC)	18	6	302	93	5	2	2	4	53	96	0	0	2	3	62	97	0	0	9	7	121	92	1	1	1	2	49	98	0	0	32	5	587	94	6	1
Hemoglobin (Hgb)	12	4	301	93	12	4	4	7	51	93	0	0	1	2	62	97	1	2	2	2	128	98	1	1	0	0	50	100	0	0	19	3	592	95	14	2
Hematocrit (Hct)*	22	7	284	87	19	6	4	7	51	93	0	0	3	5	61	95	0	0	10	8	115	88	6	5	1	2	48	96	1	2	40	6	559	89	26	4
Mean Corpuscular Volume (MCV)	17	5	250	77	58	18	3	5	46	84	6	11	1	2	53	83	10	16	0	0	100	76	31	24	0	0	47	94	3	6	21	3	496	79	108	17
Mean Corpuscular Hemoglobin (MCH)	16	5	181	56	128	39	4	7	34	62	17	31	1	2	43	67	20	31	3	2	76	58	52	40	0	0	38	76	12	24	24	4	372	60	229	37
Mean Corpuscular Hemoglobin Concentration (MCHC)	5	2	297	91	23	7	1	2	48	87	6	11	2	3	57	89	5	8	0	0	123	94	8	6	1	2	48	96	1	2	9	1	573	92	43	7
Total Differential Counts Done	325						55						64						130						49						623					
Total Neutrophils	3	1	312	96	10	3	0	0	53	96	2	4	0	0	64	100	0	0	0	0	125	96	5	4	0	0	48	98	1	2	3	*	602	97	18	3
Total Lymphocytes	3	1	322	99	0	0	0	0	55	100	0	0	4	6	60	94	0	0	1	1	128	98	1	1	1	2	47	96	1	2	9	1	612	98	2	*
Total Monocytes	10	3	315	97	0	0	2	4	53	96	0	0	7	11	57	89	0	0	5	4	125	96	0	0	0	0	49	100	0	0	24	4	599	96	0	0
Atypical WBC's	--		323	99	2	1	--		55	100	0	0	--		64	100	0	0	--		129	99	1	1	--		49	100	0	0	--		620	100	3	*
Basophilia	--		316	97	9	3	--		53	96	2	4	--		62	97	2	3	--		123	95	7	5	--		46	94	3	6	--		600	96	23	4

APPENDIX A

SHELL DEVELOPMENT COMPANY
ANALYTICAL METHOD FOR NUDRIN®

This method called for sampling to be done on packed alumina tubes and glass fiber filters; however, the samples for this analysis were received on type AA mixed cellulose ester filters and Chromosorb 102 tubes. This departure from the method necessitated the development of a different desorption solvent for the samples, as methanol is not suitable for desorbing AA filters. A 50 percent (v/v) mixture of methanol and water was used for desorption of the AA filters and Chromosorb tubes. A multilevel desorption study performed under the sample analytical conditions as were used for the sample analysis indicated a desorption efficiency of greater than 85 percent for Chromosorb 102 and greater than 90 percent for AA filters.

The samples were prepared for analysis by desorbing the filters or tube contents (both sections) in 2 mL of 50 percent (v/v) methanol/water for three hours with two two-minute periods of sonication. The resulting solutions were separated from the sampling matrix and injected into a high pressure liquid chromatography system under the following conditions:

Solvent Delivery	=	Spectra Physics SP-8700
Autosampler	=	Water Associates WISP
Integration	=	Spectra Physics SP-4100
Detector	=	Varian Vari-Chrom
Mobile Phase	=	85% water, 15% actonitrile
Elution	=	isocratic
Flow Rate	=	1.5 mL/minute
Detector Wavelength	=	233 mm
Range	=	Supelco C_{18} 250 x 4.6 mm 5 micron

Standards were prepared by placing varying amounts of solutions of known concentrations of analytes on either Millipore type AA filters or SKC Chromosorb 102 tubes, as appropriate, and allowing to air dry overnight. Each standard was then desorbed simultaneously with the samples and under identical conditions, and analyzed with the samples. The level of all standards used were comparable to those used in the aforementioned desorption study.

The wipe samples for Nudrin® and MSAO were analyzed in the following manner:

The samples were analyzed for Nudrin® (methomyl) and MSAO (methylthioacelodoxime) by a modification of an HPLC method supplied with the samples and developed by the Shell Development Company, Modesto, California.

The samples were prepared for analysis by desorbing the wipe pads in 2 mL of methanol for eight hours with 15 minutes of sonication. Each solution was then filtered through a 0.5 uM Teflon filter before injection into a high pressure liquid chromatography system under the following conditions:

Solvent Delivery	=	Spectra Physics SP-8700
Autosampler	=	Waters Associates WISP
Integration	=	Spectra Physics SP-4100
Detector	=	Perkin-Elmer LC 75
Mobile Phase	=	85% water, 15% actonitrile
Elution	=	isocratic
Flow Rate	=	1.5 mL/minute
Detector Wavelength	=	233 nm at 0.02 AUFS
Column	=	Supelco C_{18} 250 x 4.6 mm 5 micron

The results were quantitated by comparing the peak areas of the samples with peak areas generated by solutions of known concentrations of the analytes. The bulk listed as sample number 80-13504 (Nudrin®-final product) was used in the standard solutions. An HPLC analysis of this product showed its purity to be greater than 99%.

APPENDIX B

SHELL CHEMICAL COMPANY
MANUFACTURING AND DISTRIBUTION
DENVER PLANT

JH-S-83/74

Determination of CHOLINESTERASE ACTIVITY IN BLOOD Ellman Colorimetric Method

SCOPE

This method describes a procedure for the determination of cholinesterase activity in whole human blood. It is designed for routine surveillance and the results are relative. If an absolute value, expressed in enzyme activity units is desired, see the Appendix to this method. The method is sensitive to cholinesterase deactivation due to exposure to organophosphates or carbamates.

METHOD SUMMARY

A sample of blood is diluted with buffer solution. Acetylthiocholine (ATChI) and 5,5-dithiobis-(2-nitrobenzoic acid) (DTNB) are added. This solution is incubated for 15 minutes at 37 C, centrifuged to remove the erythrocytes, and the yellow color of the solution is measured at 412 nm in a spectrophotometer.

The cholinesterase in the plasma and to a lesser extent that in the erythrocytes causes the acetylthiocholine to hydrolyze to thiocholine. Thiocholine in turn reacts with DTNB to produce a yellow-colored anion whose concentration is determined spectroscopically.

APPARATUS

1. Spectrophotometer - A Coleman Junior II was used in the development of this method; however, any spectrometer capable of measuring at 412 nm could be used.
2. Centrifuge - Capable of accepting 19 x 105 mm tubes.
3. Constant Temperature Bath - Adjusted to maintain a temperature of 37 C $\pm$ 0.5 (98.6 F).
4. Cuvettes, round, 19 x 105 mm and matched to 1% transmission.
5. Volumetric Glassware - Assorted volumetric flasks and pipettes for the preparation of standard solutions.
6. Microcap Disposable Pipettes, 5 microliter.

REAGENTS

1. Buffer, pH 8.2, containing 0.114 moles (6.662 g) NaCL, .05 moles (6.057 g) tris-hydroxymethyl aminomethane (TRIS) and 7 ml of 3 N HCL in one liter of distilled water.

2. DTNB solution. Dissolve 6.3×10^{-4} moles (0.2497 g) of 5,5-dithiobis-(2,nitrobenzoic acid) in one liter of buffer solution prepared as above.

3. Acetylthiocholine iodide (ATChI) solution. Dissolve 2×10^{-4} moles (0.0578 g) of acetylthiocholine in 250 ml of water.

All of the above solutions are moderately stable but should be refrigerated at 0-4 C when not in use. They are usable for at least two weeks and their deterioration will be indicated by a change in the blank value.

PROCEDURE

1. Turn the spectrophotometer power "on" and allow the instrument to warm up.

2. Premix enough buffer-DTNB solution to handle the anticipated day's samples. Each determination requires 10 ml of this mixture. It is prepared by mixing 10 volumes of buffer and one volume of DTNB solution.

3. Measure 10 ml of this solution into each of several cuvettes.

4. When ready to run a blood sample, add 5 microliters of blood to one of these cuvettes of buffer-DTNB solution. Stopper and shake. The sample may be stored for at least an hour in this form if agitated occasionally to prevent clotting.

5. When up to three samples have been accumulated as in Step 4, add 2 ml of ATChI solution to each cuvette stopper, shake, and place in the 37 C water bath. Prepare a blank in the same manner except containing no blood. After adding the ATChI, the time and temperature are critical.

6. Incubate at 37 C for 15 minutes, remove from the bath, and centrifuge for 5 minutes.

7. While the samples are centrifuging, set the spectrophotometer to 412 nm wavelength and the filter selector knob to visible.

8. Place a cuvette of distilled water in the spectrophotometer and adjust the coarse and fine knobs to zero absorbance.

9. Remove the cuvette and substitute a piece of opaque material. Adjust zero lever to infinite absorbance (0% transmission).

10. Repeat Steps 6 [sic] and 7 [sic] until no further adjustment is required.

11. After centrifuging, wipe the outside of the cuvette clean and dry with a tissue and check to be sure no bubbles are clinging to the inside of the glass.

12. Place the cuvette in the spectrophotometer and read and record its absorbance. The blank is handled in the same manner. Save the blank for a centrifuge counterbalance.

CALCULATIONS

1. Subtract from the sample absorbance the absorbance of the blank with no blood. This absorbance is due to cholinesterase activity.

2. Corrected absorbances in the range of 0.55 to 0.75 appear to be normal. Absorbances below 0.4 indicate suppression of cholinesterase activity to a degree that the person should be restricted from further exposure to organophosphates or carbamates until the cholinesterase level has returned to the normal range.

APPENDIX

In order to express cholinesterase activity in international enzyme activity units, a calibration must be prepared. A standard solution of glutathione is used for this purpose. Glutathione undergoes the same color reaction with DTNB as does the thiocholine released by hydrolysis of ATChI, each mole of glutathione being equivalent to the hydrolysis of one mole of ATChI.

A standard solution is prepared by dissolving 0.0307 g of glutathione in 100 ml of distilled water. This solution contains 1 micromole/ml.

CALIBRATION

1. Turn spectrophotometer power "on" and allow to warm up.

2. Premix buffer-DTNB solution, mixing 100 ml of buffer and 10 ml DTNB solution.

3. Measure 10 ml of this solution into each of six cuvettes.

4. Add 2 ml of water to one of the cuvettes. This is a blank. To the other cuvettes add 0.1, 0.2, 0.3, 0.4, and 0.5 ml of glutathione standard solution and enough distilled water that the total of glutathione solution and water is 2 ml.

5. Adjust the spectrophotometer as instructed in steps 7, 8, 9, and 10 above.

6. Place each of the cuvettes of standard solution prepared above in the spectrophotometer and read and record its absorbance.

7. Plot a calibration curve of absorbance versus micromoles of glutathione, each ml of glutathione standard contains 1 micromole.

CALCULATIONS

1. Subtract from the sample absorbance the absorbance of the blank with no blood. This absorbance is due to cholinesterase activity.

2. Add to this absorbance the absorbance of the blank found in the preparation of the calibration curve. From the calibration curve, read the micromoles of glutathione equivalent to this absorbance.

3. The micromoles of glutathione multiplied by 100 gives the cholinesterase activity in units/ml of blood. A unit is defined as that amount of enzyme which will hydrolyze 0.1 micromoles of ATChI per minute of 37 C.

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APPENDIX C

Dec. 14, 1976

CHOLINESTERASE TESTING

Everyone in plant requires a baseline Cholinesterase Test.

Operators
- All Operators once every 3 months.
- All Operators working with organic phosphates or carbamates once a month. (Phosdrin workers once every week).
- Foremen and supervisors same.

Laboratory
- Technicians once a month.
- Inspectors once a month.
- Chemists once a month or once every 6 months depending on area worked in.

Maintenance
- Pipe Fitters once every month.
- Electricians once every month.
- Instrument Men once every month.
- Machinists once every month.
- Welders once every month.
- Carpenters once every 3 months.
- Painters once every 3 months.
- Foremen and supervisors once every month or once every 6 months depending on area worked in.
- Engineers once every month, 3 months or 6 months depending on area worked in.

Shipping
- Shippers once every month or once every 6 months depending on area worked in.
- Drummers once every month (Phosdrin once every week).
- Supervisors once every 3 months.

Truck Drivers
- Once every month.

Safety
- Once every 6 months.
- Inspectors once every month.

Stores
- Once every month, every 6 months or annually depending on area worked in.
- Rest of purchasing department baseline only.

Administration - Employee Relations - Treasury
- Baseline only.

Utilities
- Once every 6 months if he goes into plant area. Annually for those who do not.