IV. ENVIRONMENTAL AND BIOLOGIC METHODOLOGIES

Measurements of atmospheric concentrations of parathion within the work areas of pesticidal manufacturing and formulation plants and during application of parathion-containing pesticides in agricultural operations provide an indication of the airborne levels of parathion encountered by workers in these operations. Various experiments have also been conducted in order to determine the extent of dermal exposure to parathion during similar operations. The results of such studies define the need to wear proper protective clothing and equipment during potentially hazardous operations to prevent the occurrence of poisoning by parathion. Recommended environmental controls and work practices are essential for the control of occupational parathion exposure.

Brown and Bush[79] measured airborne parathion concentrations at several locations in and near a parathion-manufacturing and -formulating plant. Concentrations of the toxicant ranged from 0.1 to 0.8 mg/m^3. As mentioned previously, plant workers experienced significant declines in their blood ChE activities. No mention was made of engineering controls.

Several reports dealing with airborne concentrations of parathion in fields and orchards following spray application have appeared.[58,105-111] In 1951, Stearns et al[105] applied a spray mixture containing 4 lb of 15% wettable parathion and 10 lb of wettable sulfur/100 gal to a 16-acre grove of grapefruit trees at a rate of 1,173 gal/acre. Air sampling was carried out during the spraying operation and at 24-hour intervals for the next 3 days, then at 48-hour intervals for 6 days. A final air sample was collected 19 days after application. A breathing zone sample taken during application analyzed at 0.03 ppm (0.36 mg/m^3) of parathion. On the following 3 days, the maximum airborne concentration found was 0.005 ppm (0.06 mg/m^3). Seven days after application, parathion could not be detected in the orchard air.

Batchelor and Walker[106] analyzed air samples from fruit orchards sprayed with parathion and DDT at average single application rates of 1.8 and 10.1 lb/acre, respectively. The material was applied by either high-pressure hand spray equipment, air-blast equipment, or aircraft. In addition, the authors determined airborne parathion concentrations during pesticide mixing/loading of both the high-pressure hand sprayer and the air-blast sprayer in a mixing plant and in a warehouse. The results indicated that the application of parathion is considerably less hazardous than its mixing and loading into application equipment, especially in orchard operations. Application by high-pressure hand sprayers resulted in slightly higher atmospheric concentrations of parathion than were brought about by use of either air-blast ground rigs or aircraft application equipment. The mean airborne concentrations resulting from these three methods of application were 0.09, 0.03, and 0.05 mg/m^3, respectively. In contrast, mean airborne concentrations for mixing/loading operations involving ordinary water-wettable powder (WWP), antidusting WWP, and liquid concentrates were 2.15, 0.37, and 0.02 mg/m^3, respectively. By utilizing filter pads attached to various parts of the operator's body and clothing (shoulders, forearms, thighs, back of neck, and chest), estimates of the potential dermal exposure were made. Similar estimates of the potential respiratory exposure were made by measuring the parathion absorbed onto filter pads contained in respirators worn by the subjects. The dermal parathion exposure of spray operators was found to average 12.8 and 21.5 mg/sq ft/hr in high-pressure spraying and air-blast spraying, respectively. The calculated average daily dermal exposure of the workers engaged in either high-pressure hand spraying or air-blast spraying was 7.7 versus 0.02 mg/kg for respiratory exposure (using the respirator pad technique). The respirator pad technique gave values that were approximately 3-5 times as great as those calculated on the basis of the airborne samples. However, Durham and Wolfe[112] suggested that both techniques provide the same value when the data are adjusted to reflect their demonstrated ratio of impinged to inhaled toxicant. The results indicate the relative magnitudes of exposures during mixing-loading and application of parathion by the dermal and the respiratory routes, and the need for protective clothing and equipment.

By sampling within a few feet of the spray operator's breathing zone, airborne parathion concentrations ranging from 2.0 to 15.0 mg/m^3 were measured by Kay and associates[58] during the application of 15% wettable powder in the concentration of 0.75 to 1.5 lb/100 gal of water and dispersed at the rate of 300-400 gal/acre. High concentrations occurred primarily when spraying during windy conditions. Workers exposed to these concentrations of parathion experienced declines

in blood ChE activities. Air samples were also collected while workers added 15% parathion wettable powder to spray tanks. Parathion concentrations derived from two tests in which the dust cloud rose to the operator's breathing zone were 16 and 26 mg/m^3. During the application of 0.75 lb of 15% parathion wettable powder and 10 lb of sulfur in 100 gal of water (a low-concentration mixture) to apple trees, Kay et al[58] measured 14.0 mg/m^3 of parathion in the breathing zone air of the operator. The following day, the airborne concentration of parathion was diminished to 0.09 mg/m^3 and approximately 3 weeks later it was measured at 0.03 mg/m^3.

Jegier[107] reported on the health hazards to tractor operators from insecticide spraying of crops. Air samples were collected at the tractor operators' breathing zone and the results of the analyses for parathion were used to calculate respiratory exposures. Filter pads attached to double-unit respirators and to the forehead and wrists of observers riding beside the tractor drivers were used to calculate respiratory (a second method) and dermal exposures. Parathion was applied to apples as a spray in concentrations of 0.4-4.0 lb of 15% wettable powder/100 gal of water. The air concentrations of parathion ranged from 0.05 to 0.26 mg/m^3 with a mean of 0.15 mg/m^3 (10 samples). Jegier estimated a mean respiratory exposure of 0.03 mg/hour (range of 0.01-0.05 mg/hour) from analyses of the filter pads. Calculation of respiratory exposure based on the air sampling results and a lung ventilation rate of 444 liters/hour provided an estimated respiratory exposure to parathion of 0.07 mg/hour. The mean dermal exposure was estimated at 2.4 mg/hour (range of 0.7-5.8 mg/hour).

Using similar absorption pad techniques to measure the potential respiratory and dermal exposure of workers spraying parathion on vegetable crops with hand knapsack-misters, Simpson and Beck[108] estimated the daily (8 hours) dermal and respiratory exposures at 72.8 mg and 2.32 mg, respectively. A study of the blood ChE activity of the sprayers indicated that 30% of those tested had decreased levels. The investigators did not specify what level of enzyme depression they regarded as significant; however, they stated that workers with activities less than 60% of their preexposure values were removed from exposure. All samples collected in the operator's breathing zone by midget impingers contained parathion in excess of 0.1 mg/m^3.

Wolfe et al[109] studied the exposure to parathion of orchard spraymen operating low-volume spray rigs and compared it with that of spraymen using high-volume sprayers. Parathion was applied to fruit trees in the low-volume spray in 8-12 times the concentration of the high-volume mixture (0.24-0.36% vs 0.03% parathion). Both the potential dermal and respiratory exposures were calculated by attaching absorbent cellulose pads to various parts of the worker's body or clothing and by placing filter pads in special single- or double-unit respirators designed to prevent direct impingement of spray droplets onto the respirator pads. The total dermal exposure was calculated on the basis of the exposed person wearing a short-sleeved, open-necked shirt, no gloves or hat, with his clothing providing complete protection of the areas covered. Since drenching sprays can wet the worker's clothing, dermal absorption can occur through nonimpervious clothing; however, the dermal exposure values calculated by Wolfe et al[109] on the basis of minimal protective clothing would tend to provide work practice recommendations on the conservative side. The amount of parathion drawn into the respirator with sufficient velocity to reach the absorbent pad was considered to represent respiratory exposure. The calculated potential dermal exposure for operators of low-volume spray equipment was 27.9 mg/hour as compared to 19.4 mg/hour with high-volume (ie, dilute spray) equipment. The authors[109] attributed the difference to an observed greater parathion contamination of the hands of the spraymen working with the low-volume spray. Potential respiratory exposure for low-volume spraying was 0.055 mg/hour, or about 2.7 times that estimated for operators of conventional high-volume machines (0.020 mg/hour).

Samples of spray mist were taken during and after spraying operations with parathion in a study[110] of orchard workers in Quebec. Parathion was applied as a spray (a fine mist) composed of 1.5-4 lb of 15% wettable powder/1,000 lb of water to apple trees. During the spraying operations, air samples were taken in the tractor-drivers' breathing zones using fritted-glass bubblers containing alcohol. Both air residual and leaf residue analyses were performed subsequent to application. For sprays containing 3-4 lb of parathion 15% wettable powder/1,000 lb of water, applied at the rate of 0.12-0.15 lb (of 15% wettable powder) for each tree, average spray concentrations in the operators' breathing zones ranged from 0.29 to 0.52 mg/m^3 of air. Under near-windless conditions, the investigators found an airborne parathion concentration of 0.12 mg/m^3 in the orchard 1 hour after spraying. Parathion was not detected in the

orchard air after 1 hour of completing spraying in winds of 3-4 mph.

Braid et al[111] assessed the potential exposure from drifting parathion dust by taking samples of the airborne dust and of vegetation at distances up to 400 feet from the dusting machine. One percent parathion dust was applied at a rate of 40 lb/acre from a tractor-drawn duster which dispersed the material at a height of approximately 2 feet above ground. The air was sampled at a height of 4 ft above ground, corresponding to the average breathing zone height of people working in the field, using electrostatic precipitators. Thirty-nine cubic feet of air was sampled in each of five 13-minute dusting trials. Airborne dust loads were determined at distances of 50, 100, 200, 300, and 400 feet from the application equipment. Average wind speed during the 5 trials was 6.6 mph. The airborne parathion concentrations at downwind distances of 50, 100, 200, 300, and 400 feet were 3.0, 0.85, 0.22, 0.07, and 0.03 mg/m^3, respectively.

From the results of these studies, it is evident that dermal exposure to parathion is significant and actually constitutes a greater potential hazard than respiratory exposures in most occupational situations.

General room ventilation is needed in parathion-manufacturing and formulating areas. In addition, exhaust systems are needed at loaders, blenders, mills, kettles, packaging equipment, and all other possible sources of vapor, spray, or dust containing parathion. Liquid and dust exhaust systems must be so designed that neither the workers nor other human and animal life in the surrounding area are at risk. Dust exhaust systems should be vented through a dust collector and organic vapor absorber, so that air vented to the atmosphere is adequately scrubbed.[3] Detailed information on the design and installation of exhaust systems for vapor and dusts of parathion should be sought from competent sources, such as ventilation engineers or industrial hygienists.

Air Sampling Methods

The sampling of air for parathion is complicated by the fact that it may exist in vapor or particulate (ie, aerosolized liquid or dust) form. Thus sampling devices must be versatile in their ability to trap all the physical states of airborne parathion. The most widely used pesticide air sampling devices include: Greenburg-Smith or midget impingers[58,106, 108,112-118], bubblers or scrubbers (fritted glass absorbers)[58,114,116,119,120], glass fiber filters[118,121] or cellulose filter pads[106-109, 112,113,118,120], gauze pads[112,113], and packed adsorbent columns, such as alumina.[112,122] Nylon chiffon screens have also been used.[123] Each device has its advantages and disadvantages, summarized by Miles et al[118] as follows: ". . . packed columns are very efficient for trapping vapors, but recovery of the sample is frequently difficult; the filter systems permit the collection of large volumes of air in short periods of time, but their efficiency for vapors is low and unknown losses of particulate and aerosol samples occur during the sampling period; the scrubbers are good for aerosols and vapors, but the sampling rate is slow and the use of sintered glass precludes the collection of particles; and cold traps are of limited value in field work in view of the maintenance problem. Midget and Greenburg-Smith type impingers seem to offer a compromise in that they can be operated at a reasonably fast rate, they are very efficient for collection of particulate matter, and with proper selection of solvent they can collect aerosols and vapors efficiently."

Durham and Wolfe,[112] in their review of sampling methods for human respiratory exposure to pesticides, stated that the midget impinger has been reported to duplicate "reasonably well" the spectrum of particle sizes picked up by the nostrils in breathing. They further stated that the Greenburg-Smith impinger has the advantage of sampling large volumes of air in a given time, thus improving sensitivity where the concentration of pesticide is low or the exposure time is brief. Using a 4-hour sampling time for the Greenburg-Smith impinger, Miles et al[118] reported a sensitivity of 2.0 ng/m^3 of parathion in air, or 1/25,000th the airborne concentration permitted in the proposed environmental standard.

Because of the low air sampling rate inherent in the midget impinger,[117] sensitivity for similar sampling times is less than for the Greenburg-Smith impinger though still very high. However, the size of the midget impinger imparts greater adaptability to the air sampling procedure without sacrificing precision. The midget impinger appears to be the recommended collection device of choice for obtaining parathion-containing air samples. However, neither the sampling efficiency nor the overall precision of the sampling and analytical method are known. (RH Hill, Jr, written communication, March 1976) In addition, the Environmental Protection Agency has withdrawn this sampling method (ie, midget impinger using purified ethylene glycol) from its pesticide sampling and analysis manual since "a controversy concerning the reliability of the data" has arisen from using the method. (RH Hill, Jr, written communication,

March 1976) Despite this, the impinger is presently the best available sampling device for parathion in air. Since parathion may occur in air as vapor, liquid droplets, or as an adsorbed film on solid particles, it is essential that the impinger be operated at a flow rate which will efficiently collect all forms of airborne parathion. Appendix I gives details of the sampling and air flow calibration procedures to be followed when using this method. Other air sampling methods which can be shown to be equivalent, or superior, in efficiency to the impinger method may be used.

Parathion Analysis

The first step in all the analytical methods considered here is the removal of the pesticide and other compounds of interest from the substrate or trapping medium. Filters and solid adsorbents are amenable to solvent extraction or desorption. The extraction solvent must be compatible with subsequent analytical procedures unless the solvent is to be removed in the procedure. The contents of impingers or bubblers using nonvolatile solvents must be partitioned into an immiscible, volatile solvent. For example, parathion collected in ethylene glycol is extracted from it with a light hydrocarbon, preferably hexane.

The variety of techniques available for assay of parathion-containing materials covers the gamut of testing procedures from titration to the more complex instrumental methods. Several techniques are applicable to the analysis of large amounts of parathion, such as are found in the technical material or its formulations. Analysis of trace amounts of chemicals presents problems in sensitivity and specificity which can be overcome only with certain instrumental methods. The spectrophotometric methods can be used to analyze parathion directly or to assay it after derivatization.

The residue method most commonly used before the development of a gas chromatographic detector specific for phosphorus was that of Averell and Norris.[124] In this method, the nitro group of the parathion is reduced to an amino group with zinc and hydrochloric acid. The amino group is then diazotized with nitrite and coupled with N-(1-naphthyl)-ethylenediamine dihydrochloride. The resulting dye has a deep magenta color, absorbing at 555 nm. The light absorption of the colored derivative is measured at 555 nm and is compared to a standard curve for quantitation.

The spectrophotometric method of Gage[125] is a modification of the Averell-Norris method. Although it was developed as an assay method for technical parathion and formulations, it is applicable to trace analysis where relatively high concentrations of PNP or the S-ethyl isomer of parathion (O,S-diethyl-O-p-nitrophenyl phosphorothioate) are present.

Parathion, itself, has a moderate absorption maximum in the near ultraviolet spectrum at 274 nm; Hirt and Gisclard[116] utilized this property for direct analysis of the insecticide in air sampling devices. The solution from a bubbler or midget impinger is diluted to a known volume, the absorbance of the parathion being measured spectrophotometrically.

Range and sensitivity of the spectrophotometric methods are limited by two factors, the absorbance of the material analyzed and the sensitivity of the instrument used to perform the analysis. They also suffer from a variety of interferences. Many compounds absorb light in the near ultraviolet region, especially aromatic compounds; therefore, the Hirt and Gisclard[116] method is especially susceptible to interferences. Compounds that absorb in the visible spectrum are less common and would not normally be expected to appear in air sampling devices and, as such, do not represent a problem in the Averell-Norris[124] method. However, aromatic nitro or amino compounds can potentially behave like parathion by forming a dye in the color development procedure, which may absorb at the same wavelength and thus interfere. Isomers of parathion, its oxon, and p-nitrophenol are especially likely to give high parathion assays in the Averell-Norris method which is not specific for parathion.

Of the spectrophotometric methods, that of Gage[125] is the only one to have any specificity for any of the isomers of parathion; however, none of them estimates paraoxon separately from parathion, it is either lost by hydrolysis or is read as parathion. There is no UV-visible spectrophotometric scheme of analysis for the separate determination (ie, limit of detection) of paraoxon in the presence of parathion.

In 1964, the thermionic emission or alkali flame ionization detector (AFID) was introduced by Giuffrida[126]; in 1966, Brody and Chaney[127] introduced the flame photometric detector (FPD). Both detectors are modifications of the universal flame ionization detector and are highly specific for phosphorus. Since the development of the phosphorus-specific detectors, the preferred method for the analysis of parathion has been gas liquid chromatography (GLC) for the following reasons: GLC offers the advantage over the spectrophotometric methods of superior specificity in

that it separates the components of the sample under scrutiny before the compound is quantitized; that is, the instrumental signal from the gas chromatograph, as it is recorded, has a higher probability of arising from a true response to the compound being assayed than that from a spectrophotometer. Thus, GLC offers simultaneous qualitative and quantitative analysis. For parathion collected in air sampling devices, analysis should be straightforward and should require no elaborate cleanup steps.[128] Analysis follows direct extraction of filters or vapor adsorbent and concentration of the extracting solvent to an appropriate volume.

A pertinent problem in trace analysis of a pesticide is the choice of a detector system. As mentioned above, two widely used phosphorus-specific detectors have been developed for pesticide residue analysis, the FPD and the AFID.[126,127] The FPD has much less stringent requirements than the AFID for detector gas flow control and, thereby, requires less time for maintenance and adjustment of the detector. The FPD also maintains a more stable response during a period of time than the AFID and requires less frequent injection of standards for proper calibration. In addition, the AFID is responsive to organic compounds containing chlorine, nitrogen, and sometimes sulfur, though to a lesser degree than to phosphorus when the instrument is tuned properly. Therefore, the FPD is considered to be superior to AFID.

Great sensitivity is also a major advantage of the GLC-phosphorus specific detector method of analysis. Averell and Norris[124] reported that 20 μg of parathion in the final 50-ml aliquot represented the sensitivity of their method. Because of great differences in extinction coefficients, the Averell-Norris method is inherently a thousand times more sensitive than the method of Hirt and Gisclard.[116] In contrast, Guiffrida[126] detected 0.024 μg of parathion using GLC with AFID. For normal analytical work, a convenient working range for AFID is between 50-1,000 picograms (pg)/injection volume. GLC with FPD was reported[127] to be sensitive to 250 pg of parathion using a 526-nm filter; the response was linear from 6 ppb to 60 ppm.

The precision of GLC analysis depends largely on several factors. Syringe-handling technique is very important for the small volumes of samples used with the phosphorus-specific detectors. Injections are commonly made against 20-40 psi of carrier gas pressure, and a worn syringe or injection-port septum can cause serious sample loss. Use of a solvent-flush technique usually increases the reproducibility of sample analyses. Instrument stability is another factor in precision. A dirty detector, especially with the AFID, a bad column, or a faulty electrometer or recorder will cause loss of sensitivity and erratic responses. Overall precisions of ±5% are not uncommon. Factors affecting accuracy are extraction efficiency, interferences, instrument stability, and frequent use of standards. Integration of the areas of various peaks is a critical step in deriving numbers related to sample composition; it is the conversion of the record produced by the detector from analog to digital form.

All the methods for estimation of parathion discussed in this document, photometric, spectrophotometric, and GLC, quantitate their responses to unknown quantities of the insecticide by comparing them with standard curves. The standards used are originally weighed out and brought to known concentrations by serial dilutions and, as such, are secondary gravimetric standards. Thus, all the methods yield values that are in units of weight of parathion, so that the estimates obtained by different methods are comparable directly.

Air monitoring should produce samples relatively free of interferences when analyzed with a gas chromatograph equipped with a specific detector of phosphorus. Any organophosphorus compound that survives pyrolysis will be detected, but only those having a retention time close to that of parathion will interfere. Large quantities of organic material will increase background noise for the FPD, thereby reducing the accuracy of the method. In summary, GLC with FPD offers the following advantages over the photometric and spectrophotometric methods:

(1) Less subject to interferences from contaminants.

(2) Specific for parathion.

(3) Greater sensitivity.

(4) Greater precision and accuracy. The GLC with FPD method is therefore recommended.

Plasma and RBC ChE Analysis

As the identification of the various ChE enzymes developed, the determination of the catalytic ability of enzymes in tissue by various methods was performed to determine the effects of various inhibitors on tissue enzyme activities.

The early methods of determination of ChE activities used principally acetylcholine as a substrate and measured the release of H-ions as the esters were hydrolyzed. This change has been measured manometrically,[129,130] by change in an acid-base indicator,[131,132] and by electrometric pH measurement.[133]

Manometric methods for analysis of ChE's have been found to be among the most precise but have the inherent drawbacks of time-consuming manipulations and procedures. These methods have been used for both RBC and plasma ChE assays.[134-136]

Methods using a change of indicator color have been successfully used with serum ChE samples,[132] but are not applicable to hemolyzed RBC samples or plasma because of the turbidity of such solutions. Unless dialysis membranes are used,[137] the analytical precision decreases because of the turbidity.[132,138] The principle of this method has led to several useful field screening methods. Such field methods have poor precision, ±25%, but this degree of precision is not inappropriate for screening methods.[137-144]

The electrometric method of Michel[133] was developed primarily to decrease the time required for analysis and has been found to be well-suited for determinations of both RBC and plasma ChE activities. This method has been widely used in the measurement of RBC and plasma ChE in men exposed to OP ChE-inhibitors. In fact, the ΔpH method has been the one used in most of the reported determinations of normal human RBC and plasma ChE values.[134] Additionally, the best established normal values for humans were determined[145] using the original ΔpH method of Michel.[133] The studies by Vorhaus and Kark[146] of changes in serum ChE activities due to disease also used the original ΔpH method of Michel.

Variations of the original Michel method have been proposed to make the method more convenient. Procedures have been proposed using capillary blood sampling methods rather than those involving venipuncture,[147] automated systems,[148] less analysis time,[149] and a single measurement of pH.[150] The method of Wolfsie and Winter[147] has the advantage of not requiring samples as large as those of the original Michel method, without any apparent loss of precision.[151]

The production of acid has also been monitored by continuously adding base to maintain a constant pH as hydrolysis occurs. Such methods are referred to as pH-stat methods.[152,153] The pH-stat methods have not been reported in surveys and case studies of OP poisoning as often as the ΔpH methods. Equipment required is more difficult to operate and maintain than the relatively simple equipment of the ΔpH methods. The pH-stat method was found by Crane et al[151] to be less precise (1.70% relative standard deviation) than the ΔpH method (1.45% relative standard deviation), and to exhibit a high degree of interlaboratory variation. The pH-stat method employs a titration at constant pH. Although the activity of ChE enzymes has been observed to be pH-dependent, the small change in pH observed in the ΔpH methods has a comparatively small and correctible effect on the activity of ChE. Thus, the pH-stat method does not have a significant advantage in this regard; it does have the advantage that a 5-minute titration is usually sufficient for estimating the ChE activity of a sample. Furthermore, normal human values are less well established with this method than with that of Michel.[134,154]

Other methods have been used to determine the rate of hydrolysis of various substrates by enzyme-containing biologic samples. This has been done by estimating the amount of unreacted ACh after a period of incubation with a source of ChE[155-157] and by measuring the release of thiocholine from acetylthiocholine by ChE's.[158,159,160,161] The methods for the determination of unreacted ACh have been used primarily with serum samples and have not been used frequently in this determination after OP exposures. The method of Hestrin, which appears to be the standard method for serum ChE,[162,163] has been used in establishing normal values,[154] and has precision comparable with the ΔpH method.[136] The method has apparently not been used for determining ChE in plasma or RBC's, presumably because of the turbidity of such solutions. The method can be used under a great variety of experimental conditions, however, including wide ranges of pH's, substrate concentrations, enzyme concentrations, and buffer solutions.[136] A method which can accommodate variable conditions does not necessarily gain an advantage from this fact, however, because such variations usually are not encountered in the routine analysis of human ChE's.

The methods which estimate ChE by determining the amount of hydrolyzed acetylthiocholine have been used for several years since they were first developed by Koelle and Friedenwald[159] for histochemical determinations. Methods have been developed using several reagents which form colors with the thiocholine present after hydrolysis of acetylthiocholine.[158,161,164] Determinations of ChE's in plasma, serum, RBC's, and other tissues were possible using the method of Ellman et al,[164] but there are possibilities of interferences by icteric or hemolytic plasma. This method has been adapted for use with an automatic analyzer and is thus useful for the routine analysis of large numbers of samples. Normal activities of human ChE's with these methods have not been reported extensively.[134] The precision of these colorimetric

methods is not as great as that of the ΔpH methods,[164,165] and there are some additional characteristics which may detract from their suitability for routine analysis. Among these are the fact that the substrate concentration is too low for the determination of plasma ChE,[165] and that autooxidation of thiocholine is possible[165]; there is also some disagreement over the relative specificities of acetylcholine and acetylthiocholine.[159,160,164]

Several other laboratory methods have been devised, such as the amperometric method described by Einsel et al[166] and the radioassay methods of Winteringham and Disney,[167,168] and Potter.[169] A gas chromatographic method was developed by Cranmer and Peoples[170] and an acetylcholine-ion-selective electrode was developed by Baum.[171] These alternate methods have not received widespread acceptance and have not been well documented in the open literature. The principal reasons are that these methods require more expertise than the colorimetric and ΔpH methods. Equipment used in these methods is more specialized and expensive than that used in manual colorimetric and ΔpH methods. A comparison of normal values of activity for RBC ChE in humans by the Wolfsie and Winter[147] method and the original method of Michel used by Rider et al,[145] shows similar values for mean activity of RBC ChE. Wolfsie and Winter[147] found a mean of 0.861 ΔpH/hour with a standard deviation of 0.091. Rider et al[145] found a mean of 0.766 ΔpH/hour with a standard deviation of 0.081. Rider et al explained the difference between the mean RBC ChE activity that they determined and that of Wolfsie and Winter on the basis of probable contamination of red cells by plasma in the last two authors' work, since the RBC's were not washed during that study. Witter[165] suggested that the difference may have been due to increased packing of RBC's in the Wolfsie and Winter study. Also, this difference in means may be due, in part, to the fact that the same persons were not tested in the two studies. In establishing their mean, Rider et al[145] sampled 400 men, whereas Wolfsie and Winter sampled 255 men. The two groups of subjects were small enough to allow the discrepancy in mean values without necessarily concluding that the RBC's were contaminated, especially in view of the ranges and standard deviations in the studies. The ranges determined by Wolfsie and Winter and by Rider et al were 0.554-1.252 ΔpH/hr and 0.58-0.95 ΔpH/hr, respectively. The range of ChE activities of the group of subjects studied by Rider and his associates fell within the range for the group of Wolfsie and Winter. Clearly, there is much overlap of the distributions of normal ChE activities in the two studies, and the difference in means should not be given undue significance in these comparatively small samplings from the entire population.

The standard deviations for chemical analyses of ChE's by the methods of Wolfsie and Winter[147] and Rider et al,[145] 0.03 ΔpH/hr, are small in comparison to the interindividual variations observed.[145] They are included in the overall standard deviation reported.

The means of the normal populations by these two "ΔpH" methods[145,147] are closer for plasma ChE activity than for RBC ChE activity. The means of the plasma ChE activities of the 2 groups of normal subjects were found by Wolfsie and Winter [147] and Rider et al[145] to be 0.912 and 0.953 ΔpH/hr, respectively, and the standard deviations were 0.11 and 0.19, respectively. The ranges for plasma ChE in normal humans of Wolfsie and Winter and Rider et al were 0.408-1.652 ΔpH/hr and 0.52-1.39 ΔpH/hr, respectively, indicating again that the group of normal subjects used by Rider et al had plasma ChE activities included within the range determined by Wolfsie and Winter.

Based upon the consideration of means, standard deviations, and ranges, the conclusion can be made with a high degree of reliability that there is not an appreciable difference in either the normal values determined in the 2 studies or the analytical methods used in them.

In studies of serum ChE activities in various groups, different normal values have been found for men and women.[154] In the largest study reported,[145] the mean of the female plasma ChE was found to be lower than the plasma ChE of men. The female/male ratio of 0.86 found by Rider et al[145] was representative of those found in several other studies reported by Wetstone and LaMotta.[154]

Based on the foregoing, the biochemical assay method of Michel[133] has been selected as the method of analysis to be recommended because it has been the most popular, is the most widely documented, and is unsurpassed in precision. The laboratory equipment necessary is standard, relatively inexpensive, and simple to use. Although the method is not automated, it does provide small laboratories with the capability to analyze many samples without excessive expense. Normal values using this method are based upon the largest extant survey of a nonexposed population. (Table XI-2) The micromodification of the sampling method used in the original Michel method,

described by Wolfsie and Winter,[147] used in conjunction with the original biochemical assay method of Michel will provide sufficient precision in analysis without excessively great bloodletting.[148,172]

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

Parathion appeared in both the tentative Threshold Limit Value and established value lists of the American Conference of Governmental Industrial Hygienists (ACGIH) in 1954,[173] with a suggested TLV of 0.1 mg/m^3.

Documentation for the ACGIH value[174] was published in 1962. The TLV of 0.1 mg/m^3 was primarily based on conclusions drawn from the studies of Kay et al[58] and Brown and Bush.[79] Kay et al[58] measured airborne parathion levels ranging from 2 to 15 mg/m^3 in the breathing zones of workers engaged in orchard spraying. At the end of a 2-month spraying period, during which time the workers were intermittently exposed, the blood ChE levels of the sprayers were decreased about 25% below control values. The average daily exposure was estimated[174] by the Committee on Threshold Limit Values to be not more than 2.0 mg/m^3 even though the range of measured airborne parathion levels was 2-15 mg/m^3. Brown and Bush[79] measured airborne parathion levels ranging from 0.1 to 0.8 mg/m^3 in a manufacturing/formulating plant in which workers showed decreased RBC and plasma ChE activities. The TLV documentation states,[174] "Based on these calculations, 2 mg/m^3 would appear to be an excessive exposure. From the work of Brown and Bush, 0.5 mg appears excessive. It is concluded that the figure of 0.1 mg/m^3 provides the best estimate for a threshold limit from available data."

In the 1966 Documentation of Threshold Limit Values,[175] the results of various animal feeding studies were reported. In addition, the results of Edson's study[35] involving the daily oral ingestion of parathion by human volunteers were presented; "doses of 1.47 mg/man/day produced no effect in volunteers, while a dosage of 5.46 produced moderate depression of blood cholinesterase."[175] The TLV was believed to be sufficiently low to prevent significant depression of blood ChE activity provided that contamiantion of the skin was prevented.

The data of Arterberry et al[50] showing a slight depression in blood ChE activity at a urinary PNP excretion of about 2 mg/liter in workers repeatedly exposed to parathion was included in the Third Edition (1971) of the Documentation of the Threshold Limit Values.[176] The recommended TLV remained at 0.1 mg/m^3.

A federal ambient air (ie, workplace) standard for parathion of 0.1 mg/m^3, with a warning concerning skin absorption, has been promulgated by the Occupational Safety and Health Administration under the authority of the Occupational Safety and Health Act of 1970 (29 CFR Part 1910.93 published in the *Federal Register* 39:23542, June 27, 1974). This standard is based upon the recommendation of the ACGIH. The use of the word skin following parathion in the federal standard is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the ambient air limit is not invalidated. There are no state environmental limits more restrictive than the federal.

Permissible levels of toxic substances in the work environment for a number of countries in addition to the US have been published by the Joint ILO/WHO Committee on Occupational Health.[177] Finland, the Federal Republic of Germany, Japan, Rumania, and Yugoslavia all have occupational exposure standards of 0.1 mg/m^3, while Bulgaria, Hungary, and the USSR adopted 0.05 mg/m^3 as a maximal acceptable concentration (MAC). In the USSR, MAC's are defined as ". . . absolute limits that should not be exceeded during any part of the working day, regardless of lower concentrations that may have existed during any of its period. They are set at a value which will not produce, in any of the persons exposed, any deviation from normal, or any disease which can be detected by the most modern research methods available."[177] Smelyanskiy and Ulanova,[178] in a paper dealing with Russian MAC's, stated that methods for investigating CNS function and higher nervous activity, biochemical and delicate morphologic and histologic techniques, and the use of both conditioned and unconditioned reflexes, among others, are of value in detecting early manifestations of chronic toxicity of workplace substances.

Basis for the Recommended Environmental Standard

The characteristic signs and symptoms of parathion poisoning, discussed in Chapter III and listed in Table III-1, are due to cholinergic stimulation resulting from inhibition of the activity of neuroeffector and other tissue ChE's.[1] There is

evidence from experiments with DFP[71] that RBC and plasma ChE's serve as "buffers" protecting the more vital tissue ChE's from inhibition. Karczmar and Koppanyi[71] demonstrated in animals with a normal amount of neuroeffector ChE that lowered activities of plasma and RBC ChE's increased responses to ACh, BCh, and DFP. They were able to demonstrate also that, in animals in which the tissue ChE's had been reduced to near zero, the infusion of ChE-rich blood probably did not restore activity at the neuroeffector sites. In such animals, however, responsiveness to injected ACh was nearly the same as that of control animals.

The absorption and subsequent metabolic conversion[23-25] of parathion by the body reduce the ChE activities in central, peripheral, and autonomic nerve tissues, RBC's, and blood plasma.[18] Grob et al[18] demonstrated that the blood ChE's are depressed along with tissue ChE's in humans poisoned by parathion. Other investigators have shown[8,9,11,13, 17,18,34,35,61] significant depressions of both RBC and plasma ChE's in workers exposed to parathion but not exhibiting signs and symptoms of parathion poisoning as well as in those exposed and exhibiting signs and symptoms of poisoning.

In addition to blood ChE determinations, estimation of metabolites such as urinary PNP as a measure of human exposure to parathion has been proposed.[37,46,51,104,179] Determinations of blood and urine alkyl phosphates have been suggested also.[180-182] In 1970, Wolfe et al[51] reported that PNP excretion levels correlated well with exposure to parathion. The average peak excretion level occurred 8.7 hours after exposure; the levels of PNP were insignificant 48 hours after exposure. Thus, it is important to obtain urine samples soon after exposure. Arterberry et al[50] concluded in 1961 that PNP excretion is not a reliable measure of the severity of poisoning. In agreeing with the conclusion of Arterberry et al, Wolfe et al[51] stated that PNP was a more sensitive measure of exposure than were blood cholinesterase levels though the latter seemed to correlate better with occurrence of poisoning than did PNP excretion. As a hypothetical example, following an exposure to parathion sufficient to depress the RBC and plasma ChE's to 60% of their preexposure values, PNP will be excreted in the urine. In order to determine the extent of this exposure, the urine would have to be collected within approximately 9 hours of exposure.[51] About 2 days later, the urinary PNP excretion would have ended[51] whereas the blood ChE's would still be depressed from normal.[18] Subsequent significant exposures would produce the same effects, with further depression in blood ChE's and urinary excretion of PNP. Thus, the likelihood of detecting continuing parathion absorption with resultant ChE depression through a routine biologic monitoring program is greater by estimation of blood ChE's than of urinary PNP. Cholinesterase activity levels appear to be better indicators of OP exposure since the regeneration/replacement rates are slow enough[18] to integrate the exposure effectively and allow practical sampling frequencies. In addition, workers engaged in formulation, mixing, and application of parathion are likely to be simultaneously exposed to other ChE-inhibiting insecticides, such as mevinphos, monocrotophos, TEPP, azinphos-methyl, and others, which do not result in urinary excretion of PNP. In cases of exposure to mixed anticholinesterase pesticides, urinary monitoring of PNP levels would not necessarily provide warning of additional inhibition of blood ChE's. Workers exposed to parathion alone are the exception rather than the rule.

The metabolism and hydrolysis of OP pesticides in mammals result in the excretion in urine of a variety of alkyl phosphates.[181,182] Shafik et al[182] fed parathion to rats at 1/10 the LD50 for this species and recovered both O,O-diethyl phosphate (DEP) and O,O-diethyl thiophosphate (DETP) in the urine. The total DEP and DETP excreted in the urine accounted for 30-40% of the parathion initially fed. Their results suggested that the DEP arose from the action of hydrolytic enzyme(s) on paraoxon, a metabolite of parathion. Excretion of these metabolites remained relatively constant during exposure and dropped rapidly to zero upon cessation of feeding. Blood and urine alkyl phosphate (ie, phosphates, thiophosphates, and dithiophosphates) determinations are presently undergoing additional research and evaluation; they show great promise for the future as diagnostic procedures.

Electromyography (EMG)[67,68] has been used to measure the effects of mixed pesticide exposure (organochlorine and organophosphorus pesticides) on the neuromuscular system. No studies showing altered electromyographic response in workers exposed to parathion alone have been published.

Neither the alkyl phosphate metabolite method nor the EMG technique is currently acceptable since the test results cannot be satisfactorily quantitatively related to either the extent of exposure or the hazard to the worker.

Thus, because RBC ChE activity levels provide an acceptable means of correlating the extent of exposure with the immediate effect, and because

these levels are relevant to mixtures of ChE-inhibiting pesticides and allow for practical sampling frequencies, routine biologic monitoring of the RBC ChE and monitoring of both RBC and plasma ChE's in emergency exposure situations are recommended for the prevention of adverse health consequences in parathion-exposed workers.

There are daily variations, both in the plasma and RBC ChE activities of normal, healthy persons who are unexposed to ChE-inhibiting OP pesticides, including parathion.[58,135,154,172] Fryer et al[172] determined the probable daily variations of plasma and RBC ChE activities for a normal, healthy individual using a micromodification of the Michel method. In this study of 17 volunteers from a university staff with no known exposure to OP insecticides, the normal daily variation from the group mean in both plasma and RBC ChE's was determined. Five consecutive daily samples were taken from each volunteer except one; in that case, there was a one-day gap in the series. For RBC ChE activity, the range was ±23% from the group mean; for plasma, the range was ±37%. The day-to-day variation within individuals for RBC and plasma ChE activities was ±5% and ±9%, respectively, for the group as a whole. Individual maximal variations were ±13% and ±23% for RBC and plasma ChE activities, respectively. The authors[172] did not indicate race, age, or sex differences in the volunteer group. It must be noted, however, that any extrapolation of these data to a larger group must consider the possible changes in variation that may occur because of these factors. Rider et al[145] have shown that the plasma ChE levels are higher in men than in women and increase slightly with age. In men, the increase was 0.002 ± 0.001 ΔpH/hour/year of age and twice that in women. The authors did not find significant differences in RBC ChE with age or sex. On the other hand, Vorhaus and Kark[146] could not find a difference in plasma enzyme activity that could be correlated with age, sex, weight, or height. They did not evaluate differences in RBC ChE.

Reinhold et al[138] also found plasma ChE activity higher in men than in women. They noted also differences between blacks and whites in both men and women. The group mean of 0.926 for the serum ChE activity of white men was significantly higher than the observed group means of 0.814 and 0.768 for black men and women, respectively. In this study, 130 white men, 46 black men, 70 white women, and 28 black women were compared.

In addition to changes in blood ChE activities due to sex, race, and age, serum ChE activities have been reported[72-74] to be depressed in persons afflicted with liver disease, anemia, acute infectious and chronic debilitating diseases, and malnutrition. Drugs such as caffeine and related xanthine compounds,[183] chloroquine and other antimalarial drugs,[76] chloroform,[184] ether,[184] narcotic analgesics such as morphine and codeine,[77] and thiamine[185] have been shown to depress the activity of serum ChE. A few drugs have been reported to depress RBC ChE activity, including quinine,[76] other antimalarial drugs,[76] and echothiophate.[186]

Fryer et al[172] analyzed the day-to-day variations in the ChE's of the blood of 17 unexposed subjects during 5 days and concluded that 95% of normal people would have day-to-day variations of not more than 0.171 ΔpH/hr in RBC ChE and not more than 0.351 ΔpH/hr in plasma ChE. Applying these criteria to a group of 89 agricultural workers who had not knowingly been exposed to OP compounds for at least three months, they found, with 95% confidence, that there were 3 true positive reports, 12 false positive reports, and no false negative reports of decreased RBC ChE, and one false negative report and no positive report of decrease plasma ChE. The authors pointed out that a knowledge of preexposure ChE activities is necessary for any degree of accuracy in determining whether a particular individual's ChE's have been altered, but that their tolerance limits may be useful in interpreting measurements of ChE activities in blood samples submitted at random from the field.

The two populations differed somewhat in mean age: 30 years for the unexposed group and 38 years for the group of agricultural workers. Fryer et al did not give any further identification of the test populations by sex or race or give any indication of other possible exposures that might have affected blood ChE levels except that they ruled out recent known exposure to OP insecticides.

The most striking, and perhaps the most significant, difference between the handling of the blood samples from the two groups was that those from the agricultural workers were not refrigerated for about 6 hours after their collection and during that time were subjected to some agitation. The finding that the unexposed individuals had a higher mean RCB ChE activity and a lower mean plasma ChE activity than the agricultural workers could mean that their blood samples underwent slight hemolysis during transport to the laboratory. Such an effect could contribute to the false negative reports of decreased RBC ChE but would not increase the ChE activity of the plasma sufficiently to explain the excess activity there in the group of agricul-

tural workers. Some other factor seems to be involved, therefore, in generating the differences between the two groups.

Even though the effect of these limitations cannot be assessed, the estimates by Fryer et al[172] of normal daily variations in plasma (9%) and RBC (5%) ChE activities among individuals are in approximate agreement with those determined by Callaway et al[135] and Wetstone and LaMotta.[154] Callaway et al[135] found that the daily variations in the plasma and RBC ChE activities of normal, healthy men were 8.5% and 6.6%, respectively. Wetstone and LaMotta[154] reported that the overall intra-individual variation in serum ChE activity for 82 subjects tested 373 times during a 1- to 250-week interval was 8.4%. In 1975, Sidell and Kaminskis[187] reported on the temporal variability of human ChE. Twenty-two subjects were studied during a 1-year period. The coefficients of variation for plasma ChE activity were reported to be about 6% for both males and females. In agreement with previous investigators, the authors found that the activity of the RBC ChE was more constant; the average coefficient of variation was 2.1% for males and 3.1% for females.

Based on the aforementioned experimental evidence, depressions in plasma and RBC ChE activities less than 36% and 22%, respectively, from mean normal values can be due to normal daily variations. Another important consideration in selecting a particular percentage level of blood ChE depression for both worker protection and compliance purposes is the correlation between blood ChE activity depression and the appearance of signs and symptoms of parathion poisoning. The level of depression to be tolerated must be such that it will demonstrate that an exposure to parathion has occurred before the worker actually becomes ill and allows immediate steps to be taken to correct the situation leading to the exposure. It is important also that the worker not be removed from his job unnecessarily, so that a warning level of RBC ChE depression and an action level, at which the worker must be removed from potential exposure, seem desirable.

In general, the literature indicates[11,18,34,35,37,38,52,79] that normally only at depressions of plasma and RBC ChE activities considerably greater than 30% do signs and symptoms of systemic parathion poisoning appear in individuals. Certain degrees of depression of blood ChE activities are not accompanied by a significant prevalence of local or systemic effects.

In the study by Brown and Bush,[79] exposure to parathion of 5 of 12 workers in a manufacturing/formulating plant resulted in average depressions of plasma of 34% and RBC ChE activities of 61%, without the appearance of signs and symptoms of poisoning.

Rider et al[34] observed depressions in plasma ChE of 50%, 52%, and 54% in 3 subjects receiving daily oral doses of 7.5 mg parathion for approximately 30 days without signs and symptoms of poisoning. In these same individuals, the lowest RBC ChE activity levels observed during the study were 63%, 78%, and 86% of pretest levels (ie, depressions of 14-37%).

In 4 female volunteers receiving 7.2 mg parathion/day orally, the plasma and RBC ChE activities declined to 84% and 63%, respectively, of control activity after 6 weeks of exposure.[35] Neither signs nor symptoms of poisoning occurred in these subjects.

Hartwell and associates[37] observed no signs or symptoms of poisoning in a volunteer exposed for 30-minute periods on each of 4 consecutive days to vapors of heated parathion when the RBC and plasma ChE activities were depressed 30% and 53%, respectively. However, signs of parathion poisoning appeared in the subject 10 minutes after the parathion was mistakenly heated to 150 F; a subsequent determination of blood ChE activity levels indicated that RBC and plasma ChE were depressed 98% and 83%, respectively.

Plasma and RBC ChE activity levels were depressed 98.6% and 93.3% respectively, from normal, in a 15-year-old girl suffering from parathion poisoning.[52] Prior to blood ChE activity determinations, she exhibited the following signs of parathion poisoning: shallow and irregular respiration, constricted pupils, low systolic blood pressure, inspiratory rales in all lung fields, muscle fasciculations in the limbs, and bronchopharyngeal secretions, among others.

Grob et al[18] studied the effects of parathion on 40 men and women who had been exposed to the compound on one or more days during the month preceding the appearance of symptoms. Only 5 of the 40 (12.5%) poisoned individuals experienced any "warning" symptoms, including intermittent nausea, vomiting, giddiness, weakness, drowsiness, and twitching of the eyelids, prior to the day on which severe signs and symptoms appeared. The average period of exposure was 8 hours/day for 12 days. Six men died, 2 men and 2 women experienced severe but not fatal symptoms, and 24 men and 6 women had mild to moderate symptoms. Four patients who survived despite severe symptoms and 2 who died had plasma and RBC ChE depressions (compared to normal values) of

95% or greater and 78-89% (average 86%), respectively. These values averaged 90% and 78%, respectively, in 6 other subjects with symptoms of moderate degree.

Hartwell and Hayes[38] reported the case of a pilot who became ill with mild poisoning after applying both dust and liquid forms of parathion intermittently for severals days; his RBC and plasma ChE activities were depressed 48% and 44% from normal, respectively, measured on the day of onset of illness. RBC and plasma ChE activities were depressed 34% and 28%, respectively, in a second pilot engaged in crop-dusting who complained of excessive sweating and a mildly upset stomach.

In a group of 4 workers exposed to parathion residues during apple thinning, in whom signs and symptoms of parathion poisoning occurred, RBC and plasma ChE activity depressions ranged from 61-66% and 71-83%, respectively.[11] The enzyme activities were measured by the Michel method 2 days following the onset of symptoms (percent depressions were calculated using the mean values for the Michel method determined by Rider et al).[145] Nausea, vomiting, sweating, weakness, shortness of breath, headache, giddiness, and twitching of the eyelids were seen in these workers.

Important conclusions can be evolved from the preceding discussion: (1) there may be day-to-day variations in both the RBC and plasma ChE's of normal, healthy individuals,[58,135,154,172] and (2) signs and symptoms of chronic systemic parathion poisoning usually do not appear in humans until these enzyme activities are depressed by about 50% below normal levels.[11,18,34,35, 37,38,52,79] Even greater depressions of the ChE's of the blood may be incurred without the appearance of signs or symptoms of poisoning by parathion.

In many cases, individual worker preexposure blood ChE activity values will not be available, thereby necessitating the use of mean values determined for normal populations. Because of the fact that both the individual preexposure and group mean activity levels will be used as the situation warrants, it would be arbitrary to set an allowable level of blood ChE depression based solely on the variation calculated for 95% of the population at a 95% confidence level, namely, approximately 22% and 36% for RBC and plasma ChE, respectively. Therefore, in the case of RBC ChE, a depression exceeding 30% of the worker's baseline value will be considered as indicating excessive exposure to parathion. Only the RBC ChE is recommended for routine monitoring for the following reasons. Although the results of studies[18,34,81,103] involving animals and human volunteers have shown that plasma ChE is inhibited more promptly and to a greater extent than the RBC enzyme in individuals initially exposed to parathion. The rate of return of inhibited plasma ChE exceeds that of the RBC enzyme so that, during a period of consistent but moderate exposure, the ChE activity of plasma may actually be greater than that of the RBC's. [18] Grob et al,[18] in their study of 18 workers poisoned by parathion found that plasma ChE increased at an average rate of approximately 9% of normal activity during each of the first 3 days following termination of exposure, while the RBC ChE activity increased at an average daily rate of approximately 3%. However, averaged over the entire period of recovery, the rates of return approximated 1-2%/day and 3-4%/day for RBC and plasma ChE's, respectively. Thus, under certain exposure situations, the plasma ChE activity could return to normal while the RBC ChE activity remained depressed. For this reason, it is more likely that excessive absorption of parathion resulting from relatively low-level repeated exposure can be detected by routinely monitoring for RBC ChE activity. In addition, the plasma enzyme is subject to greater normal daily variation than the RBC ChE, approximately 9% versus 5%, respectively.[172] Previously, we have pointed out that the plasma ChE can be lowered in individuals with liver disease, anemia, debilitating disease, or malnutrition; drugs such as quinine,[76] morphine, and codeine[77] also depress the plasma ChE activity. Thus, monitoring plasma ChE activity increases the likelihood of false positive results. On the other hand, the RBC ChE has not been shown to be affected by such diseases; a depression in the RBC ChE activity exceeding normal variation in parathion-exposed workers is almost certainly due to the effects of the insecticide. A similar reduction in the activity of the plasma enzyme is considerably less certain to be due to exposure to parathion. Therefore, routine monitoring of RBC ChE will provide a better estimate of exposure to parathion. However, an RBC ChE monitoring program based on a preset sampling frequency should be effective in detecting the slow development of systemic parathion poisoning due to progressive inhibition of the activity of AChE at various sites throughout the body; it is intended to warn of excessive parathion absorption in a situation involving long-term, low-level exposure. Routine RBC ChE monitoring will not, in all likelihood, provide a warning of impending poisoning from massive exposures, resulting in precipitous declines in both the blood and tissue ChE's, such as in the case of inhalation exposure to high concentrations of parathion dust

or aerosol or dermal exposure to spills, sprays, or splashes of concentrated material on the skin or clothing. Also, since relatively nonsevere signs and symptoms of cholinergic stimulation can occur as the result of localized effects of parathion exposure, a biologic monitoring program based on the activity levels of the blood ChE's may not prevent or warn of the development of such signs and symptoms under certain exposure conditions. For example, miosis and blurred vision can result from direct exposure of the eyes to parathion, local fasciculations can occur in the immediate area of absorption of parathion from the surface of the skin, and bronchial secretions can result from respiratory exposure, all in the absence of significant effects on the blood ChE's. Good work practices and the use of personal protective clothing and equipment will best serve to protect workers from such effects, particularly those resulting from accidental spills, sprays, or splashes. Also, since the plasma ChE is inhibited more readily than the RBC ChE[18,34,87,103] under acute exposure conditions, the plasma ChE activity may decline precipitously in massive exposure situations while the RBC enzyme at first is relatively uninhibited. Therefore, in cases of known or suspected parathion overexposure (ie, exposure to either airborne concentrations exceeding the environmental limit or to spills or splashes, etc), both the RBC and plasma ChE activities should be determined.

Kay et al[58] demonstrated that workers engaged intermittently in the ground spraying of parathion experienced significant seasonal declines in blood ChE activities. They found no significant difference in the RBC ChE activity levels between sprayers reporting symptoms of parathion overexposure and those apparently symptom-free. However, the plasma ChE activity was 20% lower in the group with symptoms of parathion overexposure than in those not complaining of symptoms. The sprayers were exposed for a few days during each 10-day interval over a 2-month period. Airborne parathion concentrations collected in the operators' breathing zone ranged from 2.0 to 15.0 mg/m^3. Erythrocyte and plasma ChE activities were determined both during and subsequent to spraying in order to establish normal activity levels. These results of intermittent exposure demonstrate the hazard involved in a continuous exposure to airborne concentrations of parathion in the range of 2.0 to 15.0 mg/m^3. Concomitant dermal exposure, which is significant in the application of parathion,[46] compounds the hazard.

The only reported study of parathion exposure in industry in which both air samples indicating significant exposure and RBC and plasma ChE monitoring showing biologic response were obtained is the often-cited work of Brown and Bush.[79] Thirteen workers in a plant manufacturing concentrated parathion and dusts of varying concentration were studied. Twelve of the 13 workers were exposed to airborne concentrations of parathion ranging from 0.1 to 0.8 mg/m^3 (0.1 mg/m^3 being the lower limit of detectability) as determined using sintered glass absorbers, midget impingers, and Greenburg-Smith impingers. Six general location and 6 worker breathing zone air samples were collected. The average airborne parathion concentration for 8 sampling sites was 0.2-0.3 mg/m^3. Because of rotation of plant personnel, the workers were only intermittently in contact with parathion-contaminated air. Both plasma and RBC ChE activity levels were determined during a 10-month period; however, preexposure control values had been obtained for only 6 of the 12 parathion-exposed workers. A maximum of 3 blood samples was collected during a 5-month exposure period; control values for the other exposed workers were determined from blood samples collected 5 months after the end of exposure. Five of the 6 workers with preexposure ChE activities experienced the following depression of plasma and RBC ChE activities, respectively: 22% and 73%, 7% and 42%, 46% and 63%, 52% and 60%, 41% and 66%. The reductions in plasma and RBC ChE activities averaged 34% and 61%, respectively. An engineer in the plant, the sixth worker for whom baseline blood ChE values were available, experienced no significant decline in blood ChE activities. Several other workers for whom no preexposure ChE activities had been obtained appear to have exhibited significant depressions in blood ChE activities. The results of this study indicate that continuous exposure to airborne parathion in a concentration range of 0.1-0.8 mg/m^3 may pose a hazard to the health of workers. However, the data do not provide firm evidence of what airborne concentration of parathion, if any, in this range constitutes a safe exposure. The results obtained by Brown and Bush[79] can be used only to indicate a suspected unsafe continuous exposure level to airborne parathion, namely, the average value obtained for the 8 sampling sites, or approximately 0.25 mg/m^3.

In the absence of additional published data similar to that of Brown and Bush[79] upon which an environmental standard for parathion can be directly based, an indirect estimate based on extrapolation from a demonstrated safe daily oral

dose in humans must be made.

Rider et al[34] administered parathion to human volunteers at dosages of 3.0, 4.5, 6.0, and 7.5 mg/day. Each phase of the study was conducted on groups of 7 subjects, 5 of whom served as test subjects and 2 as controls. The study was divided into three periods: (1) a pretest period of approximately 30 days during which normal plasma and RBC ChE activities were determined; (2) an approximately 30-day test period during which parathion was taken orally by the subjects; and (3) a post-test period. Plasma and RBC ChE activities were measured twice each week throughout each phase. None of the subjects receiving the two lowest daily dosages, 3.0 and 4.5 mg, exhibited significant depressions in either plasma or RBC ChE activities. The investigators reported a slight but unspecified depression in plasma ChE activity in the group receiving 6.0 mg/day. Significant depressions in blood ChE activities occurred in the group receiving 7.5 mg parathion/day. Sixteen days after the start of dosing the plasma ChE activities of 2 of the 5 subjects were 50% and 52% of pretest levels, at which time administration of parathion to them was discontinued. On day 23, a third subject had a plasma ChE activity equal to 54% of his pretest level and parathion exposure was terminated. Subjects 4 and 5 completed a 35-day dosing period during which time plasma ChE activities of 78% and 86% of normal were the lowest observed. In the 3 subjects in whom the administration of parathion was discontinued because of significant plasma ChE depressions, the lowest RBC ChE activities observed were 63%, 78%, and 86% of the pretest values. No significant reduction in the RBC ChE activity occurred in the remaining 2 subjects. No signs or symptoms of parathion poisoning were reported. The results of this experiment demonstrated that the daily oral ingestion of 7.5 mg of parathion by humans resulted in a progressive and substantial depression in the activity of the blood ChE's, particularly the plasma enzyme, and thus constituted an unsafe oral exposure. In addition, the oral ingestion of 4.5 mg of parathion/day was shown to be a safe dose for man, exerting neither progressive depression of blood ChE activities nor clinical signs of illness in the subjects. Insufficient information was provided by the authors to determine the results of oral intake of 6.0 mg parathion/day.

In a similar manner, Edson[35] determined the effects of prolonged administration of small daily doses of parathion in man. Human volunteers were given parathion 5 days/week, for 25- to 70-day periods, at various dose levels. Whole blood, RBC, and plasma ChE activities were measured at various times. Daily ingestion of 0.6, 1.2, 2.4, and 4.8 mg parathion by human volunteers resulted in no significant effects on whole blood ChE activity. However, in 4 women receiving 7.2 mg parathion daily, 5 days/week, whole blood ChE activity declined to 67% of control activity after 6 weeks. At this time, RBC and plasma ChE activities were 84% and 63% of control levels, respectively. Within 28 days of withdrawal of parathion, whole blood ChE was restored to approximately 87% of control activity. Thus, the daily oral intake of 4.8 mg of parathion was shown to be safe for humans based on response of the blood ChE activity. The maximum daily no-effect level was estimated by the authors to be 0.05 mg/kg.

Rider et al[36] administered parathion, in capsules, to human volunteers in daily doses of 0.003, 0.010, 0.025, and 0.050 mg/kg. The study consisted of four successive 3-week treatment periods within a 12-week span during which 8 of 10 subjects were given the 4 doses of parathion. Baseline blood ChE activities were measured during a 3-week pretreatment period; weekly measurements were made during the periods of daily dosing. No significant depressions in either plasma or RBC ChE activities resulted from any of the 4 dosages of parathion. No adverse effects were observed in any of the volunteers.

Thus, the results of studies conducted by Rider et al[34,36] and Edson[35] demonstrate that parathion can be ingested by humans in a daily dose of 0.05 mg/kg without signs or symptoms of parathion poisoning and significant inhibitory effect on the blood ChE activities.

As a first step in calculating a no-effect (based on blood ChE activity response) respiratory dose from a safe oral dose, the assumption must be made that all parathion inhaled, particulate as well as vapor, is retained in the respiratory system and subsequently absorbed. Although such an assumption is not supported by the accumulated scientific evidence, it is necessary in order to account for all possible exposure situations. Also, calculations of the environmental limit based on 100% retention and absorption of inhaled parathion, in vapor and particulate form, provide the greatest possible margin of safety for employees exposed to this extremely toxic insecticide. An approximation of the ratio of respiratory toxicity to oral toxicity of parathion in humans is essential to the determination of a safe respiratory dose. As discussed previously, the human respiratory parathion exposure study of Hartwell et al[37] cannot be used in determining this ratio because the amounts of parathion

inhaled by the subjects were not determined by air sampling procedures but rather by extrapolation from the amount of PNP excreted in the urine. The results of other studies[105,108] in which both airborne parathion concentrations and blood ChE activities were measured are also inadequate for determining this ratio. Thus, to determine the respiratory-to-oral toxicity ratio for parathion in man, an extrapolation must be made from experimental animal data. The LCt50 (20-minute exposure) in mice was found to be about 3,800 mg min/m^3, according to a written communication from BP McNamara in October 1973. Using a ventilation rate of 0.023 liter/min and an average weight per mouse of 19.8 g,[188] this corresponds to an LD50 (inhalation) of 4.4 mg/kg. The oral LD50 of parathion in mice has been reported in the range of 18.5-20.0 mg/kg.[189-191] Thus, the ratio of respiratory to oral lethality of parathion in mice was about 0.23 to 1, or, in other words, parathion in these studies, under the existing experimental conditions, was approximately 4-5 times more lethal by inhalation than by ingestion.

As stated previously in Chapter III, it is not scientifically sound to extrapolate from minimal inhalation data in mice to a safe inhalation exposure concentration (ie, environmental limit) in man. Accordingly, the Toxicology Division, Edgewood Arsenal, Md, undertook studies of the inhalation and oral toxicities of parathion for rats and dogs. A thorough discussion of the study and results are presented in Chapter III and Appendix XV.

Groups of 34 rats were exposed for 4 hours to parathion in aerosol form at 13 concentrations ranging from 0.04 mg/m^3 to 35.0 mg/m^3. The RBC ChE50 and plasma ChE50 values, with 95% confidence limits, were calculated to be 5.43 mg/m^3 (range 4.2-7.03) and 7.28 mg/m^3 (range 5.24-10.12), respectively. The RBC and plasma ChE50 values for adult male rats exposed acutely by the oral route were 2.58 mg/kg (range 2.12-3.14) and 2.55 mg/kg (range 2.12-3.05), respectively. The approximate average weight of the rats used in these experiments was 250 g. For white rats of this weight, the average ventilation rate has been reported to be about 0.10 l/min. Thus, based on inhalation and oral RBC ChE50 values for the rat, parathion appears to be approximately 5 times more effective by the inhalation route than by ingestion in adult male rats. The corresponding value for plasma ChE was found to be approximately 3.6.

Because of the pronounced effects observed on blood ChE's at the airborne concentrations of parathion used, acute (ie, 4-hour exposures) inhalation ChE50 values for RBC's and plasma were not obtained for dogs. However, in the acute oral studies, groups of 4 dogs were exposed to 7 dose levels of parathion ranging from 0.5 to 10.0 mg/kg. The RBC ChE50 was determined to be 1.50 mg/kg (range 1.06-2.12) while the plasma ChE50 was found to be 1.67 mg/kg (range 0.94-2.96). The RBC and plasma ChE50 values for adult male beagle dogs do not appear to be significantly different from the corresponding values for male rats. Likewise, the oral LD50 for dogs determined in these experiments, 8.27 mg/kg, is not greatly different from the oral LD50 of 6.85 mg/kg determined for rats. The data strongly suggest that parathion is approximately equitoxic to both species. Thus, because of the close agreement between the results obtained from the acute oral studies in male rats and male dogs, particularly the ChE50 determinations, the assumption is made, as a first approximation, that parathion is about 4 to 5 times more effective by inhalation than by ingestion in inhibiting RBC and plasma ChE of dogs. Some confirmation for this assumption is found in Tables XVI-5 and XVI-15. If a curve is drawn through the inhibition of RBC ChE produced by exposure to the 5 concentrations stated in Table XVI-5, it is seen that the 64% inhibition caused by an oral dose of 2.5 mg/kg (Table XVI-15) is reproduced approximately by a 4-hour exposure to a concentration of 23 mg/m^3. If these dogs weighed 12 kg (no weights are stated), they would be expected to breathe about 0.356 m^3 of air during the 4-hour exposure period. This would give an inhaled amount of 8.2 mg of parathion (0.68 mg/kg) with the assumption of 100% retention. The ratio of the oral dose to the estimated inhaled dose is then 2.5/0.68, or 3.7.

Because of the extreme mammalian toxicity of parathion and the number of illnesses and deaths associated with its use in agriculture,[6-8,10,11,13] it is essential to provide the highest safety factor indicated by the experimental data. Therefore, for the purpose of establishing a safe inhalation exposure concentration (ie, environmental limit) in man, an inhalation-to-oral toxicity ratio of 5 is indicated.

The no-effect respiratory dose (Dr) of parathion accumulated during a 10-hour workday is defined as

$$Dr = 10 \times Vp \times Ca$$

where:

Vp = pulmonary ventilation rate of an average worker in m^3/hr

Ca = mean airborne concentration of parathion in mg/m^3.

Based on the demonstrated[34-36] safe daily oral parathion dose for humans of 3.5 mg, calculated on an average-man weight of 70 kg, the no-effect respiratory dose is estimated to be 0.7 mg/10-hour working day. As stated previously, no-effect exposure levels are based on insignificant depression of either the plasma or RBC ChE's from exposure to parathion.

Table XVI-4 gives minute volumes applicable to metabolic levels ranging from sleep to maximum work. Based on these data, a reasonable inhalatory minute volume for a 10-hour exposure is 25 liters/min or 1.5 m^3/hour. This 25 liters/min is an approximately median value between light and medium work. Based on the spectrum of work activity observed in various manufacturing operations, in formulation, and in mixing and application involving parathion exposures, an average pulmonary ventilation rate of 25 liters/min should encompass the workers' respiratory exposure to parathion in vapor, aerosol, and dust form. The equation thus reduces to

$$Ca = \frac{0.7}{10 \times 1.5} = 0.05 \text{ mg/cu m}$$

In summary, the human no-effect concentration of airborne parathion based on 100% retention and subsequent absorption of inhaled material for a 10-hour workday, 5-day workweek, is estimated to be 0.05 mg/m^3.

Male rats subjected to parathion aerosol (average particle diameter of 1-2 microns) in a concentration of 0.10 mg/m^3 of parathion for 7 hours/day, 5 days/week, for 6 weeks in the Edgewood Arsenal study experienced no signs of poisoning at any time during the exposure or postexposure periods. As seen in Table XV-8 the RBC and plasma ChE activities after 5 weeks' of exposure were 67% and 92% of normal activities (determined from the activities in unexposed control animals), respectively. Exposure of male rats to parathion aerosol in a concentration of 0.01 mg/m^3 for the same period of time exerted no significant effects on blood ChE's. On the other hand, significant inhibition of both RBC and plasma ChE's occurred as the result of inhalation exposure of male rats to 0.74 mg parathion/m^3 of air breathed.

In adult male dogs exposed to parathion aerosol 7-hours/day, 5-days/week, for 6 weeks, the following results were obtained: a concentration of 0.001 mg/m^3 produced no significant inhibition of either RBC or plasma ChE's; one of 0.01 mg/m^3 also produced no significant inhibition of RBC ChE during the 6-week exposure period; but the plasma ChE activity was depressed to 58% of normal after 6 weeks' exposure. No signs of overt parathion poisoning were observed in any test animal; significant inhibition of both RBC and plasma ChE's occurred as the result of exposure to airborne parathion in a concentration of 0.20 mg/m^3. Two weeks' exposure to this concentration resulted in RBC and plasma ChE activities of 54% and 26% of normal values, respectively. After 6 weeks' exposure to 0.20 mg/m^3 of parathion, the corresponding values were 41% and 36%, respectively.

The results of these chronic exposure studies with male rats and dogs indicate that continuous exposure via inhalation to a concentration of parathion of 0.10 mg/m^3 in aerosol form results in significant inhibition of the blood ChE's. These data suggest that the environmental limit of 0.05 mg parathion/m^3, derived from inhalation-to-oral toxicity ratios in mice, rats, and dogs, and recommended as safe for employees exposed to parathion, is appropriate.

It may be argued that, on the basis of the results of Rider et al,[34] 4.5 mg represents a safe continuous daily oral dose of parathion rather than 3.5 mg. However, since the weights of the subjects were not given, unlike Edson's study,[35] 4.5 mg cannot be stated unequivocably to be a safe dose for the average (ie, 70 kg) man. A daily oral dose of 3.5 mg has been shown, in 3 separate studies,[34-36] to produce no signs or symptoms of parathion poisoning and no significant depression in either RBC or plasma ChE activity levels—a no-effect exposure level. Another major factor favoring a conservative approach in estimating a safe working lifetime exposure to parathion for up to 10 hours/day, 5 days/week—the likelihood of simultaneous absorption through more than one avenue of entrance into the body (skin and gastrointestinal tract, for example) of this toxic insecticide. As stated previously, it is extremely important to emphasize that the greatest danger to employees from exposure to parathion, under most conditions, is from SKIN CONTACT. Because of nonrespiratory hazards, such as those resulting primarily from skin contact and absorption, it is recommended that appropriate work practices and protective measures be required regardless of the airborne concentration of parathion. For this reason, "occupational exposure to parathion" has been defined as employment in any area in which parathion or materials containing parathion, alone or in combination with other substances, is produced, packaged, processed, mixed, blended, handled, stored in large quantities, or applied.

VI. WORK PRACTICES

Work practices are important for the control of exposures to parathion. This is particularly true because parathion is absorbed through the intact skin, mucous membranes, and eyes, as discussed in Chapter III. Therefore, every effort must be made to avoid contamination of the skin via direct spills, splashes, or spray/dust, and indirectly via contaminated clothing or other materials. Should such contamination occur, it is essential that the worker involved be taken immediately to an uncontaminated area and the contaminated clothing or equipment removed from the body, the skin and hair thoroughly and quickly washed with water (and preferably soap) or with other suitable decontaminating solution, a physician contacted, and the exposed worker placed under observation for at least 24 hours. Contaminated clothing and other articles should be appropriately labeled and safely stored until they can be washed or destroyed. The provision for basic sanitary facilities and their use is essential in minimizing dermal exposures to parathion as reflected in the recommendations in Chapter I, Section 7.

To protect against contamination by direct spills, it is recommended that workers handling parathion wear adequate protective clothing including impervious gloves, coveralls (covering entire body) or rubber aprons, impervious footwear, and a protective head covering. It is important that personnel such as shippers and warehousemen handling nonleaking sealed containers of parathion, such as drums, wear full-body coveralls and impervious gloves. The routine maintenance of this protective clothing and equipment, usually by daily washing, is essential. Hydrogen peroxide or hypochlorous acid (dilute) should be available to decontaminate badly contaminated clothing before its subjection to laundering.

Workers engaged in the formulation of parathion and in the mixing and loading of parathion solutions and dusts into application equipment may be exposed to relatively large amounts of concentrated parathion. In these situations, the likelihood of skin contamination through spills and splashes may be great depending on the protective clothing and equipment and engineering controls being used. In addition, because of the processes involved, fairly large concentrations of airborne parathion, primarily in particulate form (ie, droplets or dusts containing adsorbed parathion), may be generated. Airborne concentrations of parathion were found to range from 0.25 to 0.4 mg/m^3 in the breathing zone of workers filling 50-lb cartons with parathion dust in the study by Brown and Bush.[79] Airborne parathion concentrations measured during mixing and loading of water-wettable powder were reported to average 2.15 mg/m^3 in a mixing plant surveyed by Batchelor and Walker.[106] Air monitoring was conducted by Kay et al[58] while workers added 15% parathion wettable powder to spray tanks. A mean airborne parathion concentration of 21 mg/m^3 was found. Such exposures are normally of short duration; however, the level of exposure may be high enough to constitute a significant hazard. Where adequate vapor and dust exhaust systems are not feasible, such as in certain field situations, workers engaged in mixing or loading of parathion in liquid or powder (dust) form must wear a suitable respiratory protective device.

Direct contamination is also possible during spray operations. The results of studies conducted by Batchelor and Walker,[106] Jegier,[107] and Simpson and Beck[108] showed that respiratory exposures of spraymen ranged from 0.03-0.26 mg/m^3 in air-blast spraying of orchards and fields to greater than 0.1 mg/m^3 during use of hand knapsack sprayers on tomatoes. Kay et al[58] in their study of Quebec apple orchards measured airborne parathion concentrations ranging from 2 to 15 mg/m^3 during the use of either hand-type or mechanical-rocker type sprayers. High-pressure hand sprayers have generated 0.09 mg/m^3 levels of airborne parathion.[106] The spraying of concentrated parathion resulted in air levels ranging from 0.29 to 0.52 mg/m^3 and a calculated respiratory exposure of 0.055 mg/hour according to Braid et al[110] and Wolfe et al.[109] These results when compared to the estimated workplace environmental limit of 0.05 mg/m^3 demonstrate that applicators may need respiratory protection under certain situations. In addition, results of several of these studies[106-109] indicate substantial simultaneous dermal exposures. Therefore, under the specified conditions (see Chapter I, Section 4), respirators or masks approved for toxic dusts and organic vapors may have to be worn in addition to protective clothing, such as coveralls (covering entire body) or waterproof rainsuits, impervious gloves, impervious footwear, goggles, and a waterproof head covering. Waterproof or repellent parkas may be used to protect the head and neck simultaneously.

Pesticide drift is a common occurrence during the aerial application of parathion and other insecticides. Based on the results of studies conducted during the period 1961-69, Ware et al[192] concluded that aerially applied insecticides in Arizona apparently deposited less than 50% on-target during the normal period of use of insecticides. Many factors, including droplet size in the spray cloud, wind speed, and the altitude of aircraft during application, play an important part in pesticide drift. During these studies, Ware et al found that windspeed changed from less than 1 to 5.6 miles/hour. In 1972, Ware[193] reported that pesticide dusts deposited 9 times as much material on a field of alfalfa 0.5 mile from target as aerosolized emulsion preparations of the same pesticides sprayed from the same height and under similar wind conditions. The smaller particle size of the dusts resulted in a larger airborne time, which led directly to greater drift.

Braid et al[111] reported airborne parathion concentrations of 3.0, 0.85, 0.22, 0.07, and 0.03 mg/m^3, measured at downwind distances of 50, 100, 200, 300, and 400 feet, respectively, during the application of 1% parathion dust. Thus, at a distance of 300 feet from the application rig, the airborne concentration exceeded the recommended air standard.

To prevent spray contamination of other workers due to drift, it is recommended that spraying not take place when excessive drift onto adjacent property is likely. Workers, except flagmen, must be removed from areas, particularly the one to be sprayed, where contamination is likely because of either fallout or spraydrift. However, care must be taken to ensure that flagmen do not receive a direct application of the spray. In addition, exposed flagging personnel should wear coveralls or waterproof rainsuits, impervious gloves, and a protective head covering. All flagmen should also be provided with a respirator approved for use against toxic dusts and organic vapors and with goggles.

The recommendation that the work environment be maintained free of unattended equipment, clothing, refuse, or natural materials contaminated with parathion reflects the experience in agriculture, in particular, of the dangers inherent to parathion contamination. Ganelin et al[194] reported several cases of poisoning from contact with contaminated equipment. In one case, a worker became ill about 2 hours after washing an aircraft previously used for applications of organophosphorus pesticides. A second worker suffered a similar exposure but, in this case, the aircraft had already been washed once since the last application of parathion. A third illness occurred after a pilot had dismantled the hopper of his aircraft for maintenance. In this last case, although parathion had been applied previously in large quantities from this aircraft, only magnesium chlorate had been used for 2 weeks preceding the illness.

Although further cases illustrating the occupational hazards of a parathion-contaminated environment are easily found, it must be mentioned that such contamination may present a serious accidental hazard to children. Eitzman and Wolfson[195] reported the deaths of 30 children in Florida during the period 1959 to 1964 due to accidental parathion poisoning. Although the majority of these deaths resulted from ingestion, dermal absorption was implicated in 8 cases. One boy and his sister died and another brother became seriously ill after playing on a swing made from a cloth-filled burlap sack found later to be heavily contaminated with parathion. Two other poisonings occurred in older children and were occupationally related.

These incidents illustrate the potential hazards posed by parathion as an environmental contaminant if not properly handled, stored, and disposed of, to workers and their families. The case for the employee education requirements recommended in Chapter I, Section 6, rests primarily on experience and common sense. These requirements are currently common practice in many agricultural operations.

Fires and large-scale accidental spills of parathion in industrial areas or while in transport present obvious hazards. It is standard operating procedure to have plans for these eventualities in dealing with any toxic substance. In particular, in any emergency situation, it is essential to inform emergency control personnel of their potential exposure. To minimize the hazard to these groups and to workers routinely exposed to concentrated parathion, the labeling requirements in Chapter I, Section 3, are recommended, as are the several reporting and advisory requirements in Chapter I, Section 6.

In the industrial workplace, the procedures for exerting proper control over exposures to parathion are relatively standardized and do not require further elaboration other than to reiterate the obvious need for the provision and use of clean clothing daily, showers at the end of a work shift, and the use of appropriate sanitary practices.

In agriculture, the problems are much more complex because the site of use of the chemical is not fixed and access to the workplace cannot be

reliably restricted. Moreover, supervision of employees is more difficult, with resulting uncertainty in ensuring that appropriate work practices are followed. The last problem area demonstrates the importance of employee education.

The recommendations regarding employee education in Chapter I, Section 6, are quite general; in practice, however, the proper instruction must be quite specific. There are myriad details associated with the use and cleaning of goggles and respirators and with the appropriate emergency procedures to be used in the event of parathion spills or fires. Such details are covered in various pesticide safety manuals,[3,196] which contain the type of material that must be made generally available to employees exposed to parathion.

It is the employer's responsibility to be informed himself of the appropriate work practices and safety procedures and to make certain that employees know, understand, and practice those precautions appropriate to their own operations. Also, it must be made very clear to all employees that parathion is a highly toxic compound and that the various safety rules are based on long-standing experience and common sense. It cannot be overemphasized that proper employee education and attendant supervision are essential in minimizing the occupational hazards posed by parathion.