V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The American Conference of Governmental Industrial Hygienists (ACGIH) [137] proposed in 1969 that its recommended threshold limit value (TLV) for methyl parathion be set at 0.2 mg/cu m. Included was a "skin" designation to indicate that measures must be taken to minimize skin exposure so that the TLV is not invalidated. According to the 1971 TLV Documentation, [138] the basis for this level was the lower toxicity of methyl parathion than that of parathion observed in human and animal studies. However, the greater toxicity of the oxon derivative of methyl parathion was not addressed in the basis given for the TLV. The TLV for parathion had previously been set at 0.1 mg/cu m. References were made in the Documentation to two animal studies [33,43] and one human study. [139] The 1974 TLV [140] is unchanged from the 1971 TLV.

Gaines' study [33] cited in the ACGIH Documentation reported the oral and dermal LD50's of methyl parathion in rats. The oral LD50's for male and female rats were 14 mg/kg and 24 mg/kg, respectively, while they were 13 mg/kg and 3.6 mg/kg, respectively, for parathion. The dermal LD50 for methyl parathion in rats of both sexes was 67 mg/kg; the dermal LD50's for parathion were 21 mg/kg (males) and 6.8 mg/kg (females).

The study by Williams et al [43] cited by the committee was an oral experiment in which technical methyl parathion was administered in the diet to dogs in concentrations of 5, 20, or 50 ppm daily for 90 days. The authors reported that the 50-ppm concentration resulted in inhibition of both plasma and erythrocyte cholinesterases to 50-60% of control values.

However, although it was not noted in the Documentation, the erythrocyte cholinesterase activity was still declining at the end of the test period in the dogs exposed to both the 20-ppm and the 50-ppm concentrations in the diet. It is likely that during a treatment period somewhat longer than 90 days, the dogs fed 20 ppm would have experienced inhibitions of blood cholinesterases equal to that of the dogs fed 50 ppm and those fed 50 ppm would have shown still greater cholinesterase inhibitions. The 50-ppm concentration corresponds to approximately 70 mg/day for a 70-kg person.

The human study cited in the Documentation was one of a series performed by Moeller and Rider. [139] In this study, groups of five men each were given methyl parathion in corn oil orally in doses of 7, 7.5, 8, or 9 mg/day for 30 days. Even with the highest dose tested, both plasma and erythrocyte cholinesterase activities were between 80-100% of preexposure values.

The methyl parathion TLV was also supported by ACGIH with the statement that: "The safety record of methyl parathion is considerably better than that of parathion." [138] The significance of the dermal absorption route was recognized in the 1971 Documentation by the word "skin" immediately following the recommended atmospheric level. Text explaining the "skin" notation stated that "this attention-calling designation is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the threshold limit is not invalidated."

No standards governing the safe handling of methyl parathion by the American National Standards Institute (ANSI) or by the International Standards Organization (ISO) were found. Methyl parathion is not mentioned in the 1969 documentation of MAC's in Czechoslovakia. [141] The only

standard found governing methyl parathion exposure in a foreign country was the MAC for the USSR, 0.1 mg/cu m. [142]

Several states currently regulate the formulation, distribution, and use of pesticides. Of these, California presently has the most comprehensive regulations. In 1974, the California Department of Food and Agriculture issued pesticide-worker-safety regulations as reported by Maddy [132] for "moderately toxic" (Category 2) and "highly toxic" (Category 1) pesticides, but established no MAC or TLV levels. Methyl parathion was included in Category 1. From the 1,474 pesticide-related occupational illnesses reported in California during 1973, the occupations "mixer-loader" and "ground applicator" were identified as most hazardous. [132] The single most hazardous activity was reported to be the pouring of concentrates. Since California had no manufacturers (but many formulators) of methyl parathion in 1973, none of the reported illnesses could have been associated with the manufacture of technical grade methyl parathion. Thus, the identification of the most hazardous pesticide occupations bears that limitation, along with the absence of denominators for the high-risk job categories.

The California regulations applicable to pesticides in toxicity Category 1 provide for medical supervision, biologic monitoring, closed mixing and loading systems, and specific work practices, including supervised training, emergency procedures, minimum employee age for certain operations, changing room facilities, personal protective clothing and equipment, and restrictions on working alone. [132]

Summaries of activities of the various states in controlling the use of pesticides are presented in Appendices VI and VII.

Basis for the Recommended Environmental Standard

The recommended standard for methyl parathion includes (1) work practices and engineering controls designed to prevent absorption of methyl parathion (especially through the skin), (2) procedures for periodic biologic monitoring to screen overexposed workers, and (3) a workplace environmental limit. In addition to these components of the recommended standard, the use of personal protective equipment and clothing also is recommended to reduce exposure of employees to methyl parathion by inhalation and dermal routes of entry. The toxicity of methyl parathion by these routes of entry has been reported by a number of investigators. [16,17,76,143]

The study by Maibach et al [133] used 14C-labeled malathion, carbaryl, and parathion with urinary radioassays to determine the dermal penetration of these pesticides when applied to different sites of the human body. All anatomic sites studied--forearm, palm, ball of the foot, abdomen, hand dorsum, fossa cubitalis, scalp, jaw angle, postauricular area, forehead, ear canal, axilla, and scrotum--showed significant penetration of the substances tested. While absorption rates and efficiencies derived in this study are not directly applicable to methyl parathion, it is likely that methyl parathion would also be absorbed from all these regions. Therefore, personal protective equipment and clothing, which will limit exposure of most, if not all, portions of the body, are recommended. Goggles and faceshields are recommended to limit eye and facial exposure to the pesticide. The use of respirators may be necessary during emergencies and during installation, testing, and maintenance of engineering controls.

Work practices and engineering controls afford additional protection to the worker by minimizing inhalation of, or exposure of the skin to, methyl parathion. Work practices are recommended to control or reduce exposure resulting from spills, splashes, leaks, or other inadvertent release of methyl parathion into the workplace environment. Engineering controls, such as the use of closed manufacturing, formulating, mixing, and loading systems, should further reduce exposure resulting from accidental release of the pesticide in the workplace.

Employees should be informed that even small amounts of methyl parathion can be hazardous and should be instructed as to the proper workplace practices. The use of good work practices and of personal protective equipment and clothing may be affected by behavioral attitudes and environmental and other conditions. Increased environmental temperatures or extremely humid environments may cause workers to avoid using certain protective equipment. When workers become fatigued as a consequence of long workdays, which may be encountered during peak formulation and application seasons, they may fail to use good work practices. Instructions to workers, therefore, should emphasize that deviation from the recommended work practices, including improper use of protective equipment and clothing, even for brief periods of time, may be dangerous.

Compliance with these recommended work practices and engineering controls as well as with the recommended workplace environmental limit for methyl parathion should limit worker exposure to this pesticide. However, available data are inadequate to establish the significance in the causation of occupational poisoning by methyl parathion of mixed active

ingredient formulations or succesive exposures to residues of single- or multiple-ingredient formulations containing methyl parathion. Exposure of the worker to anticholinesterase compounds, in addition to methyl parathion, may pose a hazard because of the cumulative effects of cholinesterase inhibition. To assess these effects in asymptomatic persons, individual monitoring is necessary.

The method of personal biologic monitoring best suited for detection of asymptomatic, progressive poisoning by anticholinesterase compounds is the periodic assay of erythrocyte cholinesterase activity. Erythrocyte cholinesterase is found in all human beings, and its activity is relatively consistent and reproducible. Determination of erythrocyte cholinesterase activity can give guidance to the physician in deciding whether an exposed worker requires extended observation, removal from the job, treatment as an outpatient, or intensive treatment. This enzyme is also affected by other organophosphorus pesticides and, thus, will aid in determining whether overexposure from other pesticides commonly found in areas of exposure to methyl parathion has occurred.

It should be emphasized that biologic monitoring will not prevent poisoning but does provide an indication of the degree to which an individual has been exposed. In addition, it may help to identify those workers exposed to low doses of methyl parathion who presently are asymptomatic but may become symptomatic because of possible cumulative effects of repeated exposure to the pesticide.

To be of protective value, biologic monitoring must be performed frequently to detect short-term increases of susceptibility to further exposure caused by changes in work activities, defective equipment,

carelessness, and changes in environmental influences. The scheme of biologic monitoring proposed by the California State Department of Health (see Appendix VI and references 132 and 144) appears inadequate in one respect: it suggests a longer interval between consecutive examinations of blood for workers exposed to Category 1 or 2 compounds for up to 2 days/week than for those exposed 3 days/week or more, without having demonstrated lessened hazard to the first group or any other supporting evidence for this difference. NIOSH recommends an interval between tests of 2 weeks for mixers, loaders, ground applicators, aerial applicators, flaggers, maintenance and janitorial personnel, checkers entering fields still wet from an application, and for manufacturing or formulating employees not working with closed production, mixing, blending, transfer, or packaging systems. If any workday exceeds 12 hours, an employee covered by the 2-week testing interval should be tested at 1-week intervals until a week passes in which no workday exceeds 12 hours. NIOSH recommends that all other employees occupationally exposed to methyl parathion, including but not limited to those indicated in Table XVI-3 but not assigned to the above 2-week interval between blood samples, be tested at 4-week intervals. Times specified here should be construed as maximum test intervals which should be shortened when conditions warrant.

A workplace environmental limit for methyl parathion has been chosen on the basis of a careful review of the available literature on the pharmacologic and toxicologic effects of this and related pesticides on animals and on humans. The literature on the toxic effects on humans of occupational exposure to methyl parathion is, however, incomplete. In addition, information is unavailable on the experimental effects of human

respiratory exposure to methyl parathion. Moreover, data which would indicate the fraction of inhaled methyl parathion actually absorbed are unavailable from epidemiologic or other studies of workers exposed to this pesticide in an occupational environment. No data were found which would allow estimation of the deposition of droplets of methyl parathion in the various sections of the respiratory apparatus from the environmental air. Data are scanty on how factors such as airstream behavior, particle size and shape, and physiologic parameters affect deposition of methyl parathion in the lungs. The mechanism by which ciliated epithelium affects the clearance of methyl parathion from the lungs is poorly understood. Furthermore, there are inadequate data on the extent of individual variation in impaction, coalescence, and absorption of particulates within the tracheobronchial tree and the alveoli of the lungs.

In contrast, the information on parathion is more extensive than that on methyl parathion and includes inhalation studies with humans [145] and with rats and dogs (Unpublished report, Edgewood Arsenal, Md, 1976), as well as studies on the toxicity of parathion by other routes in other species. These studies were used by NIOSH to recommend a TWA workplace environmental limit of 0.05 mg/cu m for parathion. Reports have been found that compare the effects of methyl parathion with those of parathion on rats [33,35,37,39,138,146] and on humans. [20-28]

Table V-1 presents a summary of several studies wherein the acute toxicities to rats of methyl parathion were compared with those of parathion.

TABLE V-1

COMPARISON OF ACUTE TOXICITIES OF PARATHION AND METHYL PARATHION IN RATS

Routes of Exposure	Sex	LD50 (mg/kg) or LC50 (mg/l)		Toxicity Ratio	Reference
		Parathion	Methyl Parathion		
Inhalation (1 hr)	Female	0.115	0.2	1.7	35
po	"	3.6	24	6.7	33
	"	7.9	18	2.3	37
	Male	13	14	1.1	41
	"	13	14	1.1	33
	"	14	12	0.9	37
iv	Female	4.5	14.5	3.2	37
	Male	6.4	9.0	1.4	37
ip	-	5.5	3.5	0.6	146
	Female	2.7	7.4	2.7	42
	Male	4.8	6.8	1.4	42
	Male (adults)	3.6	5.8	1.6	39
	Male (weanlings)	1.5	3.5	2.3	39

Although there is considerable variation between the ratios of toxicities found by different authors, the data show that methyl parathion is generally less toxic than parathion. A sex-related variation is also apparent. This agrees with the observation of Hayes [147] that the rat shows a particularly marked variation between the sexes in its response to chemicals. Variability in responsiveness to drugs and chemicals is not uncommon in animals. It may be related to inherent differences in enzyme activation and inactivation mechanisms, to differences in experimental

designs and procedures between laboratories, or to the differences in purity of the chemical used.

However, these data indicate a trend in a number of acute toxicity studies carried out in rats which, based on toxicity ratios, show that methyl parathion is less toxic than parathion. This trend was confirmed by Newell, [37] who showed that methyl parathion was considerably less toxic than parathion in female rats administered the insecticide by oral, intravenous, dermal, and inhalation routes. In the same study, methyl parathion was reported to be also less toxic in male rats by the intravenous and dermal routes; however, methyl parathion was almost seven times more toxic than parathion by inhalation. The methyl parathion used in Newell's study was stated to have been 70-80% pure, whereas the parathion was said to have been 88-94% pure. There is the possibility, then, that the methyl parathion may have contained approximately 15% more of some comparatively toxic contaminant than the parathion. Furthermore, the fact that Newell's data for the inhalatory toxicities of parathion and methyl parathion for female rats agrees reasonably well with those of Kimmerle and Lorke, and that only those estimated for parathion for male rats differ greatly from those of the latter authors, raises a question about the validity of Newell's results for the male rat. These two areas of uncertainty about Newell's study lead NIOSH to feel uncomfortable with Newell's conclusion on the toxicity of parathion for male rats exposed to the insecticide by inhalation.

The series of studies by Rider and his colleagues [20-28] compares the anticholinesterase activity of parathion and methyl parathion in humans. These data show that the oral doses of methyl parathion and

parathion required to reduce erythrocyte cholinesterase activities by 25-30% in men are about 30 mg/day and 7.5 mg/day, respectively. These figures lead to an estimate that methyl parathion is one-fourth as toxic as parathion. By applying this estimate to the recommended environmental limit of 0.05 mg/cu m for parathion, a level of 0.2 mg/cu m for methyl parathion is derived. This is the same level as the TLV currently recommended by the ACGIH. NIOSH recognizes the limited value of developing an occupational exposure limit from comparative oral data in humans and toxicity data in rats and in dogs. Nonetheless, in the absence of solid evidence that it would be unsafe, and on the basis of the relatively safe work history of methyl parathion, NIOSH recommends a TWA workplace environmental limit of 0.2 mg/cu m.

It should be noted that the contribution to human toxicity of isomers of the oxon form of methyl parathion has not been considered in development of the proposed standard, because of the scarcity of information on the occurrence of these forms of the parent substance. Adherence to the recommendations in this standard on work practices and personal protective equipment and clothing will help to reduce exposure to these more toxic analogs as well as to the parent compound.

VI. WORK PRACTICES

Occupational pesticide exposure may occur by skin penetration (including through cuts and abrasions), through inhalation, and by ingestion. [148] Methods for preventing exposure by these routes have been discussed by several investigators and groups interested in occupational safety and health. [12,127,142,148-158]

According to Wolfe, [149] over 97% of the pesticide to which the body is subjected during most application processes is deposited on the skin. Wolfe [149] stated that, in parathion spraying operations, skin exposure was potentially 950 times greater than respiratory exposure. Feldmann and Maibach [159] indicated that the spraying or dusting of pesticides may result in the deposition on exposed skin surfaces of an amount of pesticide 20-1,700 times greater than that which reaches the respiratory tract. Studies by Nemec et al [76] showed that as much as 10 mg of methyl parathion was deposited on the arms and hands of cotton checkers entering a field 2 hours after spraying with ULV equipment. The ULV technique involves application of volumes of 0.5 gallon or less/acre. This technique was reported [160] to deposit more insecticide on crops than higher-volume, water-emulsion sprays and to provide longer residual toxicity. Exposure for a 5-minute period at 2, 24, and 2 hours, respectively, after three consecutive weekly ULV applications to the same field resulted in erythrocyte cholinesterase inhibition of approximately 30% (from 90 to 60% of baseline). From these studies, [76,149,159] it is evident that a program of sound work practices, including the use of personal protection

items, must be followed to minimize skin exposure to methyl parathion.

Wolfe [161] recommended that long-sleeved outer clothing, such as coveralls, be washed daily. The author noted that rubberized or plastic waterproof clothing may be too uncomfortable for outside use because of trapping and absorption of body heat. Wolfe [161] also recommended unlined rubber gauntlet gloves, a wide-brimmed waterproof hat, and waterproof shoes or boots. According to the author, use of goggles and a respirator would offer protection from absorption of pesticide through facial skin. If high environmental temperature precludes the use of such items, other means of protection must be used.

All equipment, surfaces, and objects that become contaminated with methyl parathion must be decontaminated with 5% sodium carbonate, or with solutions of equivalent or superior decontaminating capability, to prevent employee exposure. Finley et al [162] reported that alkaline media hydrolyze methyl parathion to PNP. It has been observed [12] that periodic and emergency decontamination procedures utilizing strong alkaline solutions are commonly accepted practices in methyl parathion industries. Finley and Rogillio [163] and Finley et al [162] found that machine washing of cotton clothes contaminated with methyl parathion was effective in reducing residues. Normal laundering removed 99% of the methyl parathion applied to cotton-polyester fabric and 93% of that applied to an all-cotton fabric. [163]

A second important occupational route of entry for methyl parathion is the respiratory tract. Since high levels of airborne methyl parathion may be encountered in uncontrolled atmospheres, [77] it is necessary that filtered air enclosures or personal respiratory protection be utilized as

specified in Chapter I whenever airborne concentrations cannot be limited by engineering controls to the recommended workplace air level.

A third route of methyl parathion exposure is the oral route. Every effort must be made to avoid contamination of foodstuffs, tobacco products, and other materials that are placed in or near the mouth. Prohibiting the carrying of food, tobacco products, gum, and candy, and requiring that hands and face be washed before eating and smoking are accepted practices in methyl parathion industries. [12]

Methyl parathion must never be stored in food containers or handled with food-dispensing equipment. This requirement is necessary to prevent poisoning of individuals unaware of the presence of methyl parathion or its residues.

Wolfe et al [164] and Mail et al [165] discussed the health problems presented by discarded pesticide containers and explained the necessity for decontaminating and destroying them. Information on proper methods of disposal is readily available. [37,165,166] Such methods are routinely practiced by methyl parathion formulators and applicators. [12]

Hayes [127] stated that employees exposed to insecticides should be informed of the pertinent hazards. Industrial experience indicates that written information on insecticides is often unavailable at the worksite. However, it is generally agreed that informing employees of the hazards from methyl parathion exposure is extremely important, [12] especially in view of the absence of exposure-limiting signs or symptoms early in the course of methyl parathion intoxication.

VII. RESEARCH NEEDS

Several aspects of current knowledge regarding the acute and chronic toxicities of methyl parathion need to be verified or extended. Studies should be performed to determine the effects of long-term exposure to methyl parathion, to methyl paraoxon, and to methyl parathion isomers. The concentration of methyl paraoxon and the S-alkyl isomer of methyl parathion in technical solutions, formulations, environmental residues, and air should be determined. Inhalation exposures due to different methods of application should be quantified. Although many studies have been reported on parathion, there is limited data on the absorption, distribution, metabolism, and inhalation toxicity of methyl parathion. Epidemiologic studies of occupationally exposed populations should be designed to develop more accurate and complete data on risk.

Of particular value to the improvement of existing work practices and of environmental monitoring would be (1) research toward providing a breakthrough indicator for respirator cartridges and canisters, (2) assessment of the effectiveness of soap and water for removing methyl parathion from skin, (3) determination of the protection afforded by different materials used for impervious protective clothing, (4) investigations into the contribution to methyl parathion toxicity of methyl paraoxon in occupational environments, (5) effects of elevated ambient temperatures on the absorption and toxicity of methyl parathion, and (6) research regarding the feasibility of using membrane filters for sampling

airborne methyl parathion.

Also of significant value would be investigations into improved biologic monitoring techniques.