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Estimating the Hazard to Humans Applying Nemacur 3EC With Rat Dermal-Dose ChE Response Data

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Contamination of ground water in California by the nematocide, DBCP (dibromochloropropane) resulted in the cancellation of its use. This regulatory action provided an opportunity for the introduction of a number of cholinesterase-inhibiting organophosphates (i.e., fenamiphos, 3-methyl-4-[methylthio]penyl-(1-methylethyl) phosphoroamidate, and ethoprop, O-ethyl S-S-dipropyl phosphorodithioate) and N-methyl carbamates (i.e., oxamyl, methyl 2-[dimethylamino]-N-[(methylamino) carbonyl] oxyl-2-oxoethanimidothioate, and carbofuran, 2,3-dihydro-2, 2-dimethyl-7-benzofuranyl methylcarbamate) as DBCP replacements.

Prior to the registration of these pesticides, California regulations required registrants to conduct mixer-loader and applicator studies to determine the effectiveness of application methods and protective clothing in protecting the health of workers. This study was conducted to determine the amount of fenamiphos workers are exposed to dermally and by inhalation during the course of the work day and to relate this exposure to the adverse effects observed in studies conducted in the rat.

METHODS AND MATERIALS

The workers were two mixer-loaders and two applicators employed by a pesticide application firm located in Fresno, California. The mixer-loaders transferred formulated fenamiphos (Nemacur 3EC, Mobay Agricultural Chemicals Division, Kansas City, Missouri) in five gallon containers via a closed-transfer system to spray-mix tanks (Knaak et al., 1980a), diluted and mixed the pesticide with water (three pounds of fenamiphos per 23 gallons of water). Two mixer/loader's were monitored for a two-hour period during the workday.

The applicator drove the application equipment. The equipment consisted of a tractor, spray-mix tank mounted on the front of the tractor or a trailer drawn by the tractor. The diluted pesticide was supplied via plastic tubing from the spray-mix tank to injectors behind shanks mounted on two seven-foot tool

bars bolted to the back of the tractor. Pumps operating off the hydraulic system of the tractor in the case of a front mounted tank, or off the drive wheel in the case of a trailer mounted tank, were used to deliver the pesticide at a rate of 1.0 pounds a.i./A. Two applicators were monitored for two and one-half hours during a normal workday.

In addition to these four workers, two workers involved in both mixing-loading and application were monitored for a four-hour period during one eight-hour workday.

The concentration of fenamiphos was measured in air during mixing-loading and applications using an MSA Model C-210 personal air pump. The sampling device, an XAD-4 sampling tube connected in series with a fiberglass particulate filter, was attached to each worker's collar. Fenamiphos in particulate and vapor form, respectively, were trapped on the filter and XAD resin. The air flow was 0.2 L per min. At the end of the sampling period, resin tubes and filters were capped and refrigerated prior to analysis.

Dermal exposure was measured by using cloth patches according to the method of Durham and Wolfe (1982) and by washing hands in 250 ml of distilled water released from a separatory funnel over the hands and collected in a stainless steel bowl. The wash water was transferred to glass jars, covered with aluminum foil, sealed with screw caps and refrigerated prior to analysis. After exposure, each patch was cut up and the cloth was put into one jar while the gauze in foil sections were placed into another. Matched pairs were placed into the jars together, i.e., the cloth of both arm patches were put in one jar and the gauze and aluminum foil for both arm patches were put into a separate jar. All glass jars were covered with aluminum foil, sealed with screw caps and refrigerated prior to analysis.

All samples were extracted with methylene chloride and analyzed by gas chromatography on a 3 m x 2 mm glass column packed with 4 percent OV-17 on 100-120 mesh Chromosorb W-HP. The column was operated at a temperature of 200°C. Nitrogen at 40 ml/min was used as the carrier gas. A nitrogen-phosphorous detector was used and operated at a temperature of 300°C. The injection port temperature was 220°C.

For the dermal dose-ChE response studies, 16 male albino rats (Simmons, Inc., Gilroy, California) weighing 220 to 240 g were prepared for dosing one day prior to treatment according to the method of Knaak et al. (1980b). In this method, the hair on the back of each animal was removed using an electric animal clipper. The treatment area of 25 cm^2 was marked off using a neoprene rubber template. Queen Anne collars made of polyethylene sheeting were placed around the neck of each animal. Four dosing solutions were prepared containing 0, 2.5, 5.0 and 10 mg of fenamiphos per ml of acetone. One ml of each solution

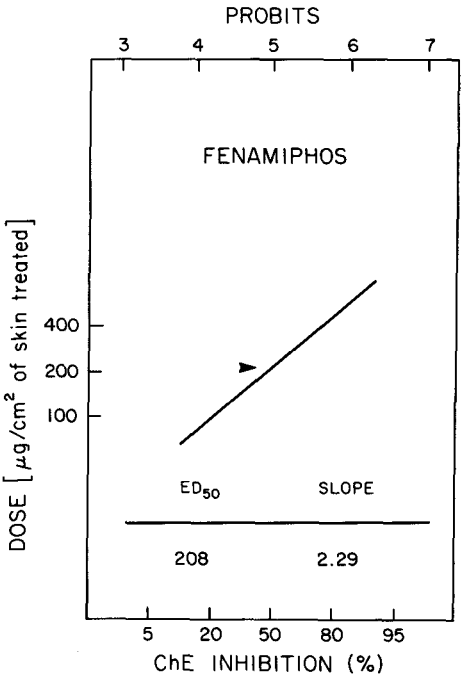

Figure 1. Dermal Dose-ChE response curve according to Knaak et al., (1980b). Male Sprague-Dawley rats weighing 220-240g were used. A 25 cm^2 area of skin was treated. Red blood cell ChE was determined 72 hours after the application of OP compound in acetone.

was applied evenly to the backs of three rats using a microliter pipet. The animals were placed in stainless steel cages and allowed free access to food and water. The animals were sacrificed 72 hours later and blood was collected and analyzed for cholinesterase activity using the method of Knaak et al., (1980b). The mean red cell cholinesterase activities from each treatment group were used to determine the dose inhibiting 10 and 50 percent of the red cell cholinesterase activity using a modification of the log-probit procedure of Finney (1972).

RESULTS AND DISCUSSION

Inhalation values were below the detectable level of 0.001 mg/hour. These inhalation values contributed negligible amounts to the total body dose. The highest levels of dermal exposure (ug/cm^2) was found on the worker's hands. Hand exposures were at least eight-fold higher than exposures to other parts of the body. The ED-10 value calculated from the cholinesterase inhibition dose response curve (see Figure 1) was designated as the practical no effect level.

Table 1. Dermal and Inhalation Exposure to Fenamiphos[a/]

Workers	Total Body Residues (Excluding Hands) in ug/hr	Residues on Hands in ug/hr	Total Residues Inhaled in ug/hr	Total Body Residues (8 Hour Day) in ug/cm^2
Applicator 1	107.0	560.0	1.0	0.267
Applicator 2	120.0	21.0	1.0	0.0564
Mixer/Loader 1	158.0	136.0	< 1.0	0.176
Mixer/Loader 2	136.0	35.0	< 1.0	0.0684
Mixer/Loader/ Applicator 1	67.0	29.0	< 1.0	0.0384
Mixer/Loader/ Applicator 2	67.0	26.0	< 1.0	0.0372

[a/] Calculations based on minimum detection level of 0.02 ppm.

The ED-10 value is below the level where cholinesterase symptoms can be detected and it can be accurately extrapolated from the straight-line equation of the dose vs. probit value at 10 percent. In order to extrapolate the rat ED-10 value to man, exposure in both rat and man was expressed in form of total body surface area. This was done by dividing the total amount of fenamiphos collected on the hands and body over an eight-hour workday by the total body skin area. The ED-10 value was found to be 4.33 ug/cm^2 of body surface area for the rat. The exposure levels in the pesticide worker was found to range from 0.037 ug/cm^2 to 0.267 ug/cm^2 of body surface (Table 1).

If the animal dermal dose response to fenamiphos is similar in humans, Nemacur 3EC may be used safely. A similar worker exposure study was done by Mobay Chemical Corporation in which patches and hand washes were used to estimate dermal exposure (1982). In addition, Mobay monitored cholinesterase activity of the workers, and found similar exposure levels result in no cholinesterase inhibition. This observation supports the use of animal dermal dose response studies to predict human response.

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