

Biological monitoring use in refining the exposure assessment of agricultural operators

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Objectives As part of the re-registration process for agriculturally active ingredients conducted by the United States Environmental Protection Agency (EPA), exposure and risk assessments are conducted for operators who mix, load, or apply agricultural products. The exposure assessment is typically based on a combination of data obtained from the Pesticide Handlers Exposure Database (PHED) and assumptions on various application parameters, such as application rates, hectares treated, and the like. However the exposure data from the PHED may not reflect current work practices for clothing as per the EPA worker protection standard and the improvements made in engineering controls for packaging, mixing–loading apparatus, and application methods. Thus the exposure assessments may overestimate the true exposure.

Methods This study consisted of 23 replicates of workers mixing, loading, or applying a formulation of ethoprop nematicide insecticide to potato fields as part of their normal work functions. The study was conducted at 13 separate sites in the south-central part of Washington State in the United States. Biomonitoring was conducted in which the urinary excretion of ethoprop and its principal metabolite was monitored on the day of exposure and for 3 days thereafter.

Results The exposure values estimated with the use of the PHED were approximately 26 to 51 times higher than the actual exposures determined in the study.

Conclusions The monitored absorbed doses found in this study should be considered representative of the range of potential absorbed doses resulting from ethoprop use with engineering controls under the conditions of this study.

Key terms engineering controls; ethoprop; Pesticide Handler's Exposure Database.

As part of the re-registration process conducted by the United States (US) Environmental Protection Agency (EPA) for agriculturally active ingredients, exposure and risk assessments are conducted for operators who mix, load, or apply agricultural products. The exposure assessment is typically based on assumptions of area treated, application rates, amount of active ingredient handled, hours of work, and the like. In addition, generic exposure values that are assumed to represent current work practices are obtained from the Pesticide Handlers Exposure Database (PHED) (1–3). These data are typically presented as exposure per amount of active ingredient handled (micrograms of exposure per kilogram of active ingredient handled). However, the assumptions for such factors as hectares treated, percentage of active ingredient dermally absorbed, and the like are

typically high-end estimates, and the mixer, loader, or applicator data in the PHED database are older data, the latest data being entered in version 1.1 in March 1995. Thus they may not reflect current work practices for clothing as per the EPA worker protection standard (4) and the improvements made in engineering controls for packaging, mixing and loading apparatus, and application methods. Thus the exposure assessments may overestimate the true exposure.

The EPA exposure assessment for ethoprop used label application rates of 6.8 and 13.6 kg of active ingredient per hectare, a default acreage value of 32 hectares treated per day, and the available data from the PHED for closed system mixing and loading and closed cab groundboom application (5). The calculated daily exposure estimates, on the assumption of the EPA default

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of 100% dermal absorption, were 95 and 190 µg/kg body weight per day [µg (kg BW · day)] for the application rates of 6.8 and 13.6 kg of active ingredient per hectare, respectively.

The objective of this study was to obtain a true assessment of exposure to ethoprop during application to potato fields using biomonitoring, the most accurate estimate of the absorbed dose, and to circumvent issues that may arise from the use of passive dosimetry, such as adjustment for dermal absorption. This study also monitored workers performing their typical worktasks, wearing their preferred clothing, using state-of-the-art loading equipment, and using modern application equipment. The actual exposures were then compared with the values estimated using the PHED in the EPA assessment.

Study population and methods

Study design and exposure assessment

The participants were 20 men who performed a total of 23 replicates, 20 to 47 years of age, 163 to 198 cm tall, and weighing 54 to 132 kg. The three workers that were monitored more than once had at least 4 days between performing their work function. All the participants were experienced in their work functions and were informed of the risks of participation and their right to withdraw from the study at any time for any reason. The participants were provided with a small monetary remuneration for their time and trouble regardless of whether or not they completed the study. This study only monitored workers performing their normal work functions in their typical manner. Four workers performed only a mixer-loader function, three performed only an applicator function, and sixteen performed a mixer-loader-applicator function.

The study was conducted at 13 separate sites in a potato-growing region in the south-central part of Washington State in the northwestern United States. Mocap® EC, a nematocide insecticide (active ingredient is ethoprop; O-ethyl-S,S-dipropyl phosphorodithioate; CAS no 13194-48-4; Bayer CropScience, RTP, NC, USA), was applied at 1.1–2.2 kg of active ingredient per hectare to vacant fields in which potatoes would soon be planted. The test material was contained in 208-l drums or 9.5-l jugs.

Eighteen mixer-loaders used a Soltera® (Soltera Systems, Fort Wayne, IN, USA) hard-coupled mechanical transfer system with a dry-lock system (Surestop™ Dry Disconnect; model DB100, Soltera Systems) connected to a digital pump (Inland Empire Distribution Systems, Inc, Pasco, WA, USA) to transfer the test material from the 208-l drums to the spray tank. An additional two

mixer-loaders used a Soltera® Securelink-G™ system (Soltera Systems) to transfer test material from the 9.5-l jugs to the spray tank.

Large, closed-cab tractors (eg, Quad Trac and Steiger ST600, Case IH Racine WI, USA; John Deere 4700, Deere & Company Moline, IL, USA) were used in these studies. Most of them were equipped with computer equipment that controlled the rate and speed of the pesticide application.

Applicators employing an injection method for the test material used a sweep injection boom attached to and followed by disc equipment, which was in turn followed and attached to a set of wheel packers in the back of the rig. Applicators employing a topical application method for the test material used a Terra-Gator-type (Ag-Chem, Duluth, GA, USA) groundboom rig. All the application equipment was precalibrated by the commercial application company.

The workers wore a variety of clothing of their choosing to meet or exceed the worker protection standard (3) requirements for handling Mocap EC. The requirements for a closed mixing-loading system are long-sleeved shirt and long pants, shoes, socks, chemical-resistant apron, and protective gloves. The workers typically wore additional clothing, such as rubber boots, coveralls over shirt and pants, jackets, goggles (when mixing), and occasionally respirators. The requirements for the applicator are long pants and a long-sleeved shirt inside the cab with chemical-resistant coveralls, gloves, and a respirator available for when work is done outside the tractor.

Inhalation exposure monitoring was performed with personal samplers (MSA, Pittsburgh, PA, USA) attached to Occupational Safety and Health Administration (OSHA) versatile sampler (OVS) tubes containing XAD-2 (SKC, Inc, Eighty Four, PA, USA) and operating at a flow rate of 2 l/min. Pumps were calibrated prior to their use and checked at the end of the exposure monitoring period prior to their being turned off and the tubes collected. Samples were collected in the breathing zone of the workers.

Ethoprop metabolism in varied organisms, such as man, animals, plants, and soil, produces at least one common metabolite, referred to as the M1 metabolite (M1M; O-ethyl S-propyl phosphorothioate). In the rat, ethoprop-radiolabeled products are excreted in the urine as a very consistent percentage of the administered dose (54% to 56%) and M1M excreted in the urine ranges from 12% to 37% of the total dose (6–8). The most recent study (8) has demonstrated that M1M from both rats and humans has the same retention time in gas chromatographic analyses (described below) and that the M1M appears to be a more predominant metabolite in humans than in rats. Thus M1M appears to serve as a reasonable marker for human exposure to ethoprop. This

conclusion was also previously proposed by the California Department of Pesticide Regulation for ethoprop exposure assessments (9).

As part of this study, another assessment of the urinary excretion of ethoprop was conducted with rats (N=10) (8). The percentage of the total dose of 4.8 mg/kg body weight (BW), administered orally on each of 3 days as [^{14}C -ethyl]-ethoprop in normal saline, excreted in urine was 54 (SD 7.1)%, a value remarkably consistent with the results of two previous studies. M1M was very consistently excreted in the urine with a mean of 12 (SD 1.9)% of the total dose. Urinary excretion of the parent ethoprop ranged from nondetectable to 6% of the total dose. Virtually complete excretion of radioactivity occurred within 24 hours. The gas chromatographic analysis of the M1M standard, the urine samples from the rats, and the urine samples from the workers had the same retention time, and it appeared that M1M was a more significant metabolite in humans than in rats. Since the rat is considered to be a suitable model for metabolism in humans and since the same urinary metabolite was found in both species, it was assumed that M1M could be used to estimate exposure to parent ethoprop in humans. A controlled metabolism study could not be conducted with humans (the EPA has not defined a policy regarding the use of human study data for pesticides); therefore, it was necessary to somehow extrapolate from the data on rats. In three metabolism studies conducted with rats, the lowest percentage that urinary M1M comprised of the total dose was 12%. This value was therefore assumed to be a conservative estimate of the percentage for urinary excretion in humans (ie, the lower this value, the higher the calculated ethoprop exposure). Therefore, to back-calculate to the absorbed dose of the parent, ethoprop, the total micrograms of M1M in the urine from day 0 through day 3 was summed and assumed to result from a single day's exposure, regardless of the actual number of days the worker handled ethoprop after the first day. The back-calculation was performed as follows: total ethoprop exposure (μg) = M1M (μg) $\times$ 0.12 $\times$ (242.3 g/mole / 184.19 g/mole), where 0.12 represents urinary M1M excretion at 12% of the total dose and 242.3 and 184.9 are the molecular weight of ethoprop and M1M, respectively.

Urine collection was conducted for the 24-hour period prior to the initiation of the study and then for 12-hour intervals for 4 days after participation in the study was begun [day 0 (day of mixing-loading-application), then for 3 additional days]. The participants were supplied with labeled collection vessels and coolers with blue ice and dry ice for storage of the samples. Samples were collected each day, weighed, and stored frozen until analysis. As a further check on the validity of the urine collection, creatinine was also analyzed in all the samples. This sampling procedure provides an

overestimate for the calculation of a single daily exposure for all the workers that continued to work with ethoprop during the 3 days following their first day's exposure. This overestimate was unavoidable since several of the workers were required to continue making applications to other farms in the area as part of their regular job. Of the 23 workers, 9 worked with ethoprop for only 1 day, 9 for 2 days, and 5 for 3 days during the urine collection period.

Field fortification of matrices

Air sampling and urine matrices were field-fortified to provide data on the stability of the analytes of interest (ethoprop and M1M) during the collection time in the field, storage time in the field facilities, shipment, and frozen storage prior to the analysis. The amount of analyte in the samples collected from the workers was corrected for losses determined in the field fortification procedures.

Air-sampling tube-field fortifications were collected on 10 days for a time similar to the collection of the worker samples (up to 545 minutes). Tubes were spiked in triplicate at 1 or 12.5 μg of ethoprop, and air was drawn through the tubes at 2 l/minute. At the end of the sample collection the tubes were treated the same as the worker samples (ie, capped, placed in a zip-type plastic bag, and then stored on dry ice until placed in a freezer). Control samples were treated in the same manner, except that the actual analyte was not included in the fortification of the tubes. Losses of ethoprop from these field-fortified samples were minimal, with mean recoveries of 102 (SD 8.3)% and 98.6 (SD 4.8)% for the low and high spike levels, respectively.

Urine samples were collected from several workers during the 24-hour period prior to participation in the study. The urine samples were pooled and aliquots of the pooled samples were then used throughout the study for field fortifications. Different sets of triplicate samples were spiked with ethoprop or M1M (Bayer, Frankfurt, Germany) at 12.5 or 62.5 μg per sample. These samples, and additional samples that were not spiked and served as controls, were immediately placed in a freezer. Losses of ethoprop and M1M from these field-fortified samples were minimal, with mean recoveries of 93.6 (SD 6.6)% and 90.4 (SD 3.5)% for the low spike levels, respectively, and 96.1 (SD 7.7)% and 88.7 (SD 3.9)% for the high spike levels, respectively.

Analytical methods and stability of the study matrices

The analytical methods for all the matrices were validated prior to the initiation of the study. The stability of all the matrices in both the ambient and frozen conditions of collection and under conditions of frozen storage

was also validated. Stability was also assessed with field-fortified samples prepared for each matrix during the study (OVS tubes—triplicate samples at each of two levels on each of 10 days; triplicate samples of urine at each of two levels for both ethoprop and M1M on each of 9 days).

XAD sorbent from the air sampling tubes was analyzed for ethoprop after extraction with 8 ml of 10% acetone in hexane. The solids were allowed to settle, a 5-ml sample was evaporated to dryness, redissolved in iso-octane, and then quantified using a gas chromatograph with a flame photometric detector in the phosphorous mode (GC/FPD-P). The sampling method was validated at three fortification levels of the OVS tubes (0.1, 1.0, and 12.5 µg/tube), which resulted in similar recoveries at all spike levels, with a mean recovery of 102 (SD 6.5)%. The limit of detection (LOD) for ethoprop was 0.0082 µg/tube.

Creatinine was analyzed using the Jaffe procedure (10) with a Cobras® Integra instrument (Roche Diagnostics, Basel, Switzerland) with creatinine Jaffe cassettes. Briefly, the urine is made alkaline and then reacted with picric acid to form a yellow dye analyzed at 512/583 nm.

The urine samples were analyzed for both ethoprop and M1M. Ten-milliliter aliquots were diluted to 100 ml with methanol, mixed vigorously, and a 30-ml aliquot was collected. The aliquot was mixed with 3 g of Dowex™ 50W resin (Dow Chemical Co, Midland MI, USA) for 20 minutes. Nuchar/attaclay (200 mg) was then added, and stirring continued for 5 minutes. This sample was filtered through a glass fiber filter, and the filtered solids were rinsed with methanol. The filtrate was then evaporated to near dryness (1–2 ml), the remaining methanol and water being removed as an azeotrope with acetonitrile (2 × 10 ml). The residue was again dissolved in methanol, the M1M being derivitized to the methyl ester with diazomethane in diethylether. The sample was then maintained at ambient conditions for 0.5 to 1 hour, glacial acetic acid was added dropwise to destroy any excess diazomethane, and then the sample was evaporated until only methanol remained. The sample was then quantitatively transferred and diluted with distilled water. The ethoprop and M1M were partitioned into dichloromethane, the extract being evaporated to dryness. The residue was again dissolved in 2 ml of iso-octane and then cleaned up on a silica gel column, which was rinsed with 15% diethylether in hexane (volume:volume). Ethoprop and M1M were eluted with 10% acetone-hexane (volume:volume), evaporated, reconstituted in iso-octane, and then analyzed using a GC/FPD-P. The sampling method was validated at three fortification levels (0.01, 0.1, and 1.0 µg/ml) of both ethoprop and M1M. The mean recoveries across the fortification levels for ethoprop were 106, 95, and 92%; for M1M they were 98, 89, and 93% for the low,

middle, and high spike levels, respectively. The overall mean recovery for ethoprop was 98.9 (SD 9.5)%; it was 93.9 (SD 5.2)% for ethoprop. The limit of detection for ethoprop was 0.0016 µg/ml and that for M1M was 0.0046 µg/ml.

Extensive evaluations were conducted to determine the stability of both ethoprop and M1M under conditions simulating the collection procedures during the study and the time spent in freezer storage until the analysis. Separate samples were spiked at 62.5 µg/ml of either ethoprop or M1M and then held at ambient conditions for 28 hours prior to being placed in the freezer, while the others were placed on blue ice plus dry ice for 24 hours prior to being placed in the freezer. Samples were analyzed after 154 days of freezer storage, and the mean recoveries for ethoprop and M1M were 73.8 (SD 2.8)% and 90.2 (SD 2.4)%, respectively. There was no breakdown of ethoprop to M1M in these samples; this finding indicates that losses occurred by some other physical (eg, sorbed to the polyethylene container) or chemical (eg, breakdown to some other product) processes. All the samples in the study were analyzed within 164 days of frozen storage. These data were further substantiated by the field fortification data already described.

Statistical methods

Statistics were calculated using the routines available in Microsoft® Excel®, Office 2000 edition. The statistics included arithmetic and geometric means and their respective standard deviations, and regression analyses. The statistical evaluation of the data for the regression analyses included the t-test and the Spearman rank correlation coefficient test.

Results

The urine creatinine and volume evaluations indicated that the participants faithfully collected all the 24-hour samples (11). However, the creatinine and volume determinations indicated that some of the 24-hour samples had obviously been collected in a single container (one of the two 12-hour containers). This practice was of no consequence to the residue determinations.

The individual replicate data from the study are presented in table 1. Notable observations were made for only two of the replicates in the study. The first replicate listed in the table (mla16) had the highest absorbed dose in the study [108 µg ethoprop/(kg BW · day)]. Not only did he handle the most active ingredient of any replicate in the study (1562 kg of active ingredient), but he also open-poured the test material into the tank from

Table 1. Summary of data from the ethoprop study on agricultural operators.

Replicate (N)	Equipment	Number of days ^a	Active ingredient handled on day 0 (kg)	Hectares treated	Time ^b of work period (min)	Total absorbed dose of ethoprop ^c	Calculated inhalation exposure contribution ^d	Calculated absorbed dose of ethoprop per kilogram ^e	Maintenance or leaks ^f
16 (mixers-loaders-applicators)	Jug or surface application	3	1562	227	324	108	0.03	1.4	Yes ^g
15 (mixers-loaders-applicators)	Closed system lock & load or surface application	2	245	24	325	84	0.02	5.2	Yes ^h
7 (mixers-loaders-applicators)	Closed system lock & load or injection application	2	448	12	490	45	0.01	1.9	Yes
1 (mixer-loader-applicator)	Closed system lock & load or injection application	3	474	66	530	22	0.03	0.6	Yes
2 (mixers-loaders-applicators)	Closed system lock & load or injection application	3	381	57	877	18	0.09	0.6	Yes
1 (mixer-loader)	Closed system lock & load	2	579	— ⁱ	573	15	0.09	0.7	No
11 (mixers-loaders-applicators)	Closed system lock & load or surface application	2	302	30	125	11	0.001	0.9	No
4 (mixers-loaders)	Closed system lock & load	3	1743	— ⁱ	586	9.3	0.03	0.1	No
8 (mixers-loaders-applicators)	Closed system lock & load or injection application	2	298	11	524	8.6	0.009	0.3	Yes
3 (mixers-loaders)	Closed system lock & load	1	204	— ⁱ	366	6.8	0.1	0.5	No
2 (mixers-loaders)	Closed system lock & load	1	72	— ⁱ	302	4.3	0.002	0.9	No
13 (mixers-loaders-applicators)	Closed system lock & load or injection application	2	377	14	439	4.2	0.002	0.2	Yes
2 (applicators)	Injection application	1	48	6	302	4.0	0.0009	1.3	No
9 (mixers-loaders-applicators)	Closed system lock & load or injection application	2	176	11	410	1.6	0.003	0.2	No
5 (mixers-loaders-applicators)	Closed system lock & load or injection application	1	148	22	362	1.2	0.0009	0.1	No
14 (mixers-loaders-applicators)	Closed system lock & load or injection application	2	265	16	433	1.2	0.002	0.1	No
4 (mixers-loaders-applicators)	Closed system lock & load or injection application	1	89	13	440	1.1	0.003	0.2	No
10 (mixers-loaders-applicators)	Closed system lock & load or injection application	2	204	15	455	1.1	0.009	0.1	No
12 (mixers-loaders-applicators)	Jug or surface application	2	272	20	152	1.0	0.006	0.05	Yes
3 (applicators)	Injection application	3	1090	162	460	1.0	0.003	0.02	Yes
3 (mixers-loaders-applicators)	Closed system lock & load or injection application	1	68	8	410	0.6	0.003	0.2	No
6 (mixers-loaders-applicators)	Closed system lock & load or injection application	1	109	13	307	0.5	0.001	0.1	No
1 applicator	Injection application	2	579	71	546	0.5	0.0009	0.02	Yes

^a Number of days the active ingredient was handled during the urine collection period.^b Time includes other normal ancillary tasks.^c Determined by biomonitoring (total M1 metabolite collected over 4 days back-calculated to the total ethoprop exposure with the assumption that exposure occurred on a single day).^d To absorbed dose on the assumption of an inhalation rate of 29 l/min as recommended by the US Environmental Protection Agency (12).^e Active ingredient handled.^f Indication of whether equipment maintenance had to be conducted during the work period or if there were leaks in the loading coupling system.^g Worker open-poured the test material from 9.5-l jugs into the tank.^h Worker had poor work habits and removed gloves during the work period.ⁱ Replicates only, mixer-loaders have no value.

9.5-l jugs (ie, he did not use a closed mixing-loading system). The second replicate listed in the table (mla15) had the second highest absorbed dose [84 µg ethoprop/(kg BW · day)]. He was observed to have removed his gloves during the study [not in compliance with the label or regulations of the EPA Workers Protection Standard (WPS)] and, in the opinion of the field observer, had poor work habits (no similar observation was made for any other worker). Removal of gloves during the work process is occasionally observed in these studies and results in an upper-end exposure value. It is also notable that the replicates with the five highest absorbed doses also performed some sort of maintenance activity (eg, cleaned boom nozzles or changed nozzles) or had leaks in the closed coupling system due to gasket corrosion.

The replicate data in table 1 were broken into several subgroups so that the effects of various pieces of equipment and work practices could be evaluated. The statistical summary data for these subgroups are presented in table 2. The data have been grouped as follows: group 1: the 12 mixers-loaders-applicators who used the closed mixing-loading system (lock-and-load system) and a soil injection application system; group 2: the 22 replicates that included mixing-loading using closed systems from 208-l or 9.5-l containers, applicators using injection or surface application techniques, and mixers-loaders-applicators using some combination of these techniques; the one replicate that open-poured from 9.5-l jugs has been excluded from this group; and group 3: all 23 replicates in the study.

The inhalation exposures were very low, regardless of the work function. For groups 1, 2, and 3, the inhalation exposure was estimated to contribute only 0.2, 0.3, and 0.1% of the absorbed dose of ethoprop, respectively (assumed 29 l/min minute volume; range of airborne concentrations of 0.0001 to 0.01 µg/l). Thus dermal exposure was probably the primary route of exposure.

None of the urine samples (approximately 184 12-hour samples) had ethoprop residues that exceeded the limit of detection of 0.0016 µg/ml. All the residues found in the urine were in the form of M1M (range of 4.2 to 982 µg of total M1M during the 4-day collection period). The elimination of M1M in urine for workers exposed for only 1 day was complete within 24 hours. No M1M was found in the urine samples during the 24- to 72-hour interval. This finding was very similar to data from rats (8). The exposure data in table 1 provide exposure values in terms of the parent ethoprop compound, and they have been back-calculated from the amount of M1M in the urine. Exposure calculations that normalize for the amount of ethoprop handled are also provided.

The geometric mean absorbed doses of ethoprop for groups 1, 2, and 3 were 3.0, 3.7, and 4.3 µg of ethoprop per kilogram of body weight per day, respectively. The mean values change very little across the groups, but the mean value for group 3 was obviously affected by the addition of data from the single replicate that open-poured from 9.5-l jugs.

Regression analyses were performed to determine if a relationship existed between the absorbed dose of the 12 mixer-loader-applicator replicates that used a closed mixing-loading-system and the ground injection application (group 1) with one of the other measured parameters for this study. The coefficient of determination (R^2) for the regressions of absorbed dose with kilogram of active ingredient handled, hectares treated, and time worked (minutes) were 0.58, 0.13, and 0.18, respectively. Figure 1 provides the regression for exposure and kilogram of active ingredient handled. There was a trend for increasing exposure with amount handled, and the results indicate that, at least from a purely statistical standpoint, some relationship between the absorbed dose and the kilograms of active ingredient handled does

Table 2. Statistical summary of the data from the ethoprop study on agricultural operators. (M=mixer, L=loader, A=applicator, M-L-A = performed all three functions using the lock-and-load system and an injection application, M-L and A performed some combination of the functions – mixing done with a closed system and application done by injection or surface sprayer)

Parameter	Group 1 ^a (M-L-A)			Group 2 ^b (M-L-A, M-L and A)			Group 3 ^c (M-L-A, M-L and A)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
Kilograms of active ingredient handled	253	142	68–474	371	386	48–1743	423	451	48–1743
Hectares treated ^d	21	19	8–66	32	38	6–162	42	58	6–227
Minutes worked	473	142	307–877	428	157	125–877	423	155	125–877
Exposure (µg ethoprop/kg active ingredient) ^e	0.2	2.5	0.1–1.9	0.3	4.5	0.02–5.2	0.3	4.6	0.02–5.2
Inhalation exposure (µg ethoprop/kg of body weight per day) ^e	0.005	4.0	0.0009–0.09	0.01	5.1	0.0009–0.1	0.006	5.1	0.0009–0.1
Absorbed dose (µg ethoprop/kg of body weight per day) ^e	3.0	4.6	0.5–45	3.7	4.0	0.5–84	4.3	4.0	0.5–108

^a 12 replicates, equipment: lock and or injection.

^b 22 replicates, equipment: all except open-pour jug.

^c 23 replicates, equipment: all.

^d For groups 2 and 3 the values are based on a number of 18; M-L did not treat acreage.

^e Values are geometric means; inhalation exposure estimates assumed a minute volume of 29 l/minute (12).

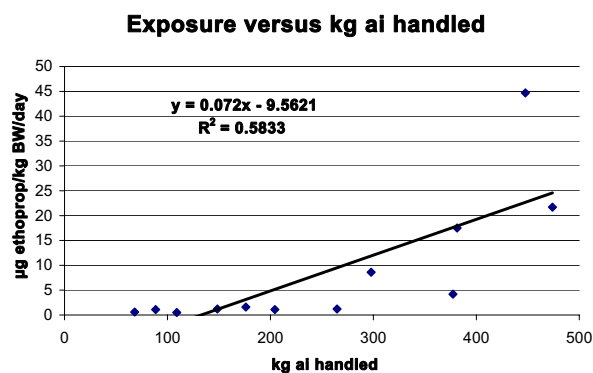


Figure 1. Absorbed dose of ethoprop versus amount (kg) handled for mixer-loader-applicators using a closed mixing-loading system and a soil injection application method (group 1, N=12). (ai = active ingredient, BW = body weight)

Table 3. Comparison of data from the assessment of ethoprop exposure made by the United States Environmental Protection Agency (EPA) for mixers, loaders and applicators in treating potato crops with data obtained from the biomonitoring of the actual workers. (PHED = Pesticide Handlers Exposure Database)

Parameter	EPA assessment	Study data ^a	
		Mean ^b	Range
Dermal absorption (%)	100	..	..
Body weight (kg)	70	84	54–132
Application rate (kg active ingredient/hectare)	6.8 & 13.6	4–12	..
Hectares treated (N) ^b	32	32	6–162
Amount amount of active ingredient handled (kg)	218 & 435	371	48–1743
PHED exposure estimate (µg exposure/kg of active ingredient handled) ^c	30.4	..	..
Exposure (µg exposure/kg of body weight per day)	95 & 190	3.7 ^d	0.5–84

^a Data are for the 22 replicates (group 2) that used a closed system for mixing or loading; the 1 replicate that open-poured from 9.5-l jugs was excluded.

^b Arithmetic mean.

^c Based on N=18; mixers and loaders did not treat acreage.

^d Geometric mean.

exist ($P < 0.004$). However, from a practical standpoint, the overall R^2 (0.58) was relatively weak.

A second regression analysis was performed to determine the relationship between the absorbed dose and the amount of active ingredient handled in the 22 group 2 replications (figure 2). The R^2 (0.0011) for the regression of the absorbed dose with kilogram of active ingredient handled was very weak, and no statistical relationship was found ($P = 0.26$).

Discussion

A comparison of the exposure assessment by the EPA with the data actually obtained in this biomonitoring

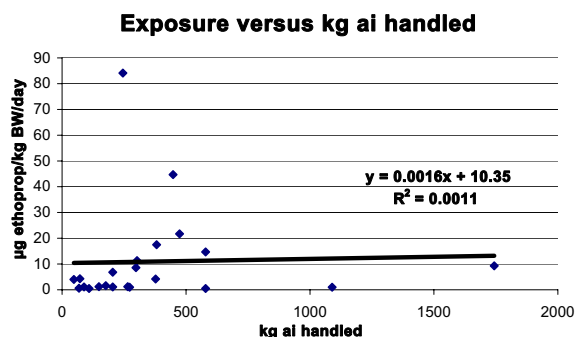


Figure 2. Absorbed dose of ethoprop versus amount (kg) handled for mixer-loader-applicators using a 208-l or 9.5-l closed mixing-loading system and a soil injection or surface application method (group 2, N=22). (ai = active ingredient, BW = body weight)

study is presented in table 3. The mean absorbed dose predicted in the EPA assessment was approximately 26 to 51 times higher than the geometric mean dose actually obtained with biomonitoring in this study. According to the data available to EPA and Bayer prior to the conduct of this study, Bayer's estimates of worker exposures were similar to the EPA's. Both the EPA and Bayer recognized the uncertainties in the EPA risk assessment and the importance of refining the uncertainties through the conduction of the biological monitoring study (13). The EPA assumption of 100% dermal absorption, which was used in the absence of ethoprop dermal absorption data, is very likely an overestimate. The biological monitoring study eliminated the need to adjust for dermal absorption. The reduction in exposure potential resulting from engineering controls such as the dry lock and mechanical transfer systems used in this study very likely also reduced the relationship between exposure and the kilograms of active ingredient handled. The use of soil injection application equipment may also have played a role. The WPS regulations and additional personal protection equipment that mixers-loaders typically wear, in addition to the required WPS clothing, probably also reduced the exposure to levels that may not be reflected in the PHED. The EPA engineering control PHED assessment assumes the use of trousers, a long-sleeved shirt, and protective gloves (during mixing-loading), and it is based on the actual monitoring of residues under such clothing during the use of closed loading systems and enclosed cab tractors.

Conversely, it should also be noted that the exposures determined in this study are actually overestimates of the exposure that would result from handling the active ingredient on a single day, as assumed in the EPA assessment, due to the fact that 11 of the 23 workers handled ethoprop for a second day during the urine collection period while 5 of 23 handled it for 3 days during the urine collection period. The extra residues found

for these workers were all attributed to a single day of exposure in the calculations in this study.

In summary, exposure estimates from the PHED, in combination with other default assumptions used in the EPA assessment for the use of ethoprop on potatoes, with mixing-loading using a closed system and application using a closed cab, overestimated the actual exposure determined for agricultural operators performing their normal routines. The estimated values were approximately 26 to 51 times higher than the actual exposures determined in the study. The monitored absorbed doses should be considered representative of the range of potential absorbed doses resulting from ethoprop use with engineering controls under the conditions of this study. However, it would not be unreasonable to assume that similar engineering controls, personal protective equipment, and work practices would result in similar exposures for ethoprop use in other bare fields. The standard regulatory approach has been to use the amount of active ingredient handled to normalize the daily exposure in operator exposure assessments. Data from this study indicate that the relationship weakens when engineering controls are used. That is, the approach tends to overestimate the exposure when large quantities of active ingredient are handled.

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