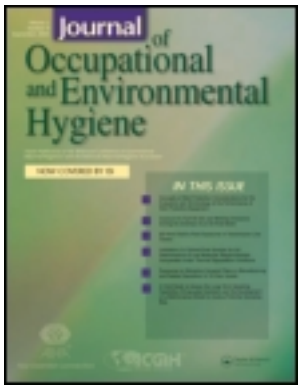

Journal of Occupational and Environmental Hygiene
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/uoeh20

A Pilot Study of Workplace Dermal Exposures to Cypermethrin at a Chemical Manufacturing Plant

Timothy J. Buckley [a], Laura A. Geer [b], Thomas H. Connor [c], Shirley Robertson [c], Deborah Sammons [c], Jerome Smith [c], John Snawder [c] & Mark Boeniger [d]

[a] Division of Environmental Health Sciences, The Ohio State University College of Public Health, Columbus, Ohio

[b] Department of Environmental and Occupational Health Sciences, SUNY Downstate School of Public Health, Brooklyn, New York

[c] National Institute for Occupational Safety and Health, Division of Applied Research and Technology, Centers for Disease Control and Prevention, Cincinnati, Ohio

[d] Consultant, Cincinnati, Ohio

Available online: 21 Sep 2011

To cite this article: Timothy J. Buckley, Laura A. Geer, Thomas H. Connor, Shirley Robertson, Deborah Sammons, Jerome Smith, John Snawder & Mark Boeniger (2011): A Pilot Study of Workplace Dermal Exposures to Cypermethrin at a Chemical Manufacturing Plant, Journal of Occupational and Environmental Hygiene, 8:10, 600-608

To link to this article: http://dx.doi.org/10.1080/15459624.2011.613269

Journal of Occupational and Environmental Hygiene, 8: 600–608
ISSN: 1545-9624 print / 1545-9632 online
DOI: 10.1080/15459624.2011.613269

A Pilot Study of Workplace Dermal Exposures to Cypermethrin at a Chemical Manufacturing Plant

Timothy J. Buckley,[1] Laura A. Geer,[2] Thomas H. Connor,[3] Shirley Robertson,[3] Deborah Sammons,[3] Jerome Smith,[3] John Snawder,[3] and Mark Boeniger[4]

[1]Division of Environmental Health Sciences, The Ohio State University College of Public Health, Columbus, Ohio
[2]Department of Environmental and Occupational Health Sciences, SUNY Downstate School of Public Health, Brooklyn, New York
[3]National Institute for Occupational Safety and Health, Division of Applied Research and Technology, Centers for Disease Control and Prevention, Cincinnati, Ohio
[4]Consultant, Cincinnati, Ohio

Exposure during the manufacture of pesticides is of particular concern due to their toxicity and because little is known about worker exposure, since most studies have focused on end-use application within agriculture or buildings. Even though dermal exposure can be expected to dominate for pesticides, little is known about workplace dermal exposures or even appropriate methods for their assessment. The current study begins to address this gap by evaluating alternative methods for assessing dermal exposure at a chemical manufacturing plant. For this pilot study, eight workers were recruited from a U.S. plant that produced the pesticide cypermethrin. Exposure was evaluated using three approaches: (1) survey assessment (questionnaire), (2) biological monitoring, and (3) workplace environmental sampling including ancillary measurements of glove contamination (interior and exterior). In each case, cypermethrin was quantified by enzyme-linked immunosorbent assay (ELISA). Environmental measurements identified two potential pathways of cypermethrin exposure: glove and surface contamination. Workplace exposure was also indicated by urine levels (specific gravity adjusted) of the parent compound, which ranged from 35 to 253 μg/L (median of 121 μg/L) with no clear trend in levels from pre- to post-shift. An exploratory analysis intended to guide future studies revealed a positive predictive association (Spearman correlation, $p \leq 0.10$) between post-shift urine concentrations and a subset of survey questions evaluating worker knowledge, attitudes, and perceptions (KAP) of workplace dermal hazards, i.e., personal protective equipment self-efficacy, and inverse associations with behavior belief and information belief scales. These findings are valuable in demonstrating a variety of dermal exposure methods (i.e., behavioral attributes, external contamination, and biomarker) showing feasibility and providing measurement ranges and preliminary associations to support future and more complete assessments. Although these pilot data are useful for supporting design and sample size considerations for larger exposure and health studies, there is a need for validation studies of the ELISA assay for quantification of cypermethrin and its metabolites in urine.

Keywords attitudes, behavior, beliefs, biological monitoring, personal protective equipment, surface sampling

Correspondence to: Timothy J. Buckley, Division of Environmental Health Sciences, The Ohio State University College of Public Health, 320 West 10th Avenue, Columbus, OH 43210-1240; e-mail: tbuckley@cph.osu.edu.

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the National Institute for Occupational Safety and Health. Mention of company names or products does not constitute endorsement by NIOSH.

INTRODUCTION

Of the many exposures faced by workers in chemical manufacturing, there is considerable uncertainty associated with the dermal route. Industrial hygienists are much better equipped to assess and manage inhalation hazards. In contrast, workplace dermal hazards are largely unrecognized and unevaluated even though there are indications that dermal absorption is a significant threat to worker health. Although Leigh et al.[1] do not classify by route of exposure in providing national estimates of worker annual deaths (60,000) and illness (over 800,000) due to chemical exposures, it is likely that the dermal route of exposure contributes substantially. Of the 655 chemicals with airborne threshold limit values (TLVs®) listed by the ACGIH®, 189 (29%) also carry the skin notation indicating "potentially significant contribution to the overall exposure by the cutaneous route."[2,p.70] Another indication of the pervasiveness of dermal exposure within the workplace is a "skin diseases or disorders" incidence rate in 2006 of 4.5 per

10,000 full-time workers representing 18% of total illness cases for all nonfatal occupational illnesses within private industry.[3]

Despite the potential for dermal exposure within pesticide manufacturing and indications that worker health is threatened,[4–6] few published reports are available on which to evaluate the dermal exposure hazard within this industry sector. This is certainly true for the pesticide cypermethrin, where a review of the literature yielded no reports of dermal exposure within pesticide manufacturing. The specific health threats associated with cypermethrin include developmental toxicity, immune suppression, and acute paresthesia.[7–9]

It is known from a number of occupational studies other than manufacturing that the dermal route can contribute as much or more to a worker's exposure relative to inhalation.[10–14] Although methods for evaluating inhalation exposure are reasonably well standardized, including the use of personal air monitoring, such is not the case for dermal exposure where a lack of consensus regarding a wide range of methods with different underlying assumptions hinders standardization.[15–18] The lack of accepted methods provides the rationale for a multifaceted approach, including biological monitoring in combination with external measures to provide a complementary assessment of exposure. Biological monitoring not only captures the dose that is absorbed through the skin, but also the dose inhaled (including the penetration of respiratory protection) and ingested. The comparison of exposure with biological monitoring is most informative when parameters of human metabolism and pharmacokinetics are characterized and available.[16,19,20]

Assessments that also incorporate measures of worker behavior can have major implications for a comprehensive picture of exposure and may lead to more options with respect to intervention. For example, worker dermal protection strategies tend to rely more on worker motivation and training in the use of personal protective equipment (PPE) and less on engineering controls.[21] Thus, worker dermal protection depends greatly on worker behavior. A behavioral focus to understanding and preventing dermal exposure is well justified since there is consistent and compelling evidence that it is a primary determinant of worker dermal exposure and protection.[21–23] For example, studies examining the impact of hygienic behavior on external and internal lead and chromium levels, respectively, found that accounting for hygienic behavior together with variation in external measures of exposure nearly doubled the amount of internal dose variation explained in comparison to considering external exposure alone.[24,25]

Recognizing the importance of behavior to the assessment of worker dermal exposure, a behavioral survey was developed and validated to semi-quantitatively estimate exposure based on worker task and behavioral observations.[26–28] This survey methodology, DeRmal Exposure Assessment Methodology (DREAM), was developed and tested in Europe and has seen very limited application within the United States. We built on their survey methodology by developing and testing a new survey, comprising seven psychosocial scales, to assess workers' dermal knowledge, attitudes, and perceptions (KAP) as underlying behavioral determinants of exposure.[29] The KAP survey was developed from the Health Belief Model premised on the concept that people partake in health protective behavior based on perception of susceptibility (personal vulnerability), severity (likelihood of getting sick), benefits of taking action (outcome expectancy), and barriers (self-efficacy).[30–32]

The current study is intended to demonstrate feasibility and provide range-finding data to inform the design of larger future studies that will assess the factors contributing to potential exposure and to characterize the current practice of hazard control, including the use of personal protective equipment. Further development of this line of research is important in two related ways. The first is in the identification of behavioral determinants of occupational dermal exposures to support better methods of exposure assessment. The second is in the development of KAP and behavior-related intervention strategies to prevent or reduce exposure.

METHODS

Worker exposure to cypermethrin was evaluated based on a combination of external measurements, biological monitoring, and the KAP behavioral assessment. The external measurements included wipe and glove sampling. Cypermethrin was analyzed in pre- and post-shift urine samples. Behavioral determinants of exposure were evaluated through a technician-administered, 115-question KAP survey based on the work of Geer et al.[29]

During December 2005– January 2006, eight workers were recruited from a chemical plant manufacturing cypermethrin and located in a northeastern U.S. city. Discussions with the plant industrial hygienist (IH) indicated that the potential existed for worker dermal exposure. The IH described anecdotal reports of paresthesia among workers, consistent with cypermethrin's known effects.[8] At the same time, air monitoring suggested that little exposure was occurring through inhalation. There had been no previous assessment of dermal exposure. Workers volunteered in response to a posted advertisement or through word of mouth. Therefore, participants were a convenience (rather than a representative) sample. Prior to study participation, workers signed an informed consent that was approved by the Johns Hopkins School of Public Health Institutional Review Board.

The workers who were monitored included those entering the manufacturing area to sample the cypermethrin product being produced. Each sampling episode required approximately 25 min and occurred 4–7 times per shift. Prior to sampling, workers donned heavy neoprene-coated, cotton-lined gloves (Scorpio; Ansell Edmont Industrial, Coshocton, Ohio). The gloves were reused, but their time in service was not ascertained. Employer-provided, standard long-sleeved uniform shirts were worn. It was standard practice for workers' shirts to be laundered by the employer after each day's use.

Hand exposure was evaluated using light cotton "dosimeter" gloves (Industrial Gloves Supply, Colorado Springs, Colo.)

as previously tested within agricultural settings.[33,34] The glove dosimeters were worn under participants' neoprene gloves during each product sampling event. Workers were instructed not to wash their hands prior to donning the cotton glove dosimeter; therefore, the glove measured contamination from a worker's hand as well as from the neoprene glove (either internal contamination or external penetration). Although this strategy precludes isolating the specific contribution from the neoprene glove, it provides a more comprehensive assessment of hand exposure.

In addition, because the glove dosimeters were worn with previously used neoprene gloves that were potentially internally contaminated, this approach did not provide the means for differentiating the cypermethrin that penetrated the glove from the internal contamination but, again, provided a more comprehensive measure of hand exposure. The cotton glove dosimeter was worn for a single donning of the neoprene gloves. On the day of monitoring, workers wore their neoprene gloves that had been previously used, although not shared among other workers. When not being worn, gloves were stored by the workers in a cubby area designed for this purpose.

At the end of the sampling event, the cotton glove dosimeters were removed by study personnel and each placed in a separate glass storage vial. The neoprene gloves were collected at the end of the work shift and placed in a glass storage vial. Fourteen cotton gloves (a pair from each of seven workers), and four neoprene gloves (a pair from each of two workers) were collected for analysis. The vial was labeled with the subject's unique identification code and placed in a Ziploc bag. At the same time, unused cotton gloves and neoprene gloves were collected as field blanks using the identical procedure. Samples were transported to the laboratory at the Johns Hopkins School of Public Health and stored at –20°C until shipped on dry ice to the National Institute for Occupational Safety and Health (NIOSH) for analysis.

Wipe samples were collected from 11 surface locations with potential for worker dermal exposure, including workers' helmets, shoes, and goggles as well as railings, doorknobs, and work surfaces. A method modified from Geno et al.[35] and recently evaluated by Bernard et al.[36] was used for sampling workplace surfaces. This methodology showed favorable sampling efficiencies from hard surfaces of 84–97% that included cypermethrin as one of the test pesticides. The modified method we employed used 4.5 × 8.5 in. EX-L Kimwipes (Kimberly Clark, Dallas, Texas). For each sample location, a 100 cm^2 area was wiped. Prior to sampling, each wipe was wetted with 1 mL of a 70% solution of isopropyl alcohol. Disposable latex gloves were worn during sampling. Surfaces were wiped three times by repeatedly folding and turning the wipe. After sampling, the wipe was placed in a glass vial, capped, and labeled. Two unused wipes were wetted with alcohol and placed in vials to serve as field blanks. As with glove samples, wipe samples were returned to the lab and stored at –20 °C until shipped to NIOSH for analysis.

Glove and wipe samples were analyzed for cypermethrin using an enzyme-linked immunosorbent assay (ELISA) kit (EnviroLogix QuantiPlate kit for synthetic pyrethroid, Portland, Maine; EP 012, Lot 143055). Wipes, cotton gloves, and neoprene gloves were extracted in methanol. Wipes were placed into 16-mL glass vials and extracted with 10 mL methanol for 180 min on a rocking platform. Cotton gloves were placed into 50-mL glass tubes and extracted with 40 or 45 mL methanol for 180 min on a rotator. The neoprene gloves were placed in 1-L mason jars and extracted with 200 mL methanol for 120 min on a rocking platform.

Sample extracts were analyzed according to ELISA kit manufacturer's directions. In brief, 31 μL of 0.2 N sodium hydroxide was mixed with 1.25 mL of the methanol extract. The mixture was equilibrated for 30 min at room temperature. The equilibrated extract was then diluted 1:21 with distilled water, and 100 μL of the diluted extract was added to appropriate wells coated with cypermethrin antibodies. Cypermethrin-enzyme conjugate (100 μL) was added to each well, and the resulting mixture was incubated for 60 min at room temperature. The cypermethrin in the sample competed with the cypermethrin-enzyme conjugate for antibody binding sites such that increasing cypermethrin in the sample resulted in decreasing enzyme conjugate bound to the wells of the ELISA plate.

The wells of the ELISA plate were then emptied and washed, and substrate for the enzyme was added and incubated in the wells for 30 min. Stop solution was added and the color was read with a spectrometric plate reader at 450 nm. Because of the competition of the cypermethrin in the sample for antibody binding sites on the wells, the developed color was inversely proportional to the amount of cypermethrin in the sample. The $\log_{10}$ of concentration was plotted against absorbance over the range 1.56–50 ppb (μg/L). If the resulting concentrations fell outside this range of linearity, sample extracts were diluted and reanalyzed.

A standard curve was generated using 98.9% pure cypermethrin (FMC Agricultural Products, Philadelphia, Pa.; FMC No 45497 Ref G0101:60) in methanol. Standard curves were linear with intercepts, slopes, and R^2 ranging from –0.4189 to –0.5882, 0.9177 to 1.227, and 0.984 to 0.999, respectively. Concentrations of the resulting sample solutions were determined from the standard curve. The mass of cypermethrin on each sample was determined by multiplying the concentration of the sample solution by the extraction volume and any additional dilution factor that was used.

Pre- and post-shift urine samples were obtained from production workers (n = 5) and an office worker (pre-shift only) on the same day that environmental sampling was conducted. Samples were placed in coolers containing frozen Blue Ice and transported to the laboratory where they were stored at –20°C until shipped to NIOSH for analysis. At NIOSH, the concentration of cypermethrin equivalents was determined for each sample—using the ELISA method described above for wipe and glove samples—except that the urine samples were diluted 1:10 with methanol before adding the sodium

hydroxide solution. A standard curve was developed in a 1:10 urine:methanol matrix using urine acquired and pooled from unexposed NIOSH laboratory personnel. A linear response in absorbance was observed with the log of concentration across a range of 6.25 to 100 ppb. Standard curves were characterized by intercepts, slopes, and R^2 values that ranged from –0.4948 to –0.55859, 1.2393 to 1.4413, and 0.941 to 0.996, respectively.

To assess background concentrations of cypermethrin or the presence of cross-reacting chemicals, blanks (i.e., unexposed) for each sample matrix (i.e., wipes n = 3, cotton gloves n = 2, and neoprene gloves n = 2) were analyzed. Recovery from the sample matrix was determined by spiking 100 μg of cypermethrin directly onto the unexposed sample matrix (wipes n = 5, cotton gloves n = 4, and neoprene gloves n = 5) and then processing through extraction and analysis.

Workers' knowledge, attitudes, and perceptions related to dermal exposure were evaluated using a technician-administered questionnaire. The KAP questionnaire was constructed using dichotomous and Likert-scale responses and shown to have both good face and content validity.[29] In addition to the dermal KAP questions, the survey instrument also included a demographic module to capture age, gender, ethnicity, and household income information. Altogether, the KAP survey contained 115 questions across seven scales: (1) Knowledge, 13 questions; (2) Information Belief, 3 questions; (3) Behavior, 5 questions; (4) PPE Self-Efficacy, 7 questions; (5) Behavior Belief, 6 questions; (6) Overall Belief, 11 questions; and (7) Training, 4 questions. Workers were provided compensation of $10 per person for their participation.

KAP scales were designed and coded so that protective factors such as higher level of knowledge, or better attitude or perception about dermal exposure and protection yielded a higher score. For example, a higher level of precautionary behavior such as reporting more frequent glove use would result in a higher score on the behavior scale. Data from the survey were entered into an Access database and descriptively analyzed using SAS version 8.0 procedures (SAS Institute, Cary, N.C.).

RESULTS

The ELISA assay showed a blank response for wipes, cotton, and neoprene gloves at (mean ± standard deviation) of 0.08 ± 0.06, 0.18 ± 0.06, and 3.0 ± 0.81 μg cypermethrin equivalents/item, respectively. The measured recoveries (mean ± standard deviation) from spiked media were 95 ± 16% for wipes, 94 ± 5% for cotton gloves, and 61 ± 1% for neoprene gloves. All reported concentrations have been blank corrected using the mean value.

The mass of cypermethrin on the wipe samples (n = 11) varied from 3.2 to 1303 μg/wipe (Table I) for the 100 cm^2 area sampled.

The median amount of cypermethrin measured on the cotton glove dosimeters worn under the neoprene gloves (7 pairs for 14 gloves) was 25 μg/glove (mean of 35 μg/glove), ranging from 1.0 to 173 μg/glove (Table II). As with the wipes, the mass of cypermethrin measured on the glove dosimeter tended to be skewed to the right. No difference was observed in right hand (median of 26 μg/glove) relative to left hand (median 24 μg/glove) contamination (p = 0.30, n = 7). The amount of cypermethrin found on glove pairs was highly correlated (Spearman r = 0.96; p = 0.0005). The amount of cypermethrin detected on glove blanks (mean of 0.18 μg) was well below the amount found on any glove (lowest of 1.0 μg/glove).

The two sampled pairs of reused neoprene gloves were heavily contaminated with cypermethrin. Amounts ranged from 1675 to 20411 with a median value of 4145 μg/glove. Measured values were well above the observed mean blank amount of 3 μg/glove. The level of glove contamination would be expected to be related to their time in service, but this information was unavailable for the two gloves sampled.

The concentration of cypermethrin in workers' (n = 5) urine ranged from 35 to 253 μg/L with a median of 121 μg/L across pre and post-shift samples. These values greatly exceeded the concentration observed for a single pre-shift unexposed office worker (OW) of 8 μg/L (Figure 1). Among the workers, there was no consistent change in concentration from pre- to post-shift where in three of five cases the concentration decreased (p = 0.57, paired t-test, n = 5).

TABLE I. Cypermethrin Loading Measured on Surfaces in Work Environment

Worker Related	Location	Loading (μg/100 cm^2)
G	Outside surface of sample jar	1300
B	Door handle	110
E	Valve handle	75
C	Valve handle	65
E	Tops of worker shoes	39
F	Worker helmet	22
D	Hand railing	19
A	Goggles	18
G	Door plate	15
A	GC equipment	6.1
F	Goggles	3.2

TABLE II. Mass of Cypermethrin (μg) Measured on Cotton Gloves Worn under Neoprene Gloves

Worker ID	Right	Left	Sum
G	1.0	1.2	2.2
D	3.8	3.3	7.1
E	22	10	32
A	26	24	51
C	26	33	59
F	32	35	67
B	98	170	268

Note: Values sorted by Sum from lowest to highest.

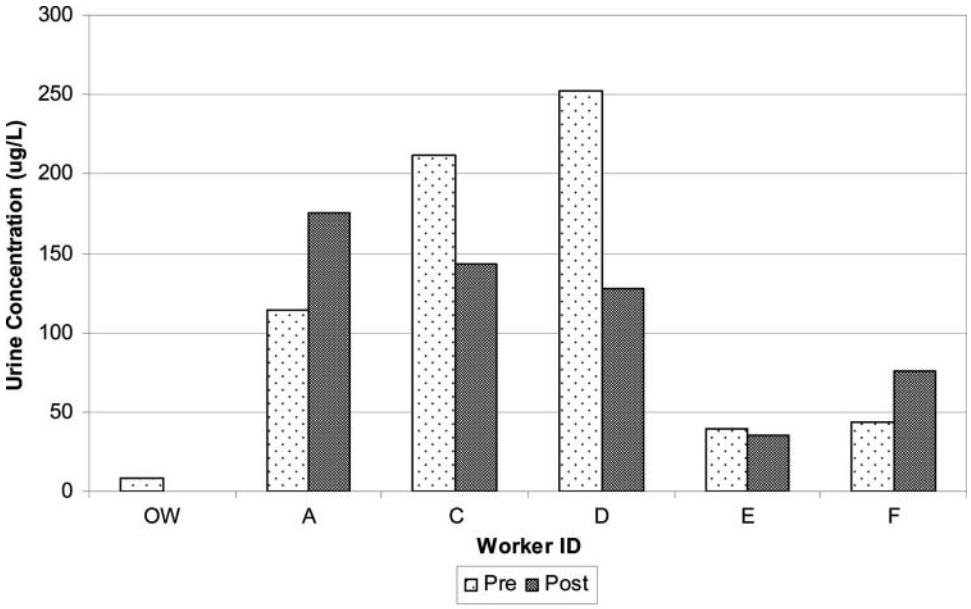

FIGURE 1. Concentration (specific gravity adjusted) of cypermethrin in worker urine pre- and post-shift relative to an office worker (OW). Workers B and G did not provide urine samples.

Worker KAP responses varied by worker and scale (Table III). Knowledge scale responses were relatively low and narrowly distributed (46% to 38% correct), whereas training scale responses were higher and more variable (100% to 44%). The average score across all seven scales ranged from 73% (workers A, C, and E) to 64% (worker G). Due to the small sample size, it was not meaningful to evaluate associations between demographic factors and KAP responses.

The sample size from this small pilot study was not sufficient to enable a robust comparison of the variability in KAP with exposure; however, Spearman correlation with a probability threshold of 0.10 was used to identify potential comparisons to consider in future studies. Each KAP scale ($n = 8$ including the overall mean) was compared with each of four metrics of exposure: (1) sum of right + left cotton glove dosimeter, (2) pre-shift urine, (3) post-shift urine, and (4) the difference between pre and post-shift urine, for a total of 32 comparisons. In only three cases did the probability satisfy the criterion of $p \leq 0.10$.

In all three cases, the correlation was observed with the post-shift urine cypermethrin concentration: (1) behavior belief scale ($r = 0.97$, $p = 0.0048$, $n = 5$); (2) information belief scale ($r = 0.87$, $p = 0.05$, $n = 5$); and (3) personal protective equipment self-efficacy ($r = -0.82$, $p = 0.089$, $n = 5$). Only in the latter case, was the relationship in the expected direction of lower exposure with increasing KAP. The positive correlation observed in the first two cases suggests either an issue with the scale or the identification of an association by chance resulting from the multiple comparisons. These results demonstrate the potential of the KAP survey for identifying both determinants

TABLE III. Average Worker Score across KAP Scales

Worker	Knowledge (%)	Information Belief (%)	Behavior (%)	PPE Self-Efficacy (%)	Behavior Belief (%)	Overall Belief (%)	Training (%)	Overall Mean (%)	Overall Rank[A]
A	46	92	60	33	93	84	100	73	1
B	46	100	50	43	70	91	94	71	2
C	46	100	50	43	80	93	100	73	1
D	46	83	60	81	80	68	75	71	2
E	46	75	100	81	63	73	75	73	1
F	38	75	100	71	70	70	63	70	3
G	46	83	60	76	70	70	44	64	4

[A] "1" indicates the highest score reflecting the most precautionary behavior, and "4" indicates the lowest score and least precautionary behavior.

of dermal exposure and targets of opportunity for intervention, e.g., PPE self-efficacy. Clearly, additional studies with a much larger sample size are required to confirm these associations. The current results will be valuable in designing future studies, and they suggest that for cypermethrin, PPE self-efficacy and post-shift urine concentration hold promise as an informative association.

DISCUSSION AND CONCLUSIONS

Lack of assessment and methodology for dermal assessment form the context and justification for the current study. We sought to test the application of methods for assessing cypermethrin dermal exposure and to provide a preliminary characterization of workplace concentrations that have dermal exposure relevance within the pesticide manufacturing industry.

The detection of low levels of cypermethrin within blank matrices (wipe, neoprene, and cotton gloves) likely suggests some cross-reactivity with extractable matrix material rather than contamination of the blank material. In each case, the blank level was well below levels found within samples, indicating that the assay was sufficiently sensitive for the measurements made. Lee et al.[37] have previously reported similar favorable sensitivity of the assay with detection limits of 1.3 ± 0.5 μg/L measured in water. We observed prevalent (11 of 11 surfaces tested) and substantial (median of 22 μg/100 cm^2 and maximum of 1304 μg/100 cm^2) cypermethrin contamination on surfaces and objects with potential for worker dermal contact. Without more detailed information of workers' activities including frequency, duration, and extent of contact with these surfaces (e.g., as provided by a detailed videotape analysis as described by Freeman et al.[38] for children's pesticide exposure or observational survey)[27] only a qualitative hazard assessment is possible from these data. A quantitative assessment is also limited by the scope of surface sampling, since only 100 cm^2 areas of 11 surfaces were sampled. Contamination of surfaces includes objects that would likely come into contact with workers wearing gloves (e.g., sampling jar, valve handle) but also surfaces/items prone to direct hand contact (e.g., door handle, shoes, helmet, and hand railing). From a para-occupational exposure standpoint, it is significant that all of the workers' PPE stayed at the work site, with the exception of shoes, which were worn home.

Our strategy for assessing worker dermal exposure also included the use of cotton glove dosimeters that were worn under neoprene gloves, the hand protection normally used by workers. Therefore, the cotton glove samplers captured the cypermethrin that otherwise would have come in contact with the skin. The source of cypermethrin sampled in this way could have originated from the workers' hands, contamination inside the glove, or penetration through the glove. Neoprene is a common glove material that is recommended by the manufacturer as resistant to "a broad range of oils, acids, caustics, and solvents."[39]

Specific penetration data or guidance for selection of glove material for dermal protection against cypermethrin could not be found within the published literature. Unfortunately, cypermethrin is not unique in this regard. Klingner and Boeniger[40] described the broader problem of inadequate test methods and data for evaluating glove protection for most chemicals. We observed a median amount of cypermethrin on cotton gloves of 25 μg/glove that ranged as high as 173 μg/glove. The level of contamination on one hand tended to be comparable to and correlated with the other. Although cotton glove dosimeters have been used to assess hand exposure to pesticides among agriculture workers,[33,34] no reports of their use among workers within pesticide or chemical manufacturing could be found for comparison.

Based on the glove dosimetry sampling and assuming a dermal absorption fraction, a rough approximation of the dermal absorption can be made. Wollen et al.[41] estimate an absorption fraction of 0.012 based on the dermal application of cypermethrin to 800 cm^2 of skin on the backs of human volunteers ($n = 6$). To account for the likely enhanced absorption occurring under the neoprene glove due to temperature, humidity, and contact, as observed by Rawson[42] (but unquantified), an additional 10-fold increase in absorption is assumed, resulting in an estimated dermal absorption factor of 0.12. Therefore, if all the cypermethrin sampled by the glove was in contact with the skin and available for absorption, a maximum and median absorbed dose of 33 (sum of 271 μg on right and left glove $\times$ 0.12) and 7.1 μg (sum of 59 μg on right and left glove $\times$ 0.12), respectively, per sampling event is estimated. Recognizing that workers conducted these sampling events typically six times per day, and assuming that this was the only activity that resulted in exposure, a total shift absorbed dose of 198 and 43 μg, respectively, is estimated. Assuming a typical body weight of 72 kg, a body weight adjusted dose of 0.6 and 2.8 μg/kg/day is estimated based on the median and maximum glove values, respectively. This can be compared with the U.S. Environmental Protection Agency's (EPA's) Integrated Risk Information System (IRIS) oral reference dose (RfD) value of 10 μg/kg/day that was last updated in 1990 and is based on the critical effect of gastrointestinal disturbances observed in a 52-week dog study.[43] With the caveat of considerable uncertainty and, likely, underestimation (given workplace objects and surface contamination identified above), the doses estimated from the glove dosimeter are within an order of magnitude of levels where adverse effects are possible. In the current study, we relied on biological monitoring as a strategy to capture workers' complete exposure, which included inhalation, ingestion, and dermal absorption, as well as non-occupational exposure likely dominated by dietary ingestion.[15] Cypermethrin was found at detectable levels for all workers tested, including a presumably unexposed office worker. Although we are limited by a small sample size, the pattern of cypermethrin concentrations among workers lacked consistency with respect to pre- vs. post-shift values (post-shift was higher in two of five cases) and predictive association with glove or surface contamination.

The time-course from exposure to urinary elimination is a key consideration in relating estimates of exposure to urinary biomarker levels.[44] Kuhn et al.[45] reported a urinary elimination half-life of 8.1 hours for cypermethrin based on two male pest control operators where the route of exposure was not specified. Based on the work of Woolen et al.,[41] it is known that absorption and elimination kinetics differ by route of exposure, with a larger fraction (36%) of an oral exposure being eliminated more slowly (half-life of 16.5 hr) relative to dermal absorption where only a total of 1.2% of the dose was detected in urine with a half-life of 13 hr. Given these relatively long half-lives and without specific information as to the time and route of exposure within a shift, we do not have the necessary information to evaluate whether the patterns in urine levels from pre- to post-shift are consistent with the pattern of exposure.

Previous studies evaluating workers' exposure to cypermethrin have relied on measurements of metabolites in urine.[15,46–48] Although the approach of measuring the parent pesticide in urine has been successfully demonstrated for the pyrethoid fenvalerate,[49] we were unable to identify any published reports of parent cypermethrin measured in urine. However, the validity of the ELISA has been previously demonstrated for other pyrethroids and their metabolites in urine[50,51] and cypermethrin detection in other complex matrices.[52,53] Nonetheless, validation of the ELISA method for cypermethrin in urine is lacking and, therefore, is a limitation of the current study.

Within the current study, parent cypermethrin concentrations ranging from 26 to 260 μg/L were observed. These levels are comparable to the aggregate of its major metabolites (including cis- and trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid, 3-phenoxybenzoic acid, and fluorophenoxybenzoic acid) detected in the urine of pest control operators, i.e., <0.05 to 277 μg/L,[54] but above concentrations observed in the general population, e.g., 3-phenoxybenzoic acid (nonspecific metabolite of pyrethroids including cypermethrin, deltamethrin, and permethrin) with an upper 95th percentile of 3.32 μg/L.[55] The general population results, along with observed urine cypermethrin concentration equivalents—observed in an office worker—that are two orders of magnitude lower than among manufacturing workers, suggest that the ELISA method provides a practical and sensitive methodology for occupational exposure assessment. Accordingly, with the caveat of small sample numbers and in the context of a pilot investigation, the current study suggests that the novel ELISA method of analysis employed in the current study is practical and sufficiently sensitive for workplace environmental and biological monitoring. Although the ELISA method appears promising, a limitation within the current study and a future research need is to validate the measurements against traditional laboratory methods. This is especially true for urine biomarker measurements which have not been previously reported by ELISA.

A detailed mass balance analysis is not feasible due to incomplete evaluation of: (1) exposure (oral, dermal, and inhalation); (2) timing of exposure relative to urine collection; and (3) the specificity of the ELISA assay for the parent cypermethrin and its metabolites. However, as a bounding exercise, the mass of cypermethrin observed in urine (median of 120 μg/L) suggests that the glove dosimeter estimate of shift absorbed dose, i.e., median of 43 μg, represented a relatively small fraction of the worker's total exposure. Additional exposure contributions likely included inhalation and dermal contact associated with other tasks over the workday that were not captured in our assessment. A rough approximation, and assuming a typical daily urine void volume of 1 L and a steady-state concentration given by the spot collection, gives a median daily dose of 120 μg. Based on this, the glove dosimeter represented approximately 36% of the dose eliminated in urine. Assuming a body weight of 72 kg, a body mass adjusted daily dose of 1.7 μg/kg/day is estimated, falling within a factor of 6 of the EPA IRIS RfD value of 10 μg/kg/day.[43]

Whereas exposure to pesticides in manufacturing has been examined for some of the older, more notorious pesticides (e.g., alachlor, chlordane, DDT, phenoxy herbicides) as reviewed in Burns,[4] the current study provides some of the first data of their kind evaluating worker exposure hazards associated with pyrethoid pesticide manufacturing. The evaluation is intended as a pilot study testing a variety of evaluative methods (i.e., behavioral attributes, external contamination, and biomarker) demonstrating feasibility and measurement ranges and variability to support a more complete assessment. These preliminary results suggest that exposures within manufacturing are similar to end-use occupational exposures (e.g., pesticide applicators) and therefore warrant further investigation. The small sample size limits the ability to interpret associations across methods; however, there are indications of associations in contamination between right-and left-handed gloves worn by workers. Furthermore, the observed associations between post-shift urine biomarker concentrations and KAP scales (especially Personal Protective Equipment Self-Efficacy but also inverse associations with Behavior Belief, Information Belief) both inform and support the need for additional confirming studies.

ACKNOWLEDGMENTS

This study was funded through a contract with the National Institute of Occupational Safety and Health (NIOSH). We are grateful for the participation of the worker volunteers and the access to them and cooperation provided by the plant management and industrial hygienist.

REFERENCES

1. **Leigh, J., S. Markowitz, M. Fahs, et al.:** Occupational injury and illness in the United States: Estimates of costs, morbidity and mortality. *Arch. Intern. Med. 57*:1557–1568 (1997).
2. **ACGIH:** *2009 TLVs and BEIs Threshold Limit Values for Chemical Substances and Physical Agents*. Cincinnati, Ohio: ACGIH, 2009.

3. "Occupational Injuries and Illnesses Statistics, 1997–2003". [Online] Available at http://www.bls.gov (Accessed January 2005).
4. **Burns, C.J.:** Cancer among pesticide manufacturers and applicators. *Scand. J. Work Environ. Health 31*(*Suppl 1*):9–17 (2005).
5. **Maroni, M., and A. Fait:** Health effects in man from long-term exposure to pesticides. A review of the 1975–1991 literature. *Toxicology 78*(*1–3*):1–180 (1993).
6. **Cheng, W.N., P.J. Coenraads, Z.H. Hao, et al.:** A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant. *Am. J. Ind. Med. 24*(*1*):81–92 (1993).
7. **Shafer, T.J., D.A. Meyer, and K.M. Crofton:** Developmental neurotoxicity of pyrethroid insecticides: Critical review and future research needs. *Environ. Health Perspect. 113*(*2*):123–136 (2005).
8. **Wilks, M.F:** Pyrethroid-induced paresthesia – A central or local toxic effect? *J. Toxicol. Clin. Toxicol. 38*(*2*):103–105 (2000).
9. **Repetto, R., and S.S. Baliga:** Pesticides and immunosuppression: The risks to public health. *Health Policy Plan*. *12*(*2*):97–106 (1997).
10. **Fenske, R.A., and K.P. Elkner:** Multi-route exposure assessment and biological monitoring of urban pesticide applicators during structural control treatments with chlorpyrifos. *Toxicol. Ind. Health 6*(*3–4*):349–371 (1990).
11. **Wolfe, H.R:** Field exposures to airborne pesticides. In *Air Pollution from Pesticides and Agricultural Processes*, R.E. Lee (ed.). Boca Raton, Fla.: CRC Press, 1976. pp.137–161.
12. **Fenske, R.A., S. Birnaum, M. Methner, et al.:** Methods for assessing fieldworker hand exposure to pesticides during peach harvesting. *Bull. Environ. Contam. Toxicol. 43*:805–813 (1989).
13. **Cattani, M., C. Krzysztof, J. Edwards, et al.:** Potential dermal and inhalation exposure to chlorpyrifos in Australian pesticide workers. *Ann. Occup. Hyg. 45*(*4*):299–308 (2001).
14. **Geer, L.A., N. Cardello, J. Roberts, et al.:** Comparative analysis of passive dosimetry and biomonitoring for assessing chlorpyrifos exposure in pesticide workers. *Ann. Occup. Hyg. 48*(*8*):683–695 (2004).
15. **Woollen, B.H.:** Biological monitoring for pesticide absorption. *Ann. Occup. Hyg. 37*(*5*):525–526 (1993).
16. **U.S. Environmental Protection Agency (USEPA):** *Harmonized OPPTS Test Guidelines Series 875- Occupational and Residential Exposure Test Guidelines, Group B Post Application Exposure Monitoring Test Guidelines*. Washington, D.C.: EPA, Office of Prevention, Pesticides, and Toxic Substances, 1998.
17. **Fenske, R.A.:** Dermal exposure assessment techniques. *Ann. Occup. Hyg. 37*(*6*):687–695 (1993).
18. **Krieger, R.I.:** Pesticide exposure assessment. *Toxicol. Lett. 82/83*:65–72 (1995).
19. **Henderson, P.T., D.H. Brouwer, J.J.G. Opdam, et al.:** Risk assessment for worker exposure to agricultural pesticides: Review of a workshop. *Ann. Occup. Hyg. 37*(*5*):499–507 (1993).
20. **Chester, G.:** Evaluation of agricultural worker exposure to, and absorption of, pesticides. *Ann. Occup. Hyg. 37*(*5*):509–523 (1993).
21. **Rutz, R., and R.I. Krieger:** Exposure to pesticide mixer/loaders and applicators in California. *Rev. Environ. Contam. Toxicol.* 129;21–39 (1992).
22. **Kromhout, H., and R. Vermeulen:** Temporal, personal, and spatial variability in dermal exposure. *Ann. Occup. Hyg. 45*(*4*):257–273 (2001).
23. **Wakefield, J.:** Human exposure assessment: Find out what's getting in. *Environ. Health Perspect. 108*(*12*):A559–A565 (2000).
24. **Lumens, M.E.G.L., P. Ulenbelt, R.F.M. Herber, et al.:** The impact of hygienic behavior and working methods on the uptake of lead and chromium. *Appl. Occup. Environ. Hyg. 9*:53–56 (1994).
25. **Ulenbelt, P., M.E.G.L. Lumens, H.M.A. Geron, et al.:** Work hygiene behavior as modifier of the lead air-lead blood relation. *Int. Arch. Occup. Environ. Health 62*:203–207 (1990).
26. **Van Wendel de Joode, B., D.H. Brouwer, R. Vermeulen, et al.:** DREAM: A method for semi-quantitative dermal exposure assessment. *Ann. Occup. Hyg. 47*(*1*):71–87 (2003).
27. **Van Wendel de Joode, B., J.J. van Hemmen, T. Meijster, et al.:** Reliability of a semi-quantitative method for dermal exposure assessment (DREAM). *J. Expo. Anal. Environ. Epidemiol. 15*(*1*):111–120 (2005).
28. **Van Wendel de Joode, B., R. Vermeulen, J.J. van Hemmen, et al.:** Accuracy of a semiquantitative method for Dermal Exposure Assessment (DREAM). *Occup. Environ. Med. 62*(*9*):623–632 (2005).
29. **Geer, L.A., D.H. Anna, B.A. Curbow, et al.:** Survey assessment of worker dermal exposure and underlying behavioral determinants. *J. Occup. Environ. Hyg. 4*:809–820 (2006).
30. **Cummings, K.M., M.H. Becker, M.C. Maile:** Bringing the models together: An empirical approach to combining variables used to explain health actions. *J. Behav. Med. 3*:123–145 (1980).
31. **Becker, M.H.:** The health belief model and personal protective behavior. *Health Educ. Monogr. 2*:409–419 (1974).
32. **Janz, N. K., and M.H. Becker:** The health belief model: A decade later. *Health Educ. Quart. 11*(*1*):1–47 (1984).
33. **Fenske, R.A., N.J. Simcox, J.E Camp, et al.:** Comparison of three methods for assessment of hand exposure to Azinphosmethyl (Guthion) during apple thinning. *Appl. Occup. Environ. Hyg. 14*:618–623 (1999).
34. **Davis, J.E., E.R. Stevens, and D.C. Staiff:** Potential exposure of apple thinners to azinphosmethyl and comparison of two methods for assessment of hand exposure. *Bull. Environ. Contam. Toxicol. 31*:631–638 (1983).
35. **Geno, P.W., D.E. Camann, H.J. Harding, et al.:** Handwipe sampling and analysis procedure for the measurement of dermal contact with pesticides. *Arch. Environ. Contam. Toxicol. 30*(*1*):132–138 (1996).
36. **Bernard, C.E., M.R. Berry, L.J. Wymer, et al.:** Sampling household surfaces for pesticide residues: Comparison between a press sampler and solvent-moistened wipes. *Sci. Total Environ. 389*(*2–3*):514–521 (2008).
37. **Lee, H.J., G. Shan, K.C. Ahn, et al.:** Development of an enzyme-linked immunosorbent assay for the pyrethroid cypermethrin. *J. Agric. Food Chem. 52*:1039–1043 (2004).
38. **Freeman, N.C., P. Hore, K. Black, et al.:** Contributions of children's activities to pesticide hand loadings following residential pesticide application. *J. Expo. Anal. Environ. Epidemiol*. *15*(*1*):81–88 (2005).
39. "Chemical and Liquid Protection Category Overview." [Online] Available at http://ansellpro.com/product-catalog/chemical-liquid-protection (Accessed March 2011).
40. **Klingner, T.D., and M.F. Boeniger:** A critique of assumptions about selecting chemical-resistant gloves: A case for workplace evaluation of glove efficacy. *Appl. Occup. Environ. Hyg. 17*:360–367 (2002).
41. **Wollen, B.H., J.R. Marsh, W.J. Laird, et al.:** The metabolism of cypermethrin in man: Differences in urinary metabolite profiles following oral and dermal administration. *Xenobiotica 22*(*8*):983–991 (1992).
42. **Rawson, B.V., J. Cocker, P.G. Evans, et al.:** Internal contamination of gloves: Routes and consequences. *Ann. Occup. Hyg. 49*(*6*):535–541 (2005).
43. "U.S. Environmental Protection Agency Integrated Risk Information System." [Online] Available at http://www.epa.gov/iris/subst/0380.htm (Accessed January 6, 2011).
44. **Calafat, A.M., X. Ye, M.J. Silva, et al.:** Human exposure assessment to environmental chemicals using biomonitoring. *Int. J. Androl. 29*(*1*):166–171 (2006).
45. **Kuhn, K.H., G. Wieseler, and H.I. Leng:** Toxicokinetics of pyrethroids in humans: Consequences for biological monitoring. *Bull. Environ. Contam. Toxicol. 62*:101–108 (1999).
46. **Wang, D., M. Kamuijma, R. Imai, et al.:** Biological monitoring of pyrethroid exposure of pest control workers in Japan. *J. Occup. Health. 49*:509–514 (2007).
47. **Lessenger, J.E.:** Five office workers inadvertently exposed to cypermethrin. *J. Toxicol. Environ. Health. 35*(*4*):261–267 (1992).
48. **Hardt, J., J. Angerer:** Biological monitoring of workers after the application of insecticidal pyrethroids. *Int. Arch. Occup. Environ. Health. 76*(*7*):492–498 (2003).

49. **Zhang, Z., J. Sun, S. Chen, et al.:** Levels of exposure and biological monitoring of pyrethroids in spraymen. *Br. J. Ind. Med. 48*:82 (1991).
50. **Ahn, K.C., S.J. Ma, H.J. Tsai, et al.:** An immunoassay for a urinary metabolite as a biomarker of human exposure to the pyrethroid insecticide permethrin. *Anal. Bioanal. Chem*. *384*(*3*):713–722 (2006).
51. **Kim, H.J., K.C. Ahn, A. González-Techera, et al.:** Magnetic bead-based phage anti-immunocomplex assay (PHAIA) for the detection of the urinary biomarker 3-phenoxybenzoic acid to assess human exposure to pyrethroid insecticides. *Anal. Biochem*. *386*(*1*):45–52 (2009).
52. **Chuang, J.C., J.M. Van Emon, M.E. Tefft, et al.:** Application of a permethrin immunosorbent assay method to residential soil and dust samples. *J. Environ. Sci. Health B 45*(*6*):516–523 (2010).
53. **Park, E.K., J.H. Kim, S.J. Gee, et al.:** Determination of pyrethroid residues in agricultural products by an enzyme-linked immunosorbent assay. *J. Agric. Food Chem*. *52*(*18*):5572–5576 (2004).
54. **Leng, G., K.H. Kühn, and H. Idel**.: Biological monitoring of pyrethroids in blood and pyrethroid metabolites in urine: Applications and limitations. *Sci. Total Environ. 199*(*1–2*):173–181 (1997).
55. **Centers for Disease Control and Prevention (CDC):** *Third National Report on Human Exposure to Environmental Chemicals* (NCEH Pub. No. 05-0570). Atlanta, Ga: CDC, 2005.