

## Human exposure to indoor residential cyfluthrin residues during a structured activity program

RYAN L. WILLIAMS, CRAIG E. BERNARD, AND ROBERT I. KRIEGER

Personal Chemical Exposure Program, Department of Entomology, and Environmental Toxicology Graduate Program, University of California, Riverside, California, USA

Estimations of absorbed daily dosage (ADD) of chemicals following contact with treated surfaces may be required for risk assessment and risk management. Measurements of ADD based upon biomonitoring are a more reliable data than estimates of ADD from environmental measurements since they require fewer default assumptions. Study participants performed a structured activity program (SAP) 24-h after an application of Tempo<sup>®</sup> 20 WP (cyfluthrin; 3-(2,2-dichloroethenyl)-2,2-dimethyl-cyclopropanecarboxylic acid cyano(4-fluoro-3-phenoxy-phenyl)-methyl ester) on a medium pile, plush nylon carpet. Measurements of total cyfluthrin residue and transferable cyfluthrin residue (cotton cloth and CDFR roller; personal sock and short dosimetry) were made at 3, 7, 12, 23, 47.5, and 407.5 h. Total cyfluthrin residue extracted from (Soxhlet extraction) carpet was  $11.1 \pm 2.7 \mu\text{g}/\text{cm}^2$  1 h prior to the SAP. Transferable cyfluthrin residue obtained through analysis of cotton cloths rolled with a weighted 30-pound cylinder was  $0.11 \mu\text{g}/\text{cm}^2$ . Cyfluthrin residues from socks and shorts were  $0.74 \pm 0.23$  and  $0.15 \pm 0.03 \mu\text{g}/\text{cm}^2$ , respectively. Urine was collected at 12-h intervals during a 72-h period following the SAP and was analyzed for the cyfluthrin biomarker, 4-fluoro-3-phenoxybenzoic acid (FPBA). The mean cyfluthrin equivalents excreted were  $8.4 \pm 5.7 \mu\text{g}/\text{person}$  (yielding an absorbed dosage of  $0.10 \mu\text{g}/\text{kg}$ ;  $n = 7$ ). The elimination half-life was  $16 \pm 5$  h. All predicted ADDs based upon environmental measurements overestimated the ADDs measured by urinary excretion.

Journal of Exposure Analysis and Environmental Epidemiology (2003) 13, 112–119. doi:10.1038/sj.jea.7500257

**Keywords:** pesticide, exposure assessment, biomonitoring, cyfluthrin, 4-fluoro-3-phenoxybenzoic acid (FPBA).

### Introduction

When chemicals are used, exposure and absorption occurs in humans. In this paper, *exposure* is contact with a chemical that may be absorbed. Although the absorbed daily dosage (ADD) is typically less than that predicted from indoor environmental measurements, the duration of indoor human exposure is longer than expected (Krieger et al., 1997). For example, elevated levels of trichloropyridinol (TCP) have been measured in urine specimens of residents approximately 2 months (67 days) following an indoor chlorpyrifos application. Other biological monitoring studies have recorded prolonged, low-level human exposure (Krieger et al., 2001).

Default assumptions used to calculate ADD from environmental measurements are the basis of overestimates of ADD relative to measurements obtained by biomonitoring. Exposure estimates as high as 3–50 mg/kg/day for

chlorpyrifos, DDVP, and propoxur have been published (Berteau et al., 1989), while measurements of ADD following indoor pesticide use normally range from 1 to  $10 \mu\text{g}/\text{kg}/\text{day}$  (Krieger et al., 1997, 2001). To develop more predictive estimates for general use, it is important to clarify the relation between environmental residue measurements and ADD in humans.

Transferable surface residue (TSR) is analogous to dislodgeable foliar residue (DFR) used in agriculture to evaluate worker exposure and to set restricted field entry intervals (Iwata et al., 1977; Zweig et al., 1985; Krieger 1999). Indoor TSRs have been used to estimate human exposure potential during structured activity studies (SAP; Jazzercise<sup>®</sup>; Ross et al., 1990) that included measurements of carpet residues transferred to cotton clothing worn as a dosimeter (Ross et al., 1991; Krieger et al., 2000). The extensive surface contact during the Jazzercise<sup>®</sup> SAP is intended to represent day long, indoor contact with treated surfaces following pesticide use. Available biomonitoring data concerning chlorpyrifos exposures in plush, nylon-carpeted residences support this assumption (Krieger et al., 2000, 2001).

TSR measured using cotton cloth and CDFR roller (Ross et al., 1991) declines rapidly following chemical application (Ross et al., 1991; Bernard et al., 1999; Williams et al.,

1. Address all correspondence to: Dr. R.I. Krieger, Personal Chemical Exposure Program, Department of Entomology, and Environmental Toxicology Graduate Program, University of California, Riverside, CA 92521, USA. Tel.: +1-909-787-3724. Fax: +1-909-787-5803.

E-mail: bob.krieger@ucr.edu

Received 27 November 2001; accepted 20 September 2002

2000). Frequently, pesticide labels designate a time to delay re-entry until treated surfaces have dried. Drying is highly correlated with reduced transferable chlorpyrifos residues (Williams et al., 2000). In general, determinants of exposure and absorbed dose are poorly defined at this time although numerous measurements that document the occurrence of indoor pesticide levels have been published.

Indoor use of pyrethroid insecticides has increased dramatically. Exposure measurements for aggregate risk assessment are not generally available in the literature. Here we report results of carpet and surface residue monitoring following an indoor application of cyfluthrin to nylon carpet. Cyfluthrin availability was studied using a SAP (Jazzercise<sup>®</sup>) and monitoring of the urinary excretion of the biomarker, 4-fluoro-3-phenoxybenzoic acid. Comparative estimates of exposure are developed from indoor environmental and biomonitoring data.

## Methods

### *Study Site*

The study was performed in a Riverside, CA, residence that had no history of recent pesticide use. The study area (5.0 m × 5.5 m) was carpeted with a medium pile, nylon plush carpet in good condition and divided into 12 (1.2 m × 1.2 m) plots. Three plots were used for cyfluthrin sampling, seven plots were used for the SAP, and two plots were not used as determined by a random draw. Cyfluthrin had never been used in that room or anywhere else on the premises.

### *Chemical Application*

Cyfluthrin was applied as Tempo<sup>®</sup> 20 WP (20% Cyfluthrin; Bayer, Kansas City, MO, USA; EPA Reg. No. 3125-380). A suspension of 7.9 g Tempo<sup>®</sup> 20 WP in 3 l deionized water was applied using a Tee-jet<sup>®</sup> nozzle system (Spraying Systems Co.<sup>®</sup>, Wheaton, IL, USA) attached to a mobile cart (Bernard et al., 2001). The spray system was pressurized to 40 psi with nitrogen and primed to remove air from spray lines prior to application. The cart was pulled at approximately 2 ft/s (ca. 60 cm/s).

### *Dosimeters and Sampling*

Each plot included the following dosimeters: 3–5 cm × 5 cm carpet squares for moisture measurements, 3–10 cm × 10 cm carpet squares for total cyfluthrin residue measurement, and an area designated for three transferable cyfluthrin measurements (TSR). The sites were undisturbed after the cyfluthrin application. Dosimeters and TSR samples were collected prior to application and after 3, 7, 12, 23, 47.5, and 407.5 h. Following collection, samples were transported on ice to the laboratory where they were stored in a freezer (–15°C) until analysis.

### *Carpet Moisture Measurement*

Percent carpet moisture was determined with a Denver Instrument IR-200 (Denver Instrument, Arvada, CO, USA). The IR-200 measured the percent moisture using an algorithm for sample weight loss during carpet drying with infrared radiation. The IR-200 working range is from 0.10 to 99.90% moisture with a balance readability of 1 mg. Moisture dosimeters were transferred to the IR-200 sample tray for analysis with clean forceps at each interval. The instrument generated a printout that measured percent moisture at the sampling time.

### *Total Cyfluthrin Residue*

Carpet swatches were extracted with ethyl acetate (Optima grade, Fisher Scientific, Fair Lawn, NJ, USA) in a Soxhlet apparatus. The apparatus was heated in a fume hood for 10 h at five extraction cycles per hour. The final volume was recorded and 20 ml was retained for cyfluthrin analysis.

### *Transferable Cyfluthrin Residue*

A 30-pound short-handled modification (Bernard et al., 2001) of the CDFA roller (Ross et al., 1990) was used to obtain transferable cyfluthrin residues from treated carpet. The transferable surface residue sampling consisted of placing a prewashed 35 cm × 35 cm 100% cotton sheet (Gerber Childrenswear, Charlotte, NC, USA) on the treated carpet that was covered with unused roofing paper and a screen template. The sampling unit was rolled forward and back 25 times. The cotton sheets were extracted with 150 ml of ethyl acetate for 20 min using an Eberbach shaker. A 20 ml extract aliquot was retained for analysis.

### *Structured Activity Program (SAP)*

SAP is a set of 20-min, high surface contact, low-impact Jazzercise<sup>®</sup> exercises and stretches (Ross et al., 1990; Krieger et al., 2000). Seven males were recruited by word of mouth from the university community for the SAP using a protocol approved by the university Human Subjects Review Committee. The study director and a physician's assistant briefed participants about the study objectives. Weights, heights, and ages of the participants are reported in Table 4.

### *Participant Clothing*

Each of the study participants wore one 100% cotton sock (500 cm<sup>2</sup>) on their right foot and 100% cotton shorts (3925 cm<sup>2</sup>). Clothing was washed with laundry detergent followed by two additional wash cycles without detergent and was dried using a home clothes dryer. Each person entered and exited the study site wearing surgical booties (Ulti-Med<sup>®</sup>, St Paul, MN, USA). Following the SAP, the sock and shorts were collected and later extracted with ethyl acetate on an Eberbach shaker. A 20 ml aliquot was retained for cyfluthrin analysis.

### Urine Collection

Each participant collected a complete 12-h urine specimen prior to the SAP and six additional 12-h urine specimens during the subsequent 72 h. A 72-h collection time was selected to capture five half-lives based on a urinary elimination half-life of  $13 \pm 5.1$  h following dermal administration of an analogous pyrethroid, cypermethrin (Woollen et al., 1992) and a urinary elimination half-life of 7 h following a dermal application of cyfluthrin in methanol (Williams and Krieger, unpublished). Woollen et al. (1992) report that 1.2% of the applied cypermethrin dose was excreted as 3-phenoxybenzoic acid metabolites. All participants completed the SAP and complied with the urine collection schedule. No other sources of cyfluthrin exposures were reported.

### Cyfluthrin and Biomarker Analysis

Cyfluthrin was measured in total cyfluthrin residue, transferable cyfluthrin residue, and participant clothing extracts by electron capture gas chromatography.

The urinary biomarker, 4-fluoro-3-phenoxybenzoic acid (FPBA; Bayer Corporation, Agriculture Division, Kansas City, MO, USA), was extracted using a modification of the procedure described by Leng et al. (1997). Urine was acidified and heated for 1 h ( $90^\circ\text{C}$ ) to free acid conjugates. Samples were alkalized to pH 13–14 with NaOH and back extracted using hexane. After reacidification to pH 1–2, acid metabolites were extracted with hexane, concentrated by heating at  $70^\circ\text{C}$ , and derivatized with diazomethane. The derivatized extract was analyzed by GC/MS. The limit of quantification for the FPBA method was 3 ng/15 ml sample.

**Table 1.** Total chemical residue, percent moisture, and transferable chemical residue following a broadcast spray application of Tempo 20 WP on carpet.

| Time (h)       | Total cyfluthrin residue ( $\mu\text{g}/\text{cm}^2$ ) <sup>a</sup> | Percent moisture <sup>a</sup> | Transferable cyfluthrin residue ( $\mu\text{g}/\text{cm}^2$ ) <sup>b</sup> | Percent transferable residue <sup>c</sup> |
|----------------|---|-------------------------------|--|---|
| Preapplication | ND  | $1.2 \pm 0.03$                | ND   | —   |
| 3              | $12.9 \pm 1.7$  | $6.0 \pm 1.40$                | 1.10   | 8.5                                       |
| 7              | $7.7 \pm 1.8$   | $2.0 \pm 0.04$                | 0.11   | 1.4                                       |
| 12             | $8.7 \pm 0.4$   | $1.7 \pm 0.09$                | 0.15   | 1.7                                       |
| 23             | $13.8 \pm 2.1$  | $1.3 \pm 0.02$                | 0.20 <sup>d</sup>  | 1.5                                       |
| 47.5           | $12.5 \pm 1.3$  | $1.4 \pm 0.04$                | 0.12   | 0.9                                       |
| 407.5          | $10.7 \pm 1.4$  | $1.4 \pm 0.05$                | 0.11   | 1.0                                       |
| Mean           | $11.1 \pm 2.7$  | —                             | —  | —   |

<sup>a</sup>Mean  $\pm$  SD ( $n = 3$ ).

<sup>b</sup>Sum of three measurements.

<sup>c,d</sup>Percent transferable residue = (transferable cyfluthrin residue<sub>time x</sub> / total cyfluthrin residue<sub>time x</sub>)  $\times$  100.

Cyfluthrin equivalents excreted from urine were calculated as follows:

Cyfluthrin equivalents

$$= \frac{\text{FW cyfluthrin}}{\text{FW FPBA}} \times \text{FPBA}_{\text{urine}} \text{urine volume}$$

The calculation includes a stoichiometric factor (ratio of formula weights of cyfluthrin to FPBA) multiplied by the measured FPBA concentration in urine and sample volume. The mean elimination half-life is calculated from the best-fit line of a semi-logarithmic plot of percent cyfluthrin equivalents remaining to be excreted *versus* time (Rowland and Tozer, 1980).

## Results

### Environmental Cyfluthrin Measurements

The results of the total chemical residue are reported in Table 1. The total cyfluthrin residue as determined by Soxhlet extraction of carpet dosimeters was  $11.1 \pm 2.7 \mu\text{g}/\text{cm}^2$  (mean  $\pm$  SD).

The results of the CDFA roller dosimeter extracts are reported in Table 1. The transferable percent of total cyfluthrin residue at any time was calculated as follows:

$$\text{Transferable percent} = \left( \frac{\text{transferable residue}}{\text{total chemical residue}} \right) \times 100$$

At 3-h sampling interval, when moisture was the highest, the transferable percent was 8.5%. Once the carpet dried, the transferable surface residue range was 0.9–1.7%. This range for transferable residue from carpet is consistent with values of 1–3% reported by Ross et al. (1991) and Bernard et al. (unpublished) during environmental sampling.

### Clothing as an Exposure Dosimeter

The results of the extracted clothing dosimeters are presented in Table 2. The mean cyfluthrin removed by sock dosimeters was  $372 \pm 114 \mu\text{g}$ . The mean cyfluthrin retained by gym shorts was  $570 \pm 101 \mu\text{g}$ . Using previous measurements of chemical transfer to sock dosimeters (Ross et al., 1990), dermal dose can be estimated. In this study, one sock would represent half a sock pair or 13% of the total amount of chemical transferred to a whole-body dosimeter (Ross et al., 1990). Total chemical transferred was calculated as follows:

$$\text{Total chemical transferred } (\mu\text{g}) \\ = \text{amount on sock } (\mu\text{g}) \div 0.13$$

Using the sock dosimeter and the above equation, the mean calculated amount of cyfluthrin transferred during the SAP was 2900  $\mu\text{g}/\text{person}$ .

### Carpet Moisture Measurement

Control and post-cyfluthrin application measurements of percent carpet moisture are listed in Table 1. The mean moisture measurement at 3-h was five times the preapplication value. Moisture returned to within 0.2% of the preapplication value by 23 h. These measurements followed a drying curve previously observed on plush carpet following a broadcast spray application (Williams et al., 2000). The small increases in percent moisture at later times are likely the result of changes in relative humidity and analytical uncertainty at low moisture levels.

### Urine Analysis

The results of the urine analysis for the cyfluthrin metabolite, FPBA, have been adjusted to cyfluthrin equivalents and are reported in Table 3. All prestudy controls were <LOQ for FPBA. There were seven samples collected following the SAP that were <LOQ (Table 3). The mean cyfluthrin equivalent excretion during the 72 h following the SAP was  $8.4 \pm 5.8 \mu\text{g}$  (range 2.2–16.8  $\mu\text{g}$ ). The mean urinary elimination half-life was  $16 \pm 5$  h (range 10–23 h).

**Table 2.** Cyfluthrin transferred to personal dosimeters during a structured activity program.

| Participant   | Sock<br>( $\mu\text{g}/\text{sock}$ ) | Sock<br>( $\mu\text{g}/\text{cm}^2$ ) <sup>a</sup> | Shorts<br>( $\mu\text{g}/\text{pair}$ ) | Shorts<br>( $\mu\text{g}/\text{cm}^2$ ) <sup>a</sup> |
|---------------|---------------------------------------|--|---|--|
| 1             | 331                                   | 0.7  | NS                                      | NS   |
| 2             | 359                                   | 0.7  | 510                                     | 0.13   |
| 3             | 414                                   | 0.8  | 469                                     | 0.12   |
| 4             | 391                                   | 0.8  | 655                                     | 0.17   |
| 5             | 416                                   | 0.8  | 614                                     | 0.16   |
| 6             | 160                                   | 0.3  | 467                                     | 0.12   |
| 7             | 536                                   | 1.1  | 702                                     | 0.18   |
| Mean $\pm$ SD | $372 \pm 113.8$                       | $0.74 \pm 0.23$                                    | $570 \pm 100.9$                         | $0.15 \pm 0.03$                                      |

<sup>a</sup>Surface area was determined gravimetrically.

### Discussion

Low levels of human cyfluthrin exposure were estimated using environmental and biological samples following an indoor application of the insecticide and a structured activity program. Environmental measurements of transferable cyfluthrin residue measured with the CDFA roller method were only 0.9–1.7% of the total cyfluthrin residue on dried carpet. The urinary biomarker of cyfluthrin, FPBA, was not detectable in pre-exposure samples. Further evaluation of the relationship between environmental measurements, contact-transfer, and human ADD will contribute to understanding the processes that govern human pesticide exposure.

### Environmental Measurements of Cyfluthrin

Cyfluthrin was measurable in all environmental samples. Observations of chemical persistence are consistent with total cyfluthrin residues and transferable cyfluthrin residue measurements previously made indoors (Williams and Krieger, unpublished). Similar observations have been made with chlorpyrifos (Krieger et al., 2001). Semivolatile chemicals such as chlorpyrifos and cyfluthrin persist indoors in small amounts for several weeks and typically produce low-level human exposures below toxicity thresholds.

The total cyfluthrin residue was relatively uniform and unchanged during the sampling period. Previous chemical applications for use with the human SAP were made with indoor foggers (Ross et al., 1990; Krieger et al., 2000) that produced variable amounts of surface residue at the study site. Uniform applications are important to reduce variability and increase the reliability of measurements of chemical persistence, transferability, and potential human exposure. In this study, a mobile spray cart was used to deliver more uniform deposition rates ( $CV < 30\%$ ) than commonly encountered using total release foggers.

Measurements of chemical transfer provide additional estimates of chemical fate, transport, and availability for

**Table 3.** Cyfluthrin equivalents ( $\mu\text{g}$ ) cleared following participation in a structured activity program.

| Participant   | Sample time (h) |                 |                |                   |                   |                   |                   |                 |
|---------------|-----------------|-----------------|----------------|-------------------|-------------------|-------------------|-------------------|-----------------|
|               | 0               | 12              | 24             | 36                | 48                | 60                | 72                | $\Sigma 0-72$   |
| 1             | 0.00            | 0.95            | 0.71           | 0.54 <sup>b</sup> | 0.37              | 0.65              | 0.13 <sup>a</sup> | 3.35            |
| 2             | 0.00            | 3.08            | 6.31           | 2.58              | 4.17              | 0.35 <sup>a</sup> | 0.29 <sup>a</sup> | 16.78           |
| 3             | 0.00            | 1.77            | 2.39           | 2.31              | 1.76              | 2.37              | 1.33              | 11.93           |
| 4             | 0.00            | 0.51            | 2.85           | 1.31              | 1.36              | 0.34              | 0.69              | 7.06            |
| 5             | 0.00            | 1.98            | 3.25           | 2.24              | 3.80              | 1.87              | 0.73              | 13.87           |
| 6             | 0.00            | 0.54            | 1.30           | 0.11 <sup>a</sup> | 0.08 <sup>a</sup> | 0.09 <sup>a</sup> | 0.04 <sup>a</sup> | 2.16            |
| 7             | 0.00            | 0.78            | 0.62           | 0.48              | 0.99              | 0.35              | 0.64              | 3.86            |
| Mean $\pm$ SD | 0.00            | $1.37 \pm 0.95$ | $2.4 \pm 1.97$ | $1.37 \pm 0.87$   | $1.79 \pm 1.55$   | $0.86 \pm 0.94$   | $0.55 \pm 0.32$   | $8.43 \pm 5.77$ |

<sup>a</sup>Sample concentration was below the limit of quantification (LOQ). Cyfluthrin equivalents were determined by multiplying half the LOQ by the urine volume.

<sup>b</sup>The urine volume was not recorded for participant 0053 sample 3 (24–36 h), so the mean volume of samples 2 and 4 was used.

exposure assessment. The amount of residue that was transferred to cotton cloth dosimeters dropped rapidly and was a small fraction of the total cyfluthrin residue at each interval. CDFA roller measurements made 3 h after the application, when the percent moisture was the highest (5 times the preapplication value), transferred only 10% (Table 1; see footnote c) of the mean total cyfluthrin residue. The mean CDFA roller measurement transferred only 1.5% of the mean total cyfluthrin residue when carpet was "dry" and percent moisture returned to within 0.5% of the preapplication value. CDFA roller measurements transferred only 1.8% of the mean total cyfluthrin residue 1 h prior to the SAP. (Table 1; see footnote d).

The increased percent transferred when the carpet moisture was higher was consistent with previous observations using chlorpyrifos (Williams et al., 2000). Measurements of chemical transferability are greatly influenced by moisture. Measurements made during the restricted entry period represent higher exposure potential than measurements made after the carpet has dried. It is also of interest that an increase in pesticide availability with higher relative humidity is observed with insect bioassays (Rust, 1995). On dry carpet, the transferable residue is relatively stable and may result in long-term, low-level human exposure.

Garments were also utilized to measure chemical transfer from treated surfaces to humans. The sock and shorts worn as personal dosimeters provided an additional measure of chemical transferability during the SAP and allow comparisons of transfer with previous studies (Ross et al., 1990; Krieger et al., 2000). Personal dosimeters transferred a small fraction of the total cyfluthrin residue. The average transferable residue based upon cotton sock dosimeters ( $0.74 \pm 0.23 \mu\text{g}/\text{cm}^2$ ) was 7% of the total cyfluthrin residue ( $11.1 \pm 2.7 \mu\text{g}/\text{cm}^2$ ). The average transferable residue on cotton shorts ( $0.15 \pm 0.03 \mu\text{g}/\text{cm}^2$ ) was only 1.4% of the total cyfluthrin residue. The amount transferred to personal dosimeters was similar to that measured with the CDFA roller: 0.74, 0.15, and  $0.20 \mu\text{g}/\text{cm}^2$  for socks, shorts, and CDFA roller, respectively. Although only a small percentage of the total chemical residue is transferred to secondary sources, clothing may represent an important protective residue sink.

Percent transfer [(amount transferred/total cyfluthrin residue)  $\times$  100] to socks and shorts probably represents the extent of chemical transfer from carpet contact during the SAP (Ross et al., 1990). Hands and feet account for a small amount of the body's total surface area, but they have more frequent surface contact than regions that incidentally contact carpet (Zartarian et al., 1998). Hands and feet remove more residue than other body regions and are an important indicator of chemical transfer. Personal dosimeters are valuable means to estimate the transfer and distribution of chemical residue, but represent residue transfer to cotton clothing, nontransferability to human skin. The relationship

of cotton dosimetry and contact-transfer to human skin requires further experimental study.

#### *Urinary Cyfluthrin Equivalent Excretion*

Owing to its specificity, stability in urine, and chromatographic characteristics, FPBA is a useful biomarker for monitoring cyfluthrin exposure even though a complete pharmacokinetic database is lacking. Urine biomonitoring following the SAP produced ADDs similar to previous results (Krieger et al., 2000). FPBA was detectable and distinguished from urine background at very low levels (3 ng/15 ml urine). FPBA was not detectable in any of the control urine samples, and was measurable in most urine specimens during the 72 h following cyfluthrin exposure. Quantification of the biomarker at such low levels makes cyfluthrin a useful pesticide for experimental and situational (opportunistic) human exposure studies.

The mean urinary excretion of cyfluthrin equivalents during the 72 h following exposure was  $8.4 \pm 5.7 \mu\text{g}$ . Excretion data were used to calculate the total absorbed dose. Following an oral administration of cyfluthrin (2.6 mg), 40% of the dose was excreted in urine as FPBA (Leng et al., 1997). Using the urinary excretion value, the absorbed dose of cyfluthrin would be  $21.1 \pm 14.4 \mu\text{g}$ . This adjustment may be high since urine excretion is probably more prominent at lower dosages.

The mean urinary excretion half-life for cyfluthrin equivalents,  $16 \pm 5$  h with a range from 12 to 28 h ( $n=7$ ), is comparable with the half-life previously reported for dermally administered cypermethrin (Woollen et al., 1992). Cyfluthrin and cypermethrin are analogous pyrethroids with similar physical and chemical properties, for example 434 versus 416 MW,  $1.6 \times 10^{-8}$  versus  $1.4 \times 10^{-9}$  mmHg, 6.0 versus 6.6 log  $K_{ow}$ , both are very poorly soluble in water, and both are metabolized rapidly by hydrolytic cleavage of the ester bond, followed by oxidation, partial conjugation, and renal excretion (Leng et al., 1997). Therefore, cypermethrin was considered a good model for cyfluthrin in these studies. Woollen et al. (1992) administered cypermethrin in an unspecified mixture of surfactants and wetting agents in soya-bean oil and observed a  $13 \pm 5$  h cypermethrin half-life with a range from 8 to 22 h ( $n=4$ ), based on total metabolite excretion. The observed urinary cyfluthrin excretion half-life is consistent with the previously reported excretion of cypermethrin (Woollen et al., 1992).

The degree of contact-transfer during the SAP probably represents a high-end exposure scenario compared to normal daily indoor activity (Krieger et al., 2000). Several factors contribute to this classification. Participants wore only cotton shorts to give maximum skin contact during the high-contact activities on the cyfluthrin-treated carpet. Under normal circumstances, clothing would act as a protective barrier that would likely retain 90% or more of the available chemical residue (Krieger, 1995; Thongsinthusak et al., 1993). Even

though the SAP is a low impact, high-contact program, humans could not sustain that level of activity for 16 h. Previous SAP studies with chlorpyrifos resulted in a urinary biomarker excretion of 14 ppb trichloropyridinol (0.58  $\mu\text{g}$  chlorpyrifos equivalents/kg day; Krieger et al., 2000). This urinary biomarker excretion was similar to the nationwide aggregate exposure estimate of 4.5 ppb (0.19  $\mu\text{g}$  chlorpyrifos equivalents/kg/day; Hill et al., 1995), taken at a time when chlorpyrifos was the most-used residential pesticide. Based on these data, the SAP seems to be a useful experimental procedure for the evaluation of high-end indoor chemical exposure.

The resulting cyfluthrin ADD following the SAP is also similar to previous studies in which chlorpyrifos was used as a model insecticide (Ross et al., 1990; Krieger et al., 2000). The chlorpyrifos ADD predictions made from environmental sampling and a chlorpyrifos dermal absorption factor (9.6%) following the SAP produced overestimates of ADD (Krieger et al., 2000). Total chlorpyrifos residue ( $11.1 \pm 2.7 \mu\text{g}/\text{cm}^2$ ) and dermal absorption yielded an estimated ADD of 31.3  $\mu\text{g}$  chlorpyrifos equivalents/kg, more than 28 times the measured ADD (3.3  $\mu\text{g}/\text{kg}$ ). When TSR was used the ADD was 7  $\mu\text{g}/\text{kg}$ , overestimating the ADD approximately 2-times. The ADD of 19  $\mu\text{g}/\text{kg}$  calculated from sock dosimetry overestimated the ADD six-times. These results are very similar to findings with cyfluthrin. Although data are limited at this time, similar exposure potential of pyrethroid and organophosphate insecticides seems likely to represent a common contact-transfer process.

### Environmental Sampling and Absorbed Dose Measurements

Accurate risk assessment and responsible risk management require detailed knowledge of relations between environmental sampling methods and the extent of human exposure. Chemicals that have stable, detectable, and readily excreted biomarkers are important for the development of relations and predictions between environmental measurements and ADD. These relations and predictions can then be used to estimate ADD of similar chemicals.

Several methods of estimating absorbed dose were used to transform environmental measurements to estimates of human exposure (Table 4). Air concentrations were assumed to be negligible based upon the low vapor pressure of cyfluthrin and previous air measurements (Krieger et al., 2001). Multiplying the total cyfluthrin residue ( $11.1 \pm 2.7 \mu\text{g}/\text{cm}^2$ ) by the surface area of an adult (20,000  $\text{cm}^2$ ; USEPA, 1997a) and assuming 100% dermal absorption yields the highest (Tier 1) estimate of ADD (2611  $\mu\text{g}/\text{kg}$ ). When total cyfluthrin residue, adult skin surface area, and a realistic dermal absorption factor (1.2% cypermethrin absorbed/24 h; Woollen et al., 1992) are used, the predicted ADD is 31  $\mu\text{g}/\text{kg}$ , more than 100 times the measured ADD (0.24  $\mu\text{g}/\text{kg}$ ). Transferable residue measurements (0.2  $\mu\text{g}/\text{cm}^2$ ) multiplied by the same factors yielded an ADD of 0.56  $\mu\text{g}/\text{kg}$ , overestimating the measured ADD by approximately two-fold. Transferable residue measurements made with a cotton cloth and CDFA roller can be used to more closely approximate the apparent absorbed dosage at short intervals after insecticide application; however, transferable residue

**Table 4.** Calculations of daily dose using various sampling methods ( $\mu\text{g}/\text{kg}$ ).

| Method  | 100% Dermal absorption | 1.2% Dermal absorption | Absorbed dose |                   |
|---|------------------------|------------------------|---------------|-------------------|
|   |                        |                        | Measured      | Calculated        |
| Total cyfluthrin residue (Soxhlet extraction)         | 2611 <sup>b</sup>      | 31.3                   | —             | —                 |
| Cotton cloth and CDFA roller                          | 47 <sup>c</sup>        | 0.56                   | —             | —                 |
| Personal sock dosimeter                               |                        |                        |               |                   |
| Residue transfer is even over entire body             | 174 <sup>d</sup>       | 2.1                    | —             | —                 |
| Residue transfer to body regions based on WBD         | 36 <sup>e</sup>        | 0.44                   | —             | —                 |
| Urine biomonitoring (cyfluthrin equivalents excreted) | —                      | —                      | 0.10          | 0.24 <sup>f</sup> |

<sup>a</sup>Mean weight, height, and age of participants was 85 kg (range 77–93), 1.84 m (range 1.75–2.13), and 27 years (range 19–31).

<sup>b</sup>(Total residue  $\times$  body surface area)/body weight;  $2611 \mu\text{g}/\text{kg} = (11.1 \mu\text{g}/\text{cm}^2 \times 20,000 \text{ cm}^2)/85 \text{ kg}$ .

<sup>c</sup>(Transferred to cotton cloth  $\times$  body surface area)/body weight;  $47 \mu\text{g}/\text{kg} = (0.2 \mu\text{g}/\text{cm}^2 \times 20,000 \text{ cm}^2)/85 \text{ kg}$ .

<sup>d</sup>(Transferred to sock  $\times$  body surface area)/body weight;  $174 \mu\text{g}/\text{kg} = (0.74 \mu\text{g}/\text{cm}^2 \times 20,000 \text{ cm}^2)/85 \text{ kg}$ .

<sup>e</sup>12% Sock contribution to whole body dosimetry (WBD) chemical transfer (Ross et al., 1990); (Transferred to sock  $\times$  factor for total chemical transferred to participant)/body weight;  $36 \mu\text{g} = (372 \mu\text{g} \times 8.3)/85 \text{ kg}$ .

<sup>f</sup>40% urine excretion of cyfluthrin following oral administration (Leng et al., 1997).

declines more rapidly than exposure potential after several days (Krieger, unpublished).

Personal dosimeters can be used to measure chemical transfer from a treated surface to humans. Dosimeters worn by participants have the same intensity and duration of contact as human skin during the SAP (Krieger et al., 2000). Calculating dermal transfer from the sock dosimeter ( $0.74 \mu\text{g}/\text{cm}^2$ ), assuming residue transfer to be uniform over the entire body, and dermal absorption yields a calculated ADD of  $2.1 \mu\text{g}/\text{kg}/\text{day}$ , overestimating the measured ADD by nine-fold. Results of previous SAP studies in which the subjects also wore whole-body dosimeters can be used to calculate chemical transfer to specific body regions (socks, torso and arms, hands, and legs; Ross et al., 1990). Sock dosimeter measurements combined with previous measures of chemical distribution and dermal absorption predict an absorbed dose of  $0.44 \mu\text{g}/\text{kg}$ , less than two times the measured ADD. Personal dosimetry, body region-specific distribution, and dermal absorption yield ADD estimates similar to biomonitoring.

Predicted (USEPA, 1997b) and measured ADDs differ considerably following USEPA standard operating procedures for residential exposure assessment. The USEPA predicted ADD is  $1.1 \text{mg}/\text{kg}/\text{day}$  (USEPA, 1997b). The estimate is more than 4600 times the measured ADD of  $0.24 \mu\text{g}/\text{kg}/\text{day}$ . According to the conditions of the SOP, this would be equivalent to removing all cyfluthrin residue from the carpet in about 40 min. Although default calculations must be health protective, extreme predictions contribute little to responsible risk management, and they may unnecessarily alarm some persons. SOPs that include more refined measures of contact-transfer potential, dermal absorption, and give consideration to clothing barriers are needed to more reliably predict residential human ADD.

Studies reported here provide data necessary to begin evaluation of the transfer coefficients concept for estimation of residential chemical exposure. When dermal dose, exposure time, and chemical concentration are known, transfer coefficients can be calculated (Ross et al., 1991). The current default transfer coefficient for adults on carpet is  $43,000 \text{cm}^2/\text{h}$  (USEPA, 1997b). Using environmental measurements from this study to calculate transfer coefficients, the respective estimates are  $200 \text{cm}^2/\text{h}$  from total residue,  $10,500 \text{cm}^2/\text{h}$  from transferable residues (roller), and  $2,850 \text{cm}^2/\text{h}$  from personal sock dosimeters. Total residues are not available during short exposure periods, but they may contribute to long-term, low-level exposure. The other two means to estimate exposure from available residue require validation and further study by persons responsible for developing estimates of residential human pesticide exposure.

### Acknowledgments

The authors are grateful to the study participants for their time, cooperation, and commitment to the requirements of

this study. Kelly Tyson provided experience, direction, and enthusiasm as instructor for the Jazzercise<sup>®</sup> activity. Anasthasia Krieger is thanked for her general assistance with all aspects of the SAP. Various donors including S. C. Johnson and Bayer Corporation, Agriculture Division, have provided unrestricted grants-in-aid.

### References

- Bernard C., Dinoff T., Nguyen H., Truong D., and Krieger R. Human exposure following indoor insecticide use. Paper Presented at the Annual Meeting of the American Chemical Society, Anaheim, CA, 1999.
- Bernard C., Nguyen H., Truong D., and Krieger R. Environmental residues and biomonitoring estimates of human insecticide exposure from treated residential turf. *Arch Environ Contam Toxicol* 2001; 41 (2): 237–240.
- Berteau P., Knaak J., Mengle D., and Schreider J. In: Wang, R., Franklin Honeycutt, R., and Reinert, J. (Eds.). *Insecticide Absorption from Treated Surfaces*. American Chemical Society Symposium Series 382. American Chemical Society, Washington, DC, 1989, pp. 315–326.
- Hill R., Head S., Baker S., Gregg M., Shealy D., Bailey S., Williams C., Sampson E., and Needham L. Pesticide residues in urine of adults living in the United States: Reference range concentrations. *Environ Res* 1995; 17: 99–108.
- Iwata Y., Knaak J., Spear R., and Foster R. Worker reentry into pesticide-treated crops. I. Procedure for the determination of dislodgeable pesticide residues on foliage. *Bull Environ Contam Toxicol* 1977; 18: 1–6.
- Krieger R. In: Curry P., Iyengar S., Maloney P., and Maroni M. (Eds.), *Methods of Pesticide Exposure Assessment*. Plenum Press, New York, 1995, pp. 129–132.
- Krieger R. In: Ragsdale N., and Seiber J. (Eds.), *Pesticides: Managing Risks and Optimizing Benefits*. American Chemical Society Symposium Series 734. American Chemical Society, Washington, DC, 1999, pp. 117–132.
- Krieger R., Bernard C., Dinoff T., Dowling K., Fell L., Nguyen H., Osimitz T., Ross J., and Thongsinthusak T. Experimental and situational exposure monitoring of human exposure to household insecticide use. *Abstr Papers Am Chem Soc* 1997: 214.
- Krieger R., Bernard C., Dinoff T., Fell L., Osimitz T., Ross J., and Thongsinthusak T. Biomonitoring and whole body cotton dosimetry to estimate potential human dermal exposure to semivolatile chemicals. *J Expo Anal Environ Epidemiol* 2000; 10: 50–57.
- Krieger R., Bernard C., Dinoff T., Ross J., and Williams R. Biomonitoring of persons exposed to insecticides used in residences. *Ann Occup Hyg* 2001; 45: S143–S153.
- Kuhn K., Leng G., Bucholski K., Dunemann L., and Idel H. Determination of pyrethroid metabolites in human urine by capillary gas chromatography–mass spectrometry. *Chromatographia* 1996; 43: 285–292.
- Leng G., Kuhn K., and Idel H. Biological monitoring of pyrethroids in blood and pyrethroid metabolites in urine: applications and limitations. *Sci Total Environ* 1997; 199: 173–181.
- Ross J., Fong H., Thongsinthusak T., Margetich S., and Krieger R. Measuring potential dermal transfer of surface pesticide residue generated from indoor fogger use: using the CDFR roller method interim report II. *Chemosphere* 1991; 22: 975–984.
- Ross J., Thongsinthusak T., Fong H., Margetich S., and Krieger R. Measuring potential dermal transfer of surface pesticide residue generated from indoor fogger use: an interim report. *Chemosphere* 1990; 20: 349–360.

- Rowland M., and Tozer T. Appendix C. Estimation of the elimination half-life from cumulative urine data. In: *Clinical Pharmacokinetics: Concepts and Applications*. Lea and Febiger, Philadelphia, PA, 1980, pp. 291–293.
- Rust M. Factors affecting control with residual insecticide deposits. In: Rust M., Owens J., and Reiersen D. (Eds.). *Understanding and Controlling the German Cockroach*. Oxford University Press, New York, 1995, pp. 149–170.
- Thongsinthusak T., Ross J., and Meinders D. Guidance for the preparation of human pesticide exposure assessment documents (HS-1612). Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA, 1993.
- USEPA. Exposure Factors Handbook Vol. 1. EPA/600/P-95/002FA. USEPA Office of Research and Development. 1997a.
- USEPA. Standard Operating Procedures (SOPs) for residential exposure assessments. Available at: <http://www.epa.gov/oscpmont/sap/1997/sepember/1sess.htm>. USEPA Office of Science Coordination and Policy 1997b.
- Williams R., Bernard C., and Krieger R. Influence of moisture on pesticide residue availability following indoor applications. Paper presented at the Annual Meeting of the American Chemical Society, San Francisco, CA, 2000.
- Woollen B., Marsh J., Laird W., and Lesser J. The metabolism of cypermethrin in man: differences in urinary metabolite profiles following oral and dermal administration. *Xenobiotica* 1992; 22: 983–991.
- Zartarian V., Ferguson A., and Leckie J. Quantified dermal activity data from a four-child pilot field study. *J Clean Technol Environ Toxicol Occup Med* 1998; 7 (3): 259–268.
- Zweig G., Leffingwell J., and Pependorf W. The relationship between dermal pesticide exposure by fruit harvesters and dislodgeable foliar residues. *J Environ Sci Health* 1985; 20: 27–59.