

# Correlation of Actual Strawberry Harvester Exposure with that Predicted from Abamectin Dislodgeable Foliar Residues

C. L. Lanning,<sup>†</sup> T. A. Wehner,<sup>‡</sup> J. A. Norton,<sup>†</sup> D. M. Dunbar,<sup>§</sup> and L. S. Grosso<sup>\*,†</sup>

Merck & Company, Inc., P.O. Box 450, Hillsborough Road, Three Bridges, New Jersey 08887-0450, Merck & Company, Inc., P.O. Box 2000, Rahway, New Jersey 07065-0900, and Merck & Company, Inc., Suite 204, 7555 North Del Mar Avenue, Fresno, California 93711

Sixteen male strawberry harvesters were monitored during two 3-h harvesting periods for dermal exposure to abamectin, a miticide/insecticide. Upper body exposures were monitored by cotton undershirt dosimetry, hand rinses, and facial washes. Exposure was greatest to the hands (833 ng/h) followed by the torso (380 ng/h) with negligible residues detected on the face. With <1% dermal penetration, the average systemic exposure was calculated to be 1.36 ng/kg/day. The ratio of the no-observed-effect level (NOEL) of 50  $\mu\text{g}/\text{kg}/\text{day}$  to the worker exposure of 1.36 ng/kg/day yielded a margin of exposure (MOE) of 36 800. Abamectin foliar residues ranged from 40.7 to 0.17 ng/cm<sup>2</sup> at 2 h and 7 days after the second application, respectively. Dislodgeable foliar residue (DFR) data at the harvest time of 3 days after the second application, 0.84 ng/cm<sup>2</sup>, combined with the Zweig transfer factor (5000 cm<sup>2</sup>/h) and a dermal penetration of 1% resulted in a predicted worker exposure of only 5.6 ng/kg/day and a corresponding MOE of 8930. These results suggest that DFR data may be used to conservatively predict worker exposure to abamectin.

**Keywords:** *Abamectin; dislodgeable foliar residues (DFR); worker exposure*

## INTRODUCTION

Abamectin belongs in the family of the naturally occurring avermectins that are produced from the fermentation of the soil microorganism *Streptomyces avermitilis*. Abamectin is a mixture of two components, avermectin B<sub>1a</sub> ( $\geq 80\%$ ) and avermectin B<sub>1b</sub> ( $\leq 20\%$ ). Biologically and toxicologically these components are considered equivalent. Abamectin is exceptionally susceptible to photodegradation. The major products resulting from photodegradation are the delta 8,9-isomer of avermectin B<sub>1a</sub> and a polar and a moderately polar fraction, of which only the 8,9-isomer was found to be toxic (Crouch et al., 1991, 1992). The total toxic residue therefore consists of avermectin B<sub>1a</sub> and its 8,9-isomer and to a lesser extent avermectin B<sub>1b</sub> and its 8,9-isomer.

Abamectin is the active ingredient found in formulations registered worldwide for control of motile mites and insect larvae on both agricultural and horticultural crops. These crops include almonds, apples, celery, citrus, cucurbit vegetables, lettuce, pears, peppers, strawberries, tomatoes, walnuts, hops, grapes, and chrysanthemums. Its use on such labor intensive crops warrants worker exposure data to ensure worker/harvester safety.

Other studies have been conducted to measure worker exposure to abamectin including exposure from airblast application to citrus groves (Grosso et al., 1989) and exposure from greenhouse chrysanthemum harvesting (Grosso et al., 1989; Jenkins et al., 1987). Because these harvester studies are both very laborious and costly, it

has been proposed that worker exposure can be safely estimated by the product of the dislodgeable foliar residues (DFR) and an appropriate transfer factor (Nigg et al., 1984; Zweig 1984; Krieger et al., 1990). In general, the Zweig factor of 5000 cm<sup>2</sup>/h (based upon a one-sided surface area) is used as the transfer factor in estimating worker exposure (Zweig et al., 1984); however, for low-growing crops such as strawberries, a transfer factor of 1000 cm<sup>2</sup>/h (based upon a two-sided surface area) may be used (Krieger et al., 1990).

Using crop-specific DFR data in combination with a transfer factor in lieu of empirical harvester exposure values may prove to be an acceptable alternative in predicting overall worker exposure and margins of exposure (MOEs) for other avermectins. The purpose of this study was to correlate actual harvester exposure with that predicted from abamectin DFR data and published transfer factors to demonstrate that DFR data are useful to conservatively estimate worker exposure.

## EXPERIMENTAL PROCEDURES

This study was conducted by Merck Research Laboratories (MRL) near Watsonville, CA, following an MRL-approved protocol that was reviewed and approved by the California Department of Pesticide Regulation (CDPR). The use of human subjects was approved by the California Committee on Human Research. Each critical phase of this project along with the raw data and study report was reviewed and approved by Quality Assurance to ensure compliance with EPA/FIFRA GLP Regulation (40 CFR 160).

**Test Subjects.** Briefing meetings were held whereby the details of this study were presented to the potential study candidates. All candidates were experienced in harvesting strawberries. Consent agreements were distributed to all of the male volunteer harvesters and read to them to ensure they understood the tasks to be performed and the nature of their involvement. All harvesters wanting to participate in this

\* Address correspondence to this author at Merial Limited, Bldg. D, 2100 Ronson Rd., Iselin, NJ 08830-3077.

<sup>†</sup> Merck & Co., Three Bridges.

<sup>‡</sup> Merck & Co., Rahway.

<sup>§</sup> Merck & Co., Fresno.

study were required to sign this agreement. After such time, 20 volunteers were selected to participate in this study. From these 20 volunteers, 4 were considered alternates. The harvesters were monitored twice following 3-h exposure periods, once in the morning and once in the afternoon at the same site.

**Description of Field Studies.** This study was conducted in 8 acres of strawberry fields of J&D Farms located in Watsonville, CA. Abamectin 0.15 EC formulation (1.8% w/v) was applied according to the Section 18 approved label of two times at 7-day intervals at the application rate of 16 fluid oz/acre [ $\approx 0.02$  lb of active ingredient (ai)/acre]. The abamectin treatments were made in 100 gal of water/acre on both dates of application. The strawberries were harvested at the approved preharvest interval (PHI) of 3 days after the second application.

**Procedure for Collecting Harvester Samples.** The harvesters were assigned an identification number, and the age, weight, and height of each worker were recorded. Exposure to the face was monitored by swabbing an area approximately 4 cm by 4 cm on the forehead, left cheek, right cheek, and throat. Each area was wiped three times through a template with swabs moistened with 10% isopropyl alcohol (IPA) in distilled water. The swabs were wrapped in aluminum foil and stored on dry ice until transfer to permanent frozen storage ( $-70$  °C).

Hand exposure was monitored by rinsing both hands in a 50% (IPA)/distilled water solution. Each hand was vigorously shaken 25 times in 250 mL of the 50% IPA/distilled H<sub>2</sub>O solution contained in a gallon Zip-loc plastic bag. The 250-mL solutions representing residues from both hands were poured directly into a 1-L polyethylene bottle and tightly capped. This procedure was repeated twice. The resulting 750 mL of rinse was stored on dry ice until transfer to permanent frozen storage ( $-20$  °C).

To best determine dermal exposure to the torso, each of the harvesters wore a lightweight, 100% cotton, long-sleeved undershirt dosimeter under his normal shirt for each of the two 3-h exposure periods. After each exposure period, the undershirt dosimeters were removed, placed in separate plastic Zip-loc bags, labeled, sealed, and stored on dry ice until transfer to a permanent frozen storage facility ( $-20$  °C). Lower body exposure was not monitored because previous studies with strawberry harvesters demonstrated minimal exposure to the lower body (Zweig et al., 1984).

Controls consisted of one long-sleeved, 100% cotton undershirt; four sets of cotton swabs moistened with 10% IPA; and 100 mL of 50% IPA, which were placed near the sampling area during each of the 3-h monitoring periods. These samples were handled in an identical manner as the field-collected samples.

**Procedure for Collecting Foliar Samples.** To determine DFR, 48 2.5-cm<sup>2</sup> leaf disk samples were collected at random from the treated and untreated strawberry fields at every specified sampling interval. Sampling times were 2 h and 3 and 7 days after the first application and 2 h and 1, 3, and 7 days after the second application. The untreated field was located 100 feet upwind and upslope from the treated field. Additionally, pretreatment leaf disk samples were collected prior to the first application. Leaf disks were collected only from fully expanded mature leaves from the tops of the strawberry plant. After collection in the field, the leaf disks were brought chilled to a nearby facility for immediate extraction with a dilute solution of aqueous Triton X-100. DFR values were calculated based on the basis of one-sided surface areas, which assumes that all abamectin residues are on one surface of the leaf. As such, a two-sided area would decrease the DFR by half.

**Field Fortifications and Recovery.** Untreated control samples (50% IPA solutions, facial swabs, cotton undershirts, and leaf disks) were fortified with various amounts of abamectin as a measure of the stability of the residues during the handling and storage process as well as a measure of the recovery method. Fortified samples were handled and stored similarly as the harvester samples.

Aliquots of 50% IPA solutions (representing the hand rinses) were fortified in triplicate by pipetting 1 mL of a standard solution containing either 25 ng/mL or 258 ng/mL avermectin B<sub>1a</sub> into the 50% IPA/water solution. Three cotton swab samples were each fortified with 0.5 mL of a standard solution containing either 51 ng/mL or 517 ng/mL avermectin B<sub>1a</sub>. Three cotton undershirts were fortified with 1.0 or 2.0 mL of a standard solution containing 258 ng/mL or 517 ng/mL avermectin B<sub>1a</sub>, respectively. The standard solution was pipetted slowly across the surface of the shirt to ensure that it would be absorbed by the cotton. The IPA solutions and the undershirts were fortified at the beginning of the morning and afternoon monitoring periods; otherwise, all other samples were fortified prior to the morning monitoring period. Leaf disks were fortified with 6, 36, or 360 ng of avermectin B<sub>1a</sub>, 26.4 ng of avermectin B<sub>1b</sub>, and 6 or 36 ng of the photolytic degradate, abamectin 8,9-Z isomer. Fortified as well as nonfortified solutions were stored near the field during the morning and afternoon 3-h monitoring periods. At the end of the monitoring periods, all control and fortified samples were frozen in dry ice and transferred to permanent frozen storage ( $-20$  °C).

**Analytical Method.** Prior to analysis of the facial swabs, hand rinses, or cotton undershirts, the method for analysis was validated. Unfortified control samples were assayed to demonstrate a lack of interference. Additionally, the fortified hand rinse, cotton undershirt, facial swab, and leaf disk samples (discussed above) were assayed to ensure proper recovery (i.e., residue does not adhere to the Zip-loc bags or to the cotton swabs or undershirts) and to validate the method. The fortified samples and the harvester samples were assayed at least in duplicate using the methods described below. Recoveries of B<sub>1a</sub> from the fortified facial swab, hand rinse, and undershirt samples were 94, 97.5, and 81%, respectively. Recoveries of B<sub>1b</sub> from the facial swab, hand rinse, and undershirt samples were 108, 114, and 89%, respectively.

**Facial Swabs.** The facial swab samples including the appropriate controls were assayed for avermectin B<sub>1a</sub> and B<sub>1b</sub> using Merck Method 5005 (Wehner and Tway, 1990). Briefly, the facial swabs were transferred into a flask and extracted three times by mechanically shaking for 30 min with 50 mL of acetonitrile each time. The acetonitrile extracts were combined into a graduated cylinder, and the volume after the final extraction was adjusted to 150 mL and mixed. Fifty milliliters of the extract (i.e., one-third of the extract) was transferred to another graduated cylinder, diluted to 500 mL with water, and mixed. The aqueous extract was quantitatively loaded onto a conditioned C<sub>8</sub> 1000-mg solid phase extraction (SPE) column on a vacuum manifold (the SPE column was conditioned with 6-mL rinses each of acetonitrile, water, and water). The extract load was discarded after eluting through the column. Then a 15-mL centrifuge tube was then placed under the column to collect the eluate. Twelve milliliters of acetonitrile was used to rinse the graduated cylinder into the SPE column, and the eluate was collected under a low vacuum. The acetonitrile eluate was evaporated to 1 mL under nitrogen using a water bath at 50 °C. The 1-mL concentrate was diluted to 5 mL with water. Five milliliters of hexane was added, and the tube was shaken for 1 min and centrifuged for 5 min at 2000 rpm (750g). The hexane phase was transferred to another tube, and the raffinate was extracted first with a 5-mL and then a 4-mL aliquot of hexane, using the same 1-min shaking, 5-min centrifuging as before. The combined hexane extract volume was 14 mL. An amino-propyl SPE column (500 mg) was conditioned by washing twice with 3 mL of hexane using a vacuum manifold. The combined hexane extract was loaded onto the prepared column. The column was washed sequentially with 4 mL of hexane, 3 mL of toluene, and 15 mL of methylene chloride, with the washes discarded. The column was eluted with 5 mL of a 50:50 mixture of acetone in methylene chloride. The eluate was evaporated to dryness and a portion derivatized. The acetic anhydride derivatization procedure was as described by Wehner et al. (1993). The derivatized residue was reconstituted in 2.0 mL of methanol and quantified by comparison with

derivatized standards. Results that were less than  $<0.3$  ng/cm<sup>2</sup> were reported as not detected (ND).

**Hand Rinse Samples.** The hand rinse samples including the appropriate controls were also assayed for avermectin B<sub>1a</sub> and B<sub>1b</sub> using Merck Method 5005 (Wehner and Tway, 1990). The hand rinse samples were transferred from the polypropylene bottles into a 2000-mL graduated cylinder. The bottle was rinsed twice with 25-mL aliquots of IPA/water, and the rinsates were transferred into the graduated cylinder. The solution was diluted to 2000 mL with water, making the composition approximately  $\approx 20\%$  organic. A 1000-mL aliquot of the solution was loaded onto a prepared C<sub>8</sub> 1000-mg SPE column, conditioned as described above. The column was eluted with 12 mL of acetonitrile. The acetonitrile eluate was evaporated to 1 mL, made aqueous, and extracted with hexane as described above for the facial swabs. The combined extracts were evaporated to dryness and derivatized with acetic anhydride according to the procedure described by Wehner et al. (1993). Quantification was based upon comparison with external standards that were derivatized and analyzed concurrently with the hand rinse samples. Hand rinse samples that were less than  $<4$  ng total were reported as ND. Samples at  $\geq 5$  ng or more were reported as the total number of nanograms found in the sample.

**Cotton Undershirt Samples.** The cotton undershirt dosimeter samples including the appropriate controls were assayed for avermectin B<sub>1a</sub> and B<sub>1b</sub> using the Merck Method ABA-501 (Mayo and Tway, 1990). Each undershirt was cut into quarters of approximately equal area (2500 cm<sup>2</sup>). Each quarter was placed in a 1-gallon Nalgene bottle along with 2 L of acetonitrile and shaken for 30 min. The acetonitrile was decanted, the procedure was repeated twice, and the pooled acetonitrile was dried to approximately  $\approx 200$  mL using a vacuum rotary evaporator. The extract was transferred to a 250-mL graduated cylinder, and brought to 250 mL with acetonitrile, and mixed. After mixing, a 50-mL aliquot was transferred to a 500-mL graduated cylinder and diluted to 500 mL with deionized water. The aqueous solution was filtered through a 63-mm porcelain funnel fitted with a piece of Whatman No. 1 filter paper in a filter flask. The filter paper was prerinsed with 3 mL of deionized water. The filtrate was collected under vacuum and transferred quantitatively to a prepared 1000-mg C<sub>8</sub> SPE column (conditioned as described above for facial swabs). The vacuum flask was rinsed with a 6-mL acetonitrile aliquot. The acetonitrile rinse was used as the eluant and collected through the C<sub>8</sub> column. Another 6-mL aliquot of acetonitrile was eluted through the column and collected in the same 15-mL centrifuge tube. The combined acetonitrile eluate was evaporated to 1 mL as described above. To the 1-mL concentrate were added 4 mL of water and 1 g of sodium chloride, and the tube was added, stoppered and shaken. Five milliliters Then, 5 mL of hexane was added and the extract was partitioned into hexane, with repeat extractions of 5 mL and 4 mL of hexane. The remaining steps were identical to those used for the facial swabs. For quantification, external standards were derivatized and analyzed concurrently with the harvester samples. The total nanograms for the quarters of each undershirt were added together to obtain the total nanograms per undershirt. The limit of detection was established as a total of 9 ng, or 3.6 pg/cm<sup>2</sup>.

**Leaf Disk Samples.** Four leaf disk samples at each time point were analyzed for avermectin B<sub>1a</sub>, B<sub>1b</sub>, and their corresponding delta 8,9-isomers using the Merck Method 3548H (Rosenthal and Tway, 1989). To each polypropylene bottle containing the collected leaf disks was added 100 mL of deionized water containing 4 drops of a Triton X-100 solution (1:50). The leaf disks were shaken on a mechanical shaker for 30 min, and the aqueous solution was decanted into a new polypropylene bottle for shipment to the analytical laboratory. The extraction of the disks was repeated with a second 100-mL aliquot of deionized water containing 4 drops of the (1:50) Triton X-100 solution. The second extraction was combined with the first. An additional 25 mL of water was used to rinse the leaf disks and decanted into the extract bottle. The leaf disks were removed from the polypropylene bottle, and the

empty bottle was rinsed twice with 10 mL of methanol. The methanol rinse was added to the extract bottle. The sample extracts were stored frozen at  $-20$  °C until shipment with dry ice and assay in the analytical laboratory.

In the analytical laboratory, the extract solution was poured from the polypropylene bottle to be filtered under vacuum through a Whatman No. 3 filter paper in a porcelain funnel that was prerinsed with 3 mL of water. The filtrate was collected in a filter flask. The polypropylene bottle was rinsed twice with 25 mL of water and twice with 10 mL of methanol and passed through the filter. The combined filtrate was transferred from the filter flask to a 500-mL graduated cylinder, and the flask was rinsed with 10 mL of methanol into the graduated cylinder to complete the quantitative transfer. The extract was diluted to 500 mL with water.

The aqueous solution was passed through a 500-mg conditioned C<sub>8</sub> column, prepared by rinsing under vacuum by 6 mL of acetonitrile followed by two rinses of 6 mL of water. The column was loaded under low vacuum and the load was discarded. A 15-mL centrifuge tube was placed under the column in the vacuum manifold, and the column was eluted twice with 6 mL of acetonitrile, to yield a collected eluate of  $\approx 12$  mL. The acetonitrile eluate was evaporated to 1 mL, diluted with 4 mL of water, and partitioned with hexane as described above for the facial swabs. The combined hexane extract totaled  $\approx 14$  mL. The 14-mL extract was further purified using a 500-mg aminopropyl column, as described above for the facial swabs. The column was eluted with 5 mL of a 50:50 mixture of acetone in methylene chloride. The acetone/methylene chloride extract was evaporated to dryness and derivatized according to the two-step trifluoroacetic anhydride derivatization procedure described by Wehner et al. (1993). The limit of detection was established as 0.02 ng/cm<sup>2</sup>. For quantification, external standards were derivatized and analyzed concurrently with the leaf disks. Results that were less than  $<0.02$  ng/cm<sup>2</sup> were reported as ND and those less than  $<0.05$  ng/cm<sup>2</sup> but greater than  $>0.02$  ng/cm<sup>2</sup> were reported as not quantifiable (NQ).

## RESULTS AND DISCUSSION

**Determining Harvester Exposure.** Reentry into pesticide-treated fields may pose risk to harvesters (Popendorf and Leffingwell, 1982). Prior to the mid 1960s, it was believed that inhalation exposure was the greatest concern, but it was later demonstrated that dermal contact is typically the route of greatest exposure (Westlake et al., 1973; Spear et al., 1977).

Researchers have demonstrated that dermal exposure of strawberry harvesters occurs predominantly to the hands and forearms (Popendorf et al., 1982; Everhart and Holt, 1982). It has been postulated that dermal body exposure could therefore be estimated by monitoring only these two anatomical regions (Zweig et al., 1983). The strawberry harvesters in this study were exposed primarily to the hands (833 ng/h) with some exposure to the torso (380 ng/h). Facial residues were 2.1 ng/h. The average overall exposure was 1215 ng/h (Tables 1 and 2).

In terms of actual risk assessment using the average weight of the workers (71.4 kg) and an 8-h work day, 1215 ng/h corresponded to a systemic exposure of 1.36 ng/kg/day (Table 4). If the standard assumed weight of 60 kg was used instead of the measured weight, the systemic exposure would be 1.62 ng/kg/day (Table 4). These low systemic exposures were a result of the  $<1\%$  dermal penetration of abamectin (Wislocki et al., 1988). This exposure information was used to derive the MOE, defined as the ratio of the NOEL to exposure. Generally, workers are not considered at risk when the MOE exceeds 100 (U.S. Congress, 1996). In this study the

**Table 1. Abamectin Harvester Exposure during 3 h Work Periods**

worker	wt (kg)	face <sup>a</sup> (ng)		hands (ng)		shirts (ng)	
		a.m.	p.m.	a.m.	p.m.	a.m.	p.m.
1	56.9	ND	NQ	1609	1693	NA	503
2	68.7	ND	NQ	1498	2471	NA	672
3	75.3	ND	17	3041	2993	NA	1000
4	72.1	ND	NQ	2030	2941	NA	697
5	73.9	ND	ND	1688	3046	457	438
6	73.7	ND	23	2166	3434	949	1094
7	70.3	ND	ND	1081	2202	292	174
8	66.7	ND	ND	1314	2277	961	792
9	65.6	ND	ND	3502	1845	303	291
10	75.7	ND	ND	3284	1503	378	298
11	63.9	ND	NQ	5041	2358	2942	829
12	68.5	ND	ND	3832	2479	344	287
13	87.6	ND	ND	3770	2895	2742	606
14	79.1	ND	ND	3138	1852	1763	530
15	64.0	ND	ND	3303	1711	1657	908
16	65.0	ND	NQ	2208	1426	2333	908
mean <sup>b</sup>	71.4 ± 8.6	ND	NQ	2657	2319	1260	607
mean residues/h		ND	NQ	886 ± 373	773 ± 205	420 ± 301	202 ± 92

<sup>a</sup> ND, not detected (see definition under Experimental Procedures); NQ, not quantifiable (approximately twice the ND); NA, not available (recoveries were <70%). <sup>b</sup> Results are not corrected for recovery and include both the B<sub>1a</sub> and B<sub>1b</sub> residues.

**Table 2. Mean Avermectin Dermal Exposures of 16 Strawberry Harvesters**

	mean dermal exposure <sup>a</sup> (ng/h)		
	face	hands	shirts
a.m.	1.0 <sup>b</sup>	837	516
p.m.	3.1	828	243
total	4.1	1665	759
av	2.1	833	380
av overall exposure	1215 ± 548		

<sup>a</sup> Residue values were corrected for recovery (recoveries ranged from 81 to 120%). <sup>b</sup> For calculation purposes ND and NQ were used at half the detection limit (Hornung and Reed, 1990).

**Table 3. DFR of Abamectin on Strawberries following Second Application<sup>a</sup>**

sampling time	total residues <sup>b</sup> (ng/cm <sup>2</sup> )
2 h postspray	40.7 ± 4.1
1 day postspray	4.3 ± 1.4
3 days postspray	0.84 ± 0.57
7 days postspray	0.17 ± 0.06

<sup>a</sup> Pesticide treatment: 0.02 lb of ai/acre. <sup>b</sup> Represents average residues of abamectin B<sub>1a</sub> and its 8,9-isomer plus abamectin B<sub>1b</sub> and its 8,9 isomer (*n* = 4).

MOE for strawberry harvesters was 36 800 (using actual weights) or 30 900 (using the assumed weight of 60 kg), indicating negligible risk to workers.

The NOEL (50 µg/kg/day) used in the determination of the MOE was based upon tremors observed in a subpopulation CF-1 mice treated with 0.075 mg/kg/day abamectin from days 6 through 15 of gestation (Lankas and Gordon, 1989). The use of the CF-1 mouse for risk assessment purposes provides a conservative estimate for predicting abamectin safety in humans since it is the most sensitive species to date in all of the toxicology studies conducted with the avermectins.

The greater sensitivity of this subpopulation of CF-1 mice has been attributed to the absence of P-glycoprotein (P-gp) in their blood-brain barrier (Lankas et al., 1997). It is known that abamectin is a substrate for P-gp and that P-gp plays a role in preventing the

**Table 4. Harvester Exposure and Safety Assessment<sup>a</sup>**

crop	basis of exposure	systemic exposure	MOE <sup>b</sup>
		(ng/kg/day)	
strawberry	actual worker	1.36	36800
strawberry	actual worker; assumed weight of 60 kg	1.62	30900
strawberry	predicted from DFR Zweig factor (5000 cm <sup>2</sup> /h) low-crop factor <sup>c</sup> (1000 cm <sup>2</sup> /h)	5.60	8930
		0.56	89300
chrysanthemum <sup>d</sup>	actual worker (60 kg)	94.5	529
chrysanthemum	predicted from DFR data (Zweig factor)	147	340

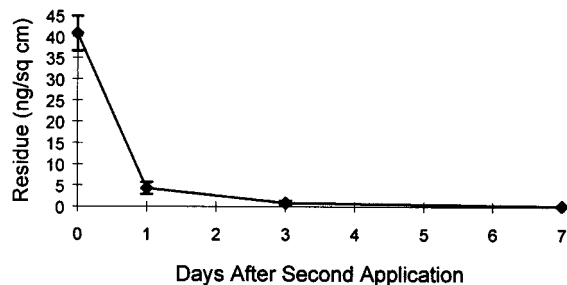
<sup>a</sup> The calculated exposures from actual harvester exposure data and that predicted from DFR data are presented. To calculate systemic exposure using actual harvester exposure data, the average weight of 71.4 g was used and the assumed weight of 60 kg was also used. However, the assumed weight of 60 kg was used in the model to predict systemic exposure using DFR data (3 days after second application) and the appropriate transfer factor. <sup>b</sup> NOEL: 50 µg/kg/day. <sup>c</sup> DFR was adjusted by half since the low-crop factor is based upon a two-sided surface area. <sup>d</sup> Grosso et al. (1989).

penetration of various hydrophobic agents including abamectin across the blood-brain barrier in various species (Schinkel et al., 1994; Lankas et al., 1997). Humans, monkeys, rats, and other strains of mice have P-gp (Juranka et al., 1989) and tolerate higher doses of the avermectins (Lankas and Gordon, 1989; Lankas et al., 1997). Given that the absence of P-gp in the CF-1 mouse is responsible for the increased sensitivity to avermectins, this strain of mouse may not be appropriate for predicting risk to humans.

Human safety to avermectins can be further supported by the worldwide use of ivermectin in human medicine. Ivermectin, the 22,23-dihydro derivative of avermectin B<sub>1</sub>, has been used extensively in humans to treat onchocerciasis, also known as river blindness. Humans have been reported to tolerate single doses as high as 1.6 mg/kg without adverse effects (Costa and Diazgranados, 1994); however, CF-1 mice treated with ivermectin or abamectin displayed signs of toxicity at doses as low as 0.2 or 0.075 mg/kg, respectively (Lankas and Gordon, 1989; Lankas, 1994). This extensive safety profile with ivermectin further supports the conservatism of risk assessments using the CF-1 mouse.

**Estimating Harvester Exposure.** Instead of conducting elaborate harvester monitoring studies, worker exposure may also be estimated by using an empirically derived transfer factor and product-specific DFR data. Abamectin DFR were determined from the foliar samples collected after the second abamectin application at 0.02 lb of ai/acre. These values ranged from 40.7 ng/cm<sup>2</sup> at 2 h postapplication to 0.17 ng/cm<sup>2</sup> at 7 days postapplication (Table 1). At the time of harvest, 3 days after the second application, abamectin foliar residues had dissipated to 0.84 ng/cm<sup>2</sup> (Figure 1).

Two transfer factors were used to estimate strawberry harvester exposure: the Zweig factor of 5000 cm<sup>2</sup>/h (based upon a one-sided surface area) and the low-crop factor of 1000 cm<sup>2</sup>/h (based upon a two-sided surface area). Originally, a 5000 cm<sup>2</sup>/h factor was proposed from a determination of the ratio of dermal exposure to DFR data for various pesticides (Zweig et al., 1984). Since specific crop groups such as citrus and low crops such as strawberries were combined in the derivation of the Zweig factor, the Zweig factor is a generic transfer factor. This generic factor will therefore tend to over-



**Figure 1.** Avermectin B<sub>1</sub> DFR dissipation curve. DFR of avermectin were determined following the second application of abamectin to the strawberry fields. Samples were analyzed as described under Experimental Procedures and plotted (ng/cm<sup>2</sup>).

estimate exposure to low-crop workers and underestimate exposure to high-crop workers.

Using the abamectin DFR data at the time for harvest (3 days after the second application), dermal penetration of 1%, an assumed weight of 60 kg, and the Zweig factor of 5000 cm<sup>2</sup>/h, systemic exposure was estimated to be 5.60 ng/kg/day. This predicted exposure combined with the NOEL of 50 μg/kg/day resulted in a MOE of 8930. The MOE of 8930 is well above the traditional safety factor of 100, suggesting minimal risk to workers.

Since the introduction of the Zweig factor, many transfer factors have been introduced that discriminate among the various types of crops. For low crops such as strawberries, the transfer factor of 1000 cm<sup>2</sup>/h is used to estimate worker exposure. Since this factor is based upon a two-sided surface area and the abamectin DFR data are based upon one-sided surface area, the abamectin DFR data can be adjusted accordingly. Using the 1000 cm<sup>2</sup>/h transfer factor, 1% dermal penetration, an assumed weight of 60 kg, and the adjusted DFR data at the time of harvest, strawberry harvester exposure to abamectin was calculated to be 0.56 ng/kg/day. This exposure combined with the NOEL of 50 μg/kg/day resulted in an MOE of 89300, suggesting minimal risk to workers (Table 4).

All calculations and estimates of abamectin exposure have been based upon residue data and worker exposure data measured at the preharvest interval of 3 days after the second application of abamectin. Since pesticide residues and potential risks to workers are greatest directly after pesticide application, there are few data regarding exposure of a worker entering a field directly after treatment. However, estimates of exposure can be derived by using DFR data and a generic transfer factor. Using the worst-case estimate derived from the Zweig factor of 5000 cm<sup>2</sup>/h, the assumed weight of 60 kg, and the DFR data directly after application (40.7 ng/cm<sup>2</sup>), systemic exposure was calculated to be 217 ng/kg/day. The resulting MOE of 185 suggests that workers entering the strawberry field directly after application of abamectin are also at little, if any, risk.

Another extensive study was conducted with abamectin to estimate the safety to workers harvesting ornamental crops (Grosso et al., 1989). The actual worker exposure in that study was 94.5 ng/kg/day, whereas the exposure predicted using the Zweig factor of 5000 cm<sup>2</sup>/h was 147 ng/kg/day (Table 4). The MOE for chrysanthemum harvesters calculated from actual harvester data was 529, whereas that calculated from the DFR data using the Zweig factor was 340 (Grosso et al., 1989). Again, the DFR method resulted in a more conservative estimate of worker exposure and safety.

MOE values derived from the actual and predicted exposures were better correlated for the chrysanthemum harvesters than for the strawberry harvesters. Since the use of the Zweig transfer factor tends to overestimate worker exposure, a better correlation between actual and predicted exposures would be expected for a more labor intensive process, such as chrysanthemum harvesting. This overestimation provides a more conservative method for predicting potential exposure.

From the current strawberry study and the previous chrysanthemum study, transfer factors (ratio of dermal exposure to DFR) for abamectin can be determined. The transfer factor generated from the use of various pesticides on strawberries has been reported to range from 500 to 6000 cm<sup>2</sup>/h (Krieger et al., 1990). For abamectin use on strawberries, the transfer factor was determined to be 1400 cm<sup>2</sup>/h, which is comparable to the transfer factors reported in the literature and that used by the EPA for low crops (Zweig et al., 1984; Krieger et al., 1990). The transfer factor of 3200 cm<sup>2</sup>/h for abamectin use on chrysanthemums was also comparable to the transfer factors reported by Krieger and supports the use of transfer factors in estimating abamectin worker exposure.

**Conclusion.** The MOEs estimated using either the Zweig transfer factor or the low-crop factor and the DFR data conservatively predicted worker exposure. This scenario may be applied to other crops as well. For example, chrysanthemum worker exposure data resulted in MOEs that were comparable to that predicted from the DFR data (Grosso et al., 1989).

Since the Zweig factor is a generic transfer factor, a more realistic exposure estimate may be generated with the use of a specific crop transfer factor, such as the use of the low-crop factor for strawberries. For regulatory purposes, it is beneficial to examine the worst-case exposure scenario predicted using the Zweig factor. The worst-case estimate can be used to determine when workers may safely enter fields.

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