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INHALATION EXPOSURE OF ORANGE HARVESTERS TO CYFLUTHRIN RESIDUE

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Abstract

In early May 1997, an outbreak of respiratory irritation was reported among orange harvesters exposed to cyfluthrin residues in Tulare County. As part of the investigation, DPR staff monitored two crews for inhalation exposure to cyfluthrin residues during orange harvest. One crew, inexperienced at the task, picked oranges 14 days after application and worked for four hours. The second crew consisted of commercial orange harvesters who worked for six hours, beginning approximately 30 hours after completion of the application. In the first study, the inexperienced crew filled 11 bins in 4 hours of picking; about 45% of the amount typically picked by a commercial crew. The three commercial harvesters also filled 11 bins in about 6 hours; about 60% of the expected amount. From the first study, only one filter sample contained detectable residues (0.24 µg/sample). That filter was worn by the only worker in the crew with some citrus harvesting experience. In the second study, all filters contained detectable levels of cyfluthrin and ranged from 2.2 to 7.6 µg/sample. Inhalation exposure appears to be below the no observable effect level (NOEL) for developmental effects (from an inhalation teratology study), resulting in a margin of exposure of 85-fold. A NOEL for human respiratory irritation is not available.

Introduction

On May 6, 1997, the Department of Pesticide Regulation (DPR) received notice that numerous citrus harvesters had received medical care on May 3, 1997. The workers experienced symptoms that primarily involved respiratory irritation; these symptoms included runny nose, sneezing, coughing and sore throat. Other symptoms experienced include headache, nausea, rash and skin and eye irritation. The workers picked in a grove treated 3 days earlier with cyfluthrin (Baythroid®). The workers were treated at a local hospital and released; most returned to work the next day. A second group of workers experienced similar symptoms on May 7, 1997, and were taken for medical evaluation. The second crew worked in a grove treated 10 days earlier. Later that afternoon, a single worker from a third harvest crew received medical care for similar symptoms. That worker was in a grove treated 11 days earlier. These incidents occurred in employees from one packing company in Tulare County, California.

The following information summarizes some recent California registration information that may have been a factor in these illness episodes. On April 2, 1997, DPR issued a Section 18 registration (emergency exemption) for cyfluthrin on navel oranges with a 150 day preharvest interval (PHI). (The PHI was set at 150 days in lieu of evaluation of citrus residue data.) On April 10, 1997, following U.S. EPA approval of a time-limited tolerance, that Section 18 registration was amended and the PHI changed to “up to day of harvest.” On April 28, 1997, the Section 18 was again amended to include all citrus. Finally, on April 30, 1997, again following U.S. EPA approval, a Section 3 registration (full registration) was issued for use on all citrus with a PHI of "up to day of harvest." The Section 3 registration restricted entry interval is 12 hours. In California, application of cyfluthrin to oranges close to harvest had not been legal prior to April 10, 1997.

DPR maintains a pesticide illness registry, the Pesticide Illness Surveillance Program (PISP). California law requires physicians to report pesticide-related illnesses and injuries. These incidents are investigated and the data entered into a database. From 1990-1995, 108 illness/injury cases were recorded in PISP as related to cyfluthrin exposure. Of those 108 cases, 15 were related to agricultural use of cyfluthrin. Only two of the 15 involved field workers exposed to residue. One worker, irrigating plants in a greenhouse 24 hours after application, developed a rash on his arms. Another worker developed a rash while pruning trees. The orchard had been treated the same day, but the spray was dry so reentry was legal at that time. The remaining 93 cases involved application in and around structures. These cases involved handler exposure, exposure to residue (after the application was complete) or exposure to drift (person present during application). Exposure to residue in the indoor setting lead to somewhat similar symptoms as May citrus harvester incidents. However, the various symptom prevalence rate between the two types of exposure (indoor residue, May incident) varied[1].

Numerous cyfluthrin toxicology studies are on file with DPR. However, a study to determine a no observable effect level (NOEL) for human respiratory irritation is not available. The lowest inhalation NOEL available comes from a teratology study. Animals dosed via inhalation demonstrated a NOEL of 0.11 mg/kg/day for developmental effects[2]. Since the exposure of concern appeared to be primarily respiratory in nature, DPR determined an inhalation exposure study was necessary. On May 13, 1997, DPR requested the citrus industry to enact a voluntary stop harvest action pending the results of the inhalation monitoring study.

Methods

Although, this study was not conducted under the FIFRA Good Laboratory Practice standards, WH&S staff followed all applicable standard operating procedures related to project identification, sample identification, sample collection, record keeping, shipping and storage. WH&S protocol procedures were not followed as the study was conducted as part of a worker illness investigation.

The study consisted of monitoring potential inhalation exposure to cyfluthrin residues during orange harvest activities. DPR conducted two separate inhalation monitoring studies. For the first study, a Valencia orange grove was selected in Tulare County. The grove had been treated on April 30, 1997 with cyfluthrin (Baythroid® 2, EPA Reg. No. 3125-351) at 0.1 lb. active ingredient per acre. Inhalation monitoring took place on May 14, 1997, 14 days after application. For the second study, also located in Tulare County, a Valencia orange grove was sprayed with Baythroid® 2 at the same rate. The application for this grove was completed at 12:00 AM on May 27, 1997; monitoring began on May 28, 1997, about 30 hours after completion of the application.

Study Dates:

Study initiation date:	May 13, 1997
Experimental start date:	May 14, 1997
Experimental termination date:	May 28, 1997
Study Completion date:	March 1998

Harvest Crews: DPR conducted these studies under the guidance of the University of California, Davis, Employee Health Services. Since the working environment appeared to present a respiratory hazard, all study volunteers were required to wear half-face respirators to prevent respiratory irritation[3]. In addition, informed consent was obtained from all participants who volunteered to participate in the studies. In the first study, the six volunteers were employed by the California Department of Food and Agriculture Tristeza Project or the University of California Extension Lindcove field station. For the most part, they were not experienced in harvesting citrus; one volunteer had worked as a citrus harvester in the past. Respiratory fit testing and respiratory training were conducted by the crew's employers. Prior to study initiation, the grower gave the crew instructions on picking oranges and safety in the grove. Each member of the crew picked oranges for four hours. Females in the crew used 50-lb. capacity picking bags while male crew members used 65-lb. capacity bags. The six volunteers were divided into two groups; each group filled separate bins. In the second study, three harvesters participated. These three participants were professional citrus harvesters and were currently working for the grower. (Five potential volunteers were provided by the grower, however, only three could be properly fitted for respiratory protection.) DPR hired a private consultant to provide respirators, fit testing and respirator use training to the second crew. As part of the respirator training, the consultant asked participants if they had any medical conditions that would interfere with wearing a respirator. Statements that no such known conditions existed were signed by the three participants. Crew 2 consisted of all male workers who used the 65-lb. capacity picking bags for the 6-hour monitoring period.

Inhalation Monitoring: DPR staff provided equipment to measure cyfluthrin in the workers' breathing zone. Cyfluthrin was trapped on 25 mm glass fiber filters housed in IOM sampling heads. The IOM samplers were attached via tubing to personal air sampling pumps. Two types of pumps were used: MSA Elf 5000 and MSA Fixt-Flo®. Prior to use, pumps were set to operate at a flow rate of 2 L/min. Pumps and sampling train were attached to the workers' clothing with the filters placed in the breathing zone. At the onset of the harvest activities, the pumps were turned on and the start times recorded. Sampling pumps remained on during harvest activities and were turned off during any lengthy breaks; on/off times were recorded. At the end of the work day, the flow rate was measured and recorded and the pumps were turned off. Samples were collected, sealed and stored on dry ice for shipment to the laboratory. No field fortifications were prepared. Blank samples were prepared and handled in the same manner as exposure samples.

Dislodgeable Foliar Residue Sampling: In addition, foliage samples were collected for analysis of dislodgeable foliar residues (DFR). DFR samples were collected with a Birkestrand® leaf punch. Each sample consisted of 40 leaf discs, each 2.523 cm in diameter, for a total sample surface area of 400 cm^2. DFR samples were collected from the same grove that the workers picked, prior to workers contacting the leaves during harvest. Leaf discs were taken at a height of 4-7 feet; harvesters contact foliage from all parts of the tree. Four DFR samples were collected during the first study, and six were collected during the second inhalation study. We were unable to collect blank samples as most groves in the area had already been treated with cyfluthrin.

Glass Fiber Filter Analytical Method: Glass fiber filter samples were analyzed for cyfluthrin. (Filter samples were not analyzed for total dust.) Cyfluthrin residues were extracted from the glass fiber filters with ethyl acetate and analyzed using a capillary gas chromatograph equipped with an electron capture detector. The column was a Hewlett-Packard 25 m x 0.2 mm ID capillary column coated with 5% phenyl methyl silicone. Column pressure was 25 psi. Operating temperatures were as follows: oven - 150 ^{o}C programmed to 270 ^{o}C at 30 ^{o}C/min., hold 20 min.; injector - 250 ^{o}C, operated in splitless mode; and detector - 300 ^{o}C. The following flow rates were used: split vent - 60 mL/min.; septum purge - 2 mL/min.; and EC detector make-up gas - 60 mL/sec. Using these conditions, cyfluthrin has a retention time of 15 minutes. The cyfluthrin isomers consists of four peaks. An integrator groups the peaks, and the combined height is treated as one compound[4]. The original filter sample limit of detection (LOD) was 2.5 µg/sample due to a request for a 1-day analysis. As time allowed, the chemist reduced the LOD to 0.20 and 0.l3 µg/sample for the first and second study, respectively.

Laboratory fortifications of filters were prepared and analyzed. At an LOD of 0.2 µg/sample, the recovery was 98.2%.

Inhalation Calculations: Filter analytical results were reported in micrograms per sample. Data were recorded into a database using Microsoft Access®. The absorbed daily dosages, in µg/kg/8-hr day, were calculated using the following formula (also in Access®):

$$\left(\frac{\text{result } (mg / \text{sample})}{\text{pump flow rate (L / min)}.*\text{min. sampled}}\right)*\begin{pmatrix}\text{breathing}\\ \text{rate (L / min)}\end{pmatrix}\div(\text{body wt (kg)})*(480 \text{ min in 8 hours})*\begin{pmatrix}\text{percent}\\ \text{uptake}\end{pmatrix}$$

This calculation assumes a breathing rate for moderate work of 26.7 L/min[5], average male/female body weight of 70 kg[6], a particulate inhalation uptake of 100% and an 8-hour workday. Results were compared to the inhalation teratology NOEL.

DFR Analytical Method: The leaf disk samples were washed three times with a surfactant/distilled water solution. The washes were combined, extracted three times with ethyl acetate and concentrated to near dryness. The extract was analyzed on a Hewlett-Packard (HP) 1050 liquid chromatograph system using a 15 cm Econosphere C8 Alltech cartridge system and water/acetonitrile gradient at 1 mL/min. Thirty microliters were injected. The detector was a HP 1050 Variable Wavelength Detector at 223 nm. Under these conditions, cyfluthrin eluted in 15 minutes. Recoveries were in the 80-120% range[7].

DFR Calculations: DFR sample results were also reported as micrograms per sample and recorded in Microsoft Access®. The results were then converted to µg/cm² by dividing the sample result by the sample surface area of 400 cm². Sample results were compared to DFR samples collected following the respiratory irritation outbreaks.

Results

Based on anecdotal information[8], a commercial orange harvester fills about 1 bin per hour. In the first study, the inexperienced 6-member crew filled 11 bins in 4 hours of picking; about 40% the amount of a commercial crew. (This low picking rate for non-commercial harvesters was also found by Popendorf[9].) The three commercial harvesters also filled 11 bins, taking about 6 hours. Although professional citrus harvesters, the second crew also picked oranges below the average rate, about 60% of the average rate. This slower rate may be due to the required respiratory protection and possibly the inhalation monitoring equipment. The volunteers stated that it was hard to breathe, they had dry throats and needed more frequent water breaks.

Table 1 contains the results of the inhalation monitoring. For the first study, only the results from the analysis with the lowest LOD are reported. Prior to lowering the LOD to 0.20 µg/sample, no residues were detected on any of the filter samples. Only one filter sample contained detectable residues above 0.20 µg/sample (0.24 µg/sample). That filter was worn by the only worker in the first crew with some citrus harvesting experience. In the second study, all filters contained detectable levels of cyfluthrin and ranged from 2.2 to 7.6 µg/sample. The observed work rate of the three workers corresponds to the amount of cyfluthrin found on the filters. During the 6-hour monitoring period, 7.6 µg/sample was found in the breathing zone of the harvester filling the most bins while 2.2 µg/sample was found in the breathing zone of the slowest harvester.

Following review of the results of the first study, the voluntary stop harvest was lifted, as it appeared that the cyfluthrin exposure was very low. However, after evaluation of the study parameters, a second study was conducted because the slow picking rate of the first crew and the 14-day period between application and worker reentry were considered inadequate to model harvester exposure close to legal reentry. As was expected, the professional harvest crew picking about 1 day after application received significantly higher cyfluthrin exposure than did the nonprofessional crew (Mann-Whitney U test, $p=0.015$)[10].

Table 1: Inhalation Exposure

Study No	*Worker No*	*Results (µg/sample)*	*Potential Inhalation[a] (µg/day)*	*Absorbed Dosage[b] (µg/kg/day)*
1	1	0.24	6.58	0.094
	2	ND	2.63	0.038
	3	ND	2.49	0.036
	4	ND	2.68	0.038
	5	ND	2.63	0.038
	6	ND	2.67	0.038
		Study Average	***3.28***	***0.047***
2	10	2.19	38.72	0.553
	11	5.60	100.24	1.432
	12	7.60	136.42	1.949
		Study Average	***91.79***	***1.311***

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[a] - Potential inhalation exposure is the cyfluthrin potentially available to the harvester in an 8-hour day.
[b] - The absorbed dosage is the amount absorbed into the body.

Table 2 lists the results of the DFR samples during each monitoring effort. The average DFR during Study 1 was less than half of the residue found in Study 2.

Table 2: Dislodgeable Foliar Residue Results from the Inhalation Studies

Study No	*Application date*	*Sample date*	*DFR (µg/sample)*	*DFR (µg/cm²)*
1	4/30/97	5/14/97	5.28	0.013
			3.93	0.010
			7.13	0.018
			8.49	0.021
		Study Average	***6.21***	***0.016***
2	5/27/97	5/28/97	16.1	0.040
			9.8	0.025
			16.9	0.042
			15.2	0.038
			15.3	0.038
			11.4	0.029
		Study Average	***14.1***	***0.035***

Table 3 shows the results of the DFR samples collected following the illness incidents. Incident-related DFR samples averaged 0.034, 0.047, 0.025, 0.048 µg/cm², respectively for the four groves associated with the episodes. DFRs from the second inhalation study fell within that range. DFR from the first inhalation study were generally lower than those found in the illness episode-related groves.

Table 3: Dislodgeable Foliar Residue Results from Illness Incidents

Incident	*Application date*	*Sample date*	*DFR (µg/sample)*	*DFR (µg/cm²)*
17-TUL-97	4/30/97	5/6/97	12.4	0.031
Ranch 1			15.7	0.039
			10.0	0.025
			13.1	0.033
			18.7	0.047
			17.8	0.045
			13.1	0.033
			10.8	0.027
			11.1	0.028
		Ranch Average	***13.6***	***0.034***
17-TUL-97	*4/30/97*	5/6/97	16.1	0.040
Ranch 2			23.1	0.058
			16.7	0.042
			13.8	0.035
			19.2	0.048
			20.8	0.052
			20.3	0.051
			24.1	0.061
			15.1	0.038
		Ranch Average	***18.8***	***0.047***
19-TUL-97	4/27/97	5/7/97	9.7	0.024
			8.7	0.022
			11.8	0.030
			9.1	0.023
		Ranch Average	***9.8***	***0.025***
97-542	4/26/97	5/8/97	18.5	0.046
			17.7	0.044
			21.0	0.053
			19.0	0.048
		Ranch Average	***19.1***	***0.048***

Discussion

All calculated absorbed dosages are below the developmental effects NOEL of 0.11 mg/kg/day (110 µg/kg/day). The average dose gives a margin of exposure (MOE) of 84-fold. Although respiratory irritation incidents led us to conduct this study, neither confirmation of cyfluthrin as a causative agent nor determination of a residue level that causes irritation has been resolved.

Pauluhn[11] summarized the toxicity of pyrethroids. Pyrethroids, especially cyano pyrethroids, are known to cause strong excitatory action on the vertebrate skin and upper respiratory tract. In studies conducted by Pauluhn[11], effects of cyfluthrin on the respiratory system appear to be related to exposure concentration rather than total dose (concentration x time). In addition, all effects noted in Pauluhn's work appeared to be transitory in nature. As part of the incident investigation, a questionnaire was administered. Many of the harvesters noted that the respiratory

irritation symptoms diminished shortly after leaving the grove or after taking a shower at home[1]. Additional support for the transitory nature of the symptoms is provided by physicians; many (but not all) of the physician's reports noted that the workers were asymptomatic at the time of examination. Investigators sought out additional affected workers from other packing companies; none were found.

Often citrus groves present a fairly dusty environment. Harvest activities may be creating a dusty micro-environment in the breathing zone of workers. Popendorf[8] found dust levels in the breathing zones of citrus harvesters that ranged from ~7 to ~85 mg/m^3. Spear *et al.*[12], found breathing zone dust levels in the range of ~10 to 22 mg/m^3 in citrus groves. The American Conference of Governmental Industrial Hygienists recommend a TLV® for nuisance dust of 10 mg/m^3. According to data from both Popendorf and Spear, the dust levels in a citrus grove are generally above the nuisance dust standard. In addition to dust, both Popendorf and Spear found organophosphates in the breathing zone samples of those citrus harvesters. Thus, it is conceivable that the workers are stirring up both dust and cyfluthrin during their harvest activities. This is supported by the fact that the noncommercial harvesters had significantly less exposure than the commercial harvesters and that the faster commercial harvesters had higher exposures. The filters were visibly dirty at the completion of the sampling period in both DFR studies. However, at the completion of harvest activities for the second study, considerable dust was also visible on the skin and clothing.

It is also possible that the harvesters were affected by pollen. Both citrus and olive groves are in the immediate area where the harvesters were working. However, this doesn't appear to be a plausible explanation because pollens are commonly in the environment. In addition, pollens usually cause symptoms only in individuals with specific allergies[1].

Conclusions

Several citrus harvesters developed respiratory irritation symptoms while harvesting oranges treated with cyfluthrin. Since dust and pollen seem to be part of the normal working environment, something different in the work environment probably led to the respiratory irritation symptoms. Application of cyfluthrin close to harvest had not taken place in previous years because of label preharvest restrictions. Thus, it appears plausible that cyfluthrin applied close to harvest led to the symptoms experienced.

Recommendations

From the data collected to date, it is plausible that cyfluthrin applied close to harvest led to the symptoms experienced. However, without a human respiratory irritation NOEL, we cannot make a determination. We recommend that data be developed to determine the human respiratory NOEL.

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