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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

October 22, 2001

Memorandum

SUBJECT: Review of "*Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Walnut Harvesting Following Applications of Penncap-M® Microencapsulated Insecticide*"(MRID # 453677-01 and 453915-01 amended)

FROM: Renee Sandvig, Environmental Protection Specialist
Reregistration Branch II
Health Effects Division (7509C)

THROUGH: Al Nielsen, Branch Senior Scientist
Reregistration Branch II
Health Effects Division (7509C)

Al Nielsen 10/23/01

TO: Laura Parsons, Chemical Review Manager
Reregistration Branch I
Special Review and Reregistration Division (7508C)

DP Barcode: D274054 and D274752

Pesticide Chemical Codes: 053501

EPA MRID Numbers: 453677-01 and 453945-01

Attached is a review of the post-application biomonitoring data submitted by Cerexagri, Inc. (formerly Elf Atochem North America, Inc.). This review was completed by Versar, Inc. on May 18, 2001, under supervision of HED. It has undergone secondary review in the HED and has been revised to reflect Agency policies.

Executive Summary

The data collected reflecting the workers exposure to methyl parathion from leaf surfaces of treated walnut trees meet most of the criteria specified in the U.S. Environmental Protection Agency's (US EPA) OPPTS Guidelines, Occupational and Residential Exposure Test Guidelines: Group B: Postapplication Exposure Monitoring Test Guidelines, 875.2500, Inhalation Exposure and 875.2600, Biological Monitoring. The data will be considered in future methyl parathion REDs.

Summary

The insecticide methyl parathion was applied to walnut trees in California. Walnut trees were treated with PENNCAP-M® Microencapsulated Insecticide, containing approximately 20.9 percent methyl parathion as the active ingredient (a.i.). The product is a flowable formulation consisting of a water suspension of polymeric-type microcapsules. Biological monitoring was used to measure exposure levels of walnut harvesters to methyl parathion after a seasonal regime of Penncap-M®. All four applications were made with an airblast sprayer at 21-day intervals. The insecticide was applied at 100 to 200 gallons per acre spray volume. The minimum application volume referenced on the product label is 10 gallons/acre.

The study was conducted at two sites in southern California (Fresno and Porterville). Fourteen (Fresno) or fifteen days (Porterville) after the last Penncap-M® application, fifteen subjects harvested walnuts during a single work period, which lasted about 8 hours (in-field), including breaks. Twenty-four hour urine samples were collected from each worker beginning 2 days prior to harvesting, and for 4 days after harvesting. The workers were housed in a hotel during this period, leaving only to perform hand-harvesting on the day of exposure and to eat meals. Methyl parathion exposure was quantified by measuring 4-nitrophenol and its sulfate and glucuronide conjugates in urine samples (the analytical method used converts these two biological conjugates to 4-nitrophenol). Creatinine levels were measured in the urine samples as a qualitative check on the urine output of the monitored subjects.

Results for all 24 hour worker urine samples from all 15 workers for both sites ranged from 2.58 μg/sample to 10.2 μg/sample for pre-exposure samples and from 1.76 μg/sample to 13.1 μg/sample for exposure samples. On the day of exposure, residue levels in the samples ranged from 0.88 μg to 7.68 μg. Total net normalized 4-NP excreted (expressed as μg/70 kg body weight) from Day 0 through 96 hours after exposure ranged from -0.44 to 40.49 μg/70 kg body weight. Creatinine levels measured in each harvester's daily urine sample were fairly consistent across the monitoring period, except for one high value for a worker at the Fresno site.

Results from selected air monitoring, using OVS air monitoring tubes, produced no detectable methyl parathion and methyl paraoxon residues (less than 0.05 μg/sample). According to the authors, the results indicate that inhalation exposure was minimal during harvesting activities.

The study followed the OPPTS Series 875 Occupational and Residential Exposure Test Guidelines in most respects. The following issues of potential concern were identified:

- Inhalation monitoring was done using OVS air monitoring tubes affixed to portable stands at the height representative of the breathing zone of the rakers, stationed in the work space. Personal air samplers measure possible inhalation exposure more accurately, since the intake area is closer to the workers actual breathing zone. Work may not be performed near the stationary sampling pumps during the entire course of the sampling period.

- Only five inhalation monitoring replicates were monitored at each of the two sites. EPA's guidelines states that *"Each study should include a minimum of 15 individuals (replicates) per activity."*

- Creatinine levels, after the exposure event, were unusually low for two workers at the Portersville site and unusually high for one worker at the Fresno site, relative to the other workers. The two Portersville workers, subjects #11 and #13, had creatinine levels of 0.830 and 1.00 g/24hrs, respectively. The Fresno worker, subject # 5, had a creatinine level of 5.12 g/24hrs.

- 4-NP values that were lower after exposure than before the exposure event for one worker at the Fresno site, subject #1, and three workers at the Portersville site, subjects #11, #12, and #13.

MEMORANDUM

TO: Renee Sandvig cc: 1000.001.01
FROM: Marit Espevik/Pat Wood
DATE: May 18, 2001
SUBJECT: Review of "*Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Walnut Harvesting Following Applications of Penncap-M® Microencapsulated Insecticide*" (MRID # 453677-01 and 453915-01 amended)

This report reviews a study entitled *"Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Walnut Harvesting Following Applications of Penncap-M® Microencapsulated Insecticide,"* submitted to US-EPA in support of the reregistration requirements for *Penncap-M®*. Study requirements were specified by the U.S. Environmental Protection Agency under OPPTS Guidelines, Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines: 875.2500 Inhalation Exposure and 875.2600 Biological Monitoring.

The following information may be used to identify the study:

Title:	*Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Walnut Harvesting Following Applications of Penncap-M® Microencapsulated Insecticide;* 461 pages (2 volumes)	
Sponsor:	Timothy M. Formella Cerexagri (formerly Elf-Atochem North America, Inc.) Agrichemicals Division 2000 Market Street, 21st Floor Philadelphia, PA 19103-3222	
Field Study Sites and Principle Investigators:	Brian Lange Excel Research Services, Inc. 3021 W. Dakota Avenue, Suite 110 Fresno, CA 93722	Dave Ennes Research For Hire 1696 S. Leggett Street Porterville, CA 93257
Analytical Laboratory:	Richard Reed, II and Gary L. Westberg (Author of Analytical Report) Morse Laboratories, Inc. 1525 Fulton Avenue Sacramento, CA 95825	
Author/Study Director and Testing Facility:	Tami I. Belcher Excel Research Services, Inc. 3021 W. Dakota Avenue, Suite 110 Fresno, CA 93722	
Report Date:	March 27, 2001	
Identifying Codes:	MRID # 453677-01 and 453915-01 amended; Cerexagri Study No. KP-2000-06; Excel Study No. ERS20004	

EXECUTIVE SUMMARY

The purpose of this study was to quantify potential worker exposure due to hand-harvesting of walnuts following four treatments of the crop with the restricted use, organophosphate insecticide methyl parathion. Biological monitoring was used to measure exposure levels of walnut harvesters to methyl parathion after a seasonal regime of Penncap-M®. All four applications were made with an airblast sprayer at 21-day intervals. Penncap-M® Microencapsulated Insecticide was applied at the maximum label application rate (i.e., 2.0 lbs. ai/A) for each application. The insecticide was applied at 100 to 200 gallons per acre spray volume. The minimum application volume referenced on the product label is 10 gallons/acre.

The study was conducted at two sites in southern California (Fresno and Porterville). Fourteen (Fresno) or fifteen days (Porterville) after the last Penncap-M® application, fifteen subjects harvested walnuts during a single work period, which lasted about 8 hours (in-field), including breaks. While hand harvesting walnuts, study subjects wore identical, new clothing: long-sleeved shirts, undershirts, long pants, socks and underwear. All wore closed shoes, some also wore jackets and hats, but none wore gloves. Twenty-four hour urine samples were collected from each worker beginning 2 days prior to harvesting, and for 4 days after harvesting. The workers were housed in a hotel during this period, leaving only to perform hand-harvesting on the day of exposure and to eat meals.

Methyl parathion exposure was quantified by measuring 4-nitrophenol and its sulfate and glucuronide conjugates in urine samples (the analytical method used converts these two biological conjugates to 4-nitrophenol). Creatinine levels were measured in the urine samples as a qualitative check on the urine output of the monitored subjects. Twenty-four hour urine samples were collected for a total of 7 days (i.e., 2 days prior to exposure, the day of exposure, and for 4 days following exposure).

Results for all 24 hour worker urine samples from all 15 workers for both sites ranged from 2.58 μg/sample to 10.2 μg/sample for pre-exposure samples and from 1.76 μg/sample to 13.1 μg/sample for exposure samples. On the day of exposure, residue levels in the samples ranged from 0.88 μg to 7.68 μg. Total net normalized 4-NP excreted (expressed as μg/70 kg body weight) from Day 0 through 96 hours after exposure ranged from -0.44 to 40.49 μg/70 kg body weight. Creatinine levels measured in each harvester's daily urine sample were fairly consistent across the monitoring period, except for one high value for a worker at the Fresno site.

Results from selected air monitoring, using OVS air monitoring tubes, produced no detectable methyl parathion and methyl paraoxon residues (less than 0.05 μg/sample). According to the authors, the results indicate that inhalation exposure was minimal during harvesting activities.

The study followed the OPPTS Series 875 Occupational and Residential Exposure Test Guidelines in most respects. The following issues of potential concern were identified:

- Exposure data from the Portersville site were not corrected for the site's field recovery results for 4-NP in urine which averaged 81 percent ± 11 (n=27). EPA' s guidelines states that *"Field data should be corrected if any appropriate field fortified, laboratory fortified or storage stability recovery is less than 90 percent."* .

- There were only two test locations in this study. EPA' s guidelines require *"a minimum of 15 replicates per activity and preferably 5 replicates (i.e. individuals) for each of three monitoring periods... in three geographical locations."* A third geographic location in Ripon, California was to be included as a test site, but the commercial grower rescinded on his agreement to allow use of the orchard to monitor the reentry activities. However, a total of 15 individuals were monitored at the two sites.

- In this study, a formal discussion of activities performed by subjects within the last two weeks prior to biomonitoring was not provided. EPA' s guidelines states that *"Prior exposures to the test pesticide or structurally related compounds may interfere with study results. For blood, a brief history should be taken relating to known prior exposures to pesticides for at least the last 2 weeks, including reentry into potentially treated fields..."*.

- Inhalation monitoring was done using OVS air monitoring tubes affixed to portable stands at the height representative of the breathing zone of the rakers, stationed in the work space. Personal air samplers measure possible inhalation exposure more accurately, since the intake area is closer to the workers actual breathing zone. Work may not be performed near the stationary sampling pumps during the entire course of the sampling period.

- Only five inhalation monitoring replicates were monitored at each of the two sites. EPA' s guidelines states that *"Each study should include a minimum of 15 individuals (replicates) per activity."*

- Creatinine levels were unusually low for two workers at the Portersville site and unusually high for one worker at the Fresno site, relative to the other workers.. The two Portersville workers, subjects #11 and #13, had creatinine levels of 0.830 and 1.00 g/24hrs, respectively. The Fresno worker, subject # 5, had a creatinine level of 5.12 g/24hrs.

- 4-NP values that were lower after exposure than before the exposure event for one worker at the Fresno site and three workers at the Portersville site.

STUDY REVIEW

Study Background

The purpose of this study was to quantify potential exposure of walnut harvesters to the restricted use, organophosphate insecticide methyl parathion (i.e., O, O-dimethyl O-p-nitrophenylphosphorothioate, CAS No. 298-00-0). Methyl parathion was formulated as a 20.9 percent product in Penncap-M® Microencapsulated Insecticide. Penncap-M® is a flowable formulation consisting of a water suspension of polymeric-type microcapsules used to control insect pests in a variety of commercial crops including, nuts. This study was conducted in California where Penncap-M® has a Section 24(c), Special Local Needs label; Penncap-M® is used to control codling moth, navel orange worm, San Jose scale, and walnut scale. Four foliar applications of Penncap-M®, each at the maximum application rate of 2 pounds ai per acre were made to walnuts at 21-day intervals. All applications were made using ground airblast application equipment. Volunteer study subjects performed a single day of harvesting either fourteen days (Fresno) or fifteen days (Porterville) after the last Penncap-M® application.

Methyl parathion exposure was quantified by measuring 4-nitrophenol and its sulfate and glucuronide conjugates in urine samples (the analytical method used converts these two biological conjugates to 4-nitrophenol). Creatinine levels were measured in the urine samples as a qualitative check on the urine output of the monitored subjects. Twenty-four hour urine samples were collected for a total of 7 days (i.e., 2 days prior to exposure, the day of exposure, and for 4 days following exposure).

All field and analytical operations were overseen by Excel Research Services, Inc. of Fresno, California. On-site field operations were conducted by Excel Research Services, Inc. of Fresno, California and Research For Hire of Porterville, California. All samples were analyzed by Morse Laboratories, Inc. of Sacramento, California.

Study Subjects

The study subjects were males or females, ranging from 19 to 58 years old, 5' 3" to 6' 0" in height, 150 to 240 pounds (68 to 109 kg) in weight, that had prior experience in harvesting crops. Worker experience varied in duration from less than 1 year to 20 years. All workers read and signed Informed Consent forms, which explained the purpose of the study, the procedures, and a statement of their rights. The workers were sequestered (November 1, 2000) in a hotel beginning two days prior to the exposure at the Fresno site and three days prior to exposure (October 31, 2000) at the Porterville site. The workers were released from sequestration on November 7, 2000. The study subjects were warned to avoid exposing themselves to a list of substances, e.g. polishes, paint solvents, any product containing almond essence, and certain drugs (see Appendix I of the Study Report for a complete list).

Protective Clothing & Work Practices

Study subjects wore identical, new standardized clothing while scouting cotton. The clothing consisted of: long-sleeved shirt and long pants over their choice of undergarments. The shirt and pants were made of 65 percent polyester and 35 percent cotton blend. All subjects wore socks and shoes. No other protective clothing was worn at the Fresno site. At the Porterville site, two replicates (Replicates 9 and 13) wore jackets at the start of the reentry event, but removed them during the early portion of the activity. Four replicates (Replicates 9, 10, 14, and 15) wore hats at the start of the reentry, but the hats were also removed during the course of the activity.

Test Plots

The test sites were located in Fresno (Fresno County) and Porterville (Tulare County), representing two walnut growing regions of California. The test sites were selected to represent the climatic and walnut-growing conditions for use of Penncap-M's the intended-use area. According to July 2000 National Agricultural Statistics Service data, in 1997, California produced 269 tons of walnuts, representing 100 percent of the total U.S. walnut production. A third geographic location in Ripon, California was to be included as a test site, however, the commercial grower rescinded his agreement to allow use of the orchard to monitor reentry activities.

A portion of the same treated area was monitored for both foliar and soil dislodgeable residues and reported separately in, "Foliar and Soil Dislodgeable Residue Dissipation of Methyl Parathion Residues Following Applications of Penncap-M® Microencapsulated Insecticide to Walnuts," Atochem Study No. KP-2000-03. Study No. KP-2000-03 provides a complete dissipation profile for each of the two reentry sites, including the actual reentry day of harvest for the workers. This report provides a review of the reentry study only.

A single treated and a single untreated (control) plot were established at each test site. The plots were maintained under typical cultural and irrigation practices. The walnut variety tested was Frankette, and was suited to the geographical region in which walnuts are grown. The approximate ages of the trees were 50 years (Fresno) and 44 years (Porterville). The overall treated test site at Fresno consisted of 7.86 acres to accommodate the walnut harvesting reentry plot and the dislodgeable and soil residue plot. Approximately 6.57 acres of the total treated acreage were dedicated to the walnut harvesting reentry study. The test site had a less than 2 percent slope. (Sample plot diagram is provided on page 40 of the Study Report.) The overall treated test site in Porterville consisted of 9.37 acres. This accommodated a concurrent walnut dislodgeable and soil residue study. Approximately 7.86 acres of the total acreage were dedicated to the walnut harvesting reentry study. The test site had an estimated slope of 0.5 percent. (Sample plot diagram is provided on page 41 of the Study Report.)

Field and Pesticide Use History

Walnuts were grown on both tests sites for three years (1997-1999) prior to the current study. In 1999, at the Fresno test site, two herbicides (Valor WDG® and Roundup Ultra®) were applied to the test site. Prior to the current study in 2000, Roundup Ultra® was applied monthly from February to July (except April). No pesticides were applied in 1997 or 1998. A complete listing of the pesticides with their rates of application is provided on page 135 of the Study Report. No maintenance chemicals were applied during the in-life portion of the trial.

Maintenance chemicals were not applied to the Porterville test site for the three years prior to the current study (1997-2000). Also, maintenance chemicals were not applied during the course of the current study.

Materials and Application

A Special Local Needs label for Penncap-M® (EPA Reg. No. 4581-393 and EPA SLN No. CA-000001) was provided in the Study Report. Penncap-M® is a flowable formulation insecticide consisting of a water suspension of polymeric-type microcapsules which contain 2 pounds ai per gallon. The formulation is packaged in 2.5 gallon containers. In California, Penncap-M® can be applied to walnuts using ground or aerial equipment, and a sufficient water volume for thorough coverage. For aerial applications, a minimum of 10 gallons per acre total spray volume should be used. The total spray volume should be increased depending on the size of the trees being treated. The maximum application rate for walnuts is 8 pints of formulated product per acre or 2.0 pounds ai per acre. Applications should not be made within 14 days of harvest. The minimum spray interval is 21 days and the maximum application is 32 pints (8 pounds ai) per season, including dormant and post-harvest applications.

In this study, four applications of Penncap-M® were made before exposure monitoring began, each at the maximum label rate of 2.0 pounds ai per acre per application[1]. The total nominal amount represents the maximum total seasonal application rate of 8.0 ai per acre per season. The four applications were made using ground airblast application equipment calibrated to deliver an approximate 100 to 200 gallons per acre spray volume. The four applications were made at 21-day intervals at both sites. Actual application rates were within 95 to 110 percent (actual rates were 7.9 to 8.1 pints per acre) of the target rate for all applications at both sites. The equipment was calibrated based on the total output from the sprayer measured in duplicate or triplicate over 30 seconds. The average output was calculated and the speed was determined based on the desired output in gallons per acre.

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[1]Penncap-M® was applied on: August 18, September 8, September 29, and October 20, 2000 in Fresno, and on August 17, September 7, September 28, and October 19, 2000 in Porterville.

The four applications at the Fresno site were made using a tractor-mounted Rears airblast sprayer equipped with a 150-gallon tank with paddle agitation. The sprayer was equipped with 10 TeeJet D6 and D7 nozzles with No. 46 swirl plates operating at approximately 200 psi. The actual spray volume was 100-101 gallons per acre. At the time of applications, the growth stage varied from nut sizing at the initial application to mature by the fourth application.

The four applications at the Porterville site were made using a tractor-mounted Air-O-Fan Airblast GB36 sprayer equipped with a PTO pump. Mechanical agitation was used for each application. The sprayer was equipped with 10 TeeJet D7 and D8 nozzles with 4-hole cores operating at 110 to 120 psi. The actual spray volume was 121-125 gallons per acre. At the time of the applications, the growth stage varied from nut sizing at the initial application to near maturity by the fourth application.

Work Performed

Fifteen study subjects performed harvesting activities from designated treated rows for a typical 8-hour work period which included approximately 6 hours of high activity in the orchard and approximately 2 hours of breaks. The study subjects took short breaks throughout the work day to use the lavatory, smoke, eat, drink water, or rest. All breaks were taken inside the treated orchard so all study subjects were continuously exposed to potential methyl parathion residues. Harvesting activities included mechanical shaking of trees to dislodge nuts, hand-raking nuts from around the tree trunks and off berms, and mechanically blowing and sweeping nuts into windrows. Fifteen replicates were included in the study; eight replicates at the Fresno site and seven replicates at the Porterville site. Both test sites included one shaker replicate, one sweeper replicate and the rest were raker replicates. The shakers at both sites were closed-cab units while the sweepers were open-cab. However, at the Porterville site, the sweeper was equipped with a cage for overhead protection. The activities performed by each worker are summarized in Table 1.

Table 1. Summary of Job Functions Performed by The Workers

Fresno, California Site			Porterville, California Site		
Replicate No.	Activity	Total Exposure Time[2]	Replicate No.	Activity	Total Exposure Time
1	Shaker	7 hrs	9	Raker	8 hrs, 15 min
2	Raker/Sweeper	7 hrs, 59 min	10	Raker	8 hrs, 15 min
3	Raker	8 hrs	11	Raker	8 hrs, 15 min
4	Raker	8 hrs	12	Raker	8 hrs, 15 min
5	Raker	8 hrs	13	Raker	8 hrs, 15 min
6	Raker	7 hrs, 59 min	14	Shaker	8 hrs
7	Raker	7 hrs, 59 min	15	Raker/ Sweeper	8 hrs, 15 min
8	Raker	7 hrs, 59 min			

Meteorology

The statement of GLP Compliance prepared for the study states that weather data (current and/or historical) were not collected per the GLP regulations. Average 10-year (1990-1999) or 30-year (1961-1990) historical meteorological data (monthly air temperature and precipitation) were provided in the Study Report. Hand-held weather instruments were used to periodically monitor conditions during the reentry day at the Porterville site. Air temperature, relative humidity, wind speed and wind direction were monitored during the reentry event at both sites. Rainfall did not occur at either site during the reentry event. The report states that "there were no significant departures from normal air temperatures during the trial period. Rainfall was above normal in October and below normal for November at both test sites. This did not appear to adversely impact walnut growth or vigor at the test sites."

At the Fresno site, precipitation data were collected from a rain gauge placed near the treated plot. Other current weather data were collected from Excel's Weather Station No. 1, located approximately 20 miles northwest of the test site. Historical data were collected from the NOAA Fresno weather station located approximately 14 miles southeast of the test site. During the exposure monitoring, air temperatures ranged from mid 40°F to low 70°F and relative

[2] Total Exposure Time includes all breaks, but the workers remained in the treated orchard during breaks; therefore, exposure to the test chemical was continuous.

humidity ranged from 45 percent to 97 percent. Wind speeds ranged from 0.1 mph to 1.5 mph. No supplemental irrigation was used after the test applications and sampling began.

At the Porterville site, precipitation data were collected from an on-site Tru-chek rain gauge. Other current weather data were collected from the Research For Hire weather station, 6.5 miles south of the test site. Historical data were collected from the NOAA weather station located in Porterville, approximately 3.5 miles southeast of the test site. During the exposure monitoring, air temperatures ranged from upper 40°F to mid 60°F and relative humidity ranged from 58 percent to 88 percent. Wind speeds ranged from 0.5 mph to 2.8 mph. Supplemental irrigation was applied to the test plots by microsprinklers. Approximately 2.0 inches of water were applied in August, 3.5 inches in September, and 1.5 inches in October. Irrigation amounts were estimated by the grower.

Sampling

Sampling consisted of biological monitoring (urine analysis for the metabolite 4-NP) and personal air monitoring. Urine samples were collected from each worker at both sites for 48 hours prior to exposure and for 96 hours after exposure. Baseline urine samples were collected from each worker at 24 hour intervals for 72 hours (Porterville only) or 48 hours prior to exposure and Day 0 (the day of exposure). Urine samples were also collected at 24 hour intervals from inception of walnut harvesting activities (Day 0), and up to 96 hours after exposure activities ended. Samples were collected from the workers at the Porterville site only for 72 to 48 hours prior to initial exposure, but these samples were neither preserved nor subsampled and were not used in the study since they were not stabilized properly.

All urine was collected from each worker during the exposure monitoring period. The workers were provided with pre-weighed and labeled Urisafe® containers (3 L). Their urinary output was collected for 24 hours into a single Urisafe® container. Each day the filled Urisafe® containers were collected and the workers were given new, pre-weighed and labeled Urisafe® containers. Samples were stored in coolers with blue ice packs during the sampling period. After the urine samples were collected from the workers, the entire sample was weighed, and the density and volume were determined before the samples were placed in freezer storage. The sample density was determined by weighing 100 mL of the urine. Samples were stabilized by adding 3 drops of 37 percent aqueous HCl per 100 mL of urine. This was equivalent to 1 mL of HCl to 700 mL of urine based on the conversion of 20 drops of HCl being equivalent to 1 mL. Each Urisafe® container was subsampled into duplicate 50 mL samples.

Air monitoring was conducted at each site during walnut harvesting using OVS air monitoring tubes. The sampling train consisted of a 13 mm glass fiber filter attached to an OVS sampling tube (SKC, lot number 1461) containing XAD-2 sorbent. The OVS tubes consisted of a glass fiber filter secured with a Teflon retaining ring, followed by 270 mg of XAD-2 in the primary sorbent bed and 140 mg in the backup bed. The pump air flow rate was calibrated at approximately 2 liters per minute (Lpm) with a BIOS, DC Lite Dry Cal flow meter. Flow rates were measured before and after each exposure monitoring period. Three air sampling pumps

with attached OVS tubes were affixed to portable stands at a height representative of the breathing zone of rakers, and one air sampling pump was placed in each equipment cab of the shaker and the sweeper.

QA/QC

Sample Handling and Storage

Applications of the test substance at the Fresno site were made on August 18, September 8, September 29, and October 20, 2000. In Porterville, applications of the test substance were made on August 17, September 7, September 28, and October 19, 2000. Harvesting at both sites was conducted on November 3, 2000.

At the field facilities, urine samples were stored cool in ice chests containing blue ice. After completion of the 24-hour period, study personnel retrieved the containers from the workers and placed them in freezer storage until shipment to the analytical laboratory. OVS tubes were placed in a pre-labeled plastic bag in a cooler containing dry ice and transported to the field facilities freezer. Samples were stored in freezers set to maintain temperatures below -10°C. During the period from sample collection to sample shipment, the freezer storage temperatures ranged from -13°F to 1°F for the untreated freezer and -17°F to -2°F.

All samples were shipped from the test sites within 1 to 21 days of sample collection. Samples were shipped frozen to the analytical laboratory, Morse Laboratories, in Sacramento, California, either on dry ice via Federal Express overnight service, by ACDS freezer truck service, or hand-delivered. The control samples, urine samples, and field fortification samples were packaged and shipped in separate containers. All samples were transported to the analytical laboratory.

Upon arrival at Morse Laboratories, the samples were transferred to a limited-access freezer for storage where they remained until thawed for analysis. All worker urine samples were extracted between 10 and 73 days and OVS tubes samples between 32 and 33 days of collection. Freezer storage temperatures were monitored on a daily basis and were at -20 ± 5°C.

Product and Tank Mix Analysis

Prior to study initiation, the sponsor made determinations of purity, strength, stability, and composition of the formulation. The substance was assayed at 20.2 percent ai with an expiration date of June 23, 2001. Tank mix analyses were not performed.

Analytical Methodology

4-nitrophenol (Urine) Analysis:

The analytical method used for the analysis of 4-Nitrophenol in urine samples was Morse Laboratories, Inc. Analytical Method No. Meth-120, Revision No. 3, dated April 28, 2000, entitled, *"Determination of 4-nitrophenol in Urine."* The 4-nitrophenol is a urinary metabolite of methyl parathion. The 4-nitrophenol was isolated from urine by treating it with sodium bisulfite and subjecting it to acid hydrolysis to free any conjugated residues. An aliquot of the resulting hydrolysate was then extracted with toluene. MTBSTFA [N(tert-Butyldimethylsilyl)-N-methyltrifluoroacetamide] was added to a concentrated form of the toluene extract to convert any 4-nitrophenol present to a more volatile tert-butyldimethylsilyl derivative. Detection and quantitation of 4-nitrophenol were conducted using a gas chromatograph equipped with a mass selective detector.

Creatinine (urine) analysis:

Creatinine levels were measured in the urine samples as a qualitative measure of renal function of the monitored workers. The analytical method used for this analysis of creatinine was Morse Laboratories, Inc. Analytical Method No. Meth-111, dated June 1998, entitled *"Quantitative Determination of Creatinine in Urine."* Creatinine, an anhydride of creatine, is excreted as a waste product by the kidney and synthesized in the body at a fairly constant rate. In this analytical method, creatinine was reacted with alkaline picrate reagent in sodium borate to form an amber-colored creatinine picrate complex. The concentration of creatinine in the urine sample was calculated against a known standard creatinine concentration based on absorbance of the resulting creatinine picrate complex at 520 nm.

Methyl parathion/methyl paraoxon (OVS sampling tube) analysis:

The analytical method used for the analysis of OVS air monitoring tubes for methyl parathion and methyl paraoxon was Morse Laboratories, Inc. Analytical Method No. Meth-124, dated February, 2000, entitled *"Determination of Methyl Parathion and 4-Nitrophenol in OVS Air Sampling Tubes."* The authors noted that "the contents of each OVS air sampling tube (referred to as "sorbent tube") were in most cases, divided into two separate samples, each representing a specific section of the tube (front or rear) and analyzed as such. In some cases, however, both sections were analyzed together as one sample (the entire tube). The method did provide for this." Methyl parathion and methyl paraoxon were extracted from each sorbent tube section with acetone. Aliquots of the extract were evaporated to dryness, reconstituted in solvent appropriate for either methyl parathion or methyl paraoxon, and then submitted to gas chromatographic analysis using flame photometric detection (FPD) detection.

Limits of Detection (LOD) and Limits of Quantitation (LOQ)

1. Urine Samples: For 4-nitrophenol and its conjugates in urine sample, the target limit of quantitation (LOQ) was 1.0 μg/L and the target limit of detection (LOD) was 0.3 μg/L as 4-nitrophenol (or in the case of the conjugates, as 4-nitrophenol equivalents).

2. Creatinine in Urine: Method sensitivity was 0.6 mg/dL based on instrument resolution of 0.01 absorbance units.

3. Inhalation Exposure Samples: The limit of quantitation (LOQ) was 0.05 µg/sample for both methyl parathion and methyl paraoxon.

Compositing of Control Urine

Samples obtained from exposed study subjects did not require compositing, since each 24-hour sample was collected in a single container. However, Elf Atochem provided a specific procedure for compositing control urine from 12-hour urine samples to yield 24-hour samples (see page 416 of the Study Report).

Control Samples

Urine samples (24-hour output) from Morse Laboratory personnel were screened for use in the study as control samples for procedural quality control (concurrently analyzed controls and fortified controls) and field fortifications. According to the authors, "urine for laboratory control use was considered acceptable for this if its endogenous content of 4-NP (corrected for reagent blank) was less than approximately 1.0 μg/L."

In this study, all control urine samples were found to contain less than 1.13 μg/L 4-NP except for one sample that contained 1.32 μg/L.

Concurrent Laboratory Recovery

4-Nitrophenol (urine)

Overall 4-NP procedural recoveries (including fresh fortifications for field fortification runs), across the two sites, prepared in-house, yielded a mean and standard deviation of 92 percent ± 15 (n=67) and ranged from 70 percent to 131 percent. Overall 4-NP glucuronide procedural recoveries (including fresh fortifications for field fortification runs), across the two sites, prepared in-house, yielded a mean and standard deviation of 75 percent ± 4.7 (n=33) and ranged from 62 percent to 83 percent. Overall 4-NP sulfate (potassium salt) procedural recoveries, prepared in-house, yielded a mean and standard deviation of 99 percent ± 18 (n=6) and ranged from 80 percent to 119 percent.

Methyl parathion/methyl paraoxon (OVS tubes)

Overall methyl parathion OVS tube procedural recoveries (including fresh fortifications for field fortification runs), across the two sites, prepared in-house, yielded a mean and standard deviation of 103 percent ± 5.4 (n=4), and ranged from 97 percent to 110 percent. Overall methyl paraoxon OVS tube procedural recoveries (including fresh fortifications for field fortification runs), across the two sites, prepared in-house, yielded a mean and standard deviation of 114 percent ± 6.2 (n=4), and ranged from 107 percent to 121 percent. Individual analytical results for procedural recovery can be found on pages 289 to 299 of the study report.

Field Fortification Recovery

4-Nitrophenol (urine)

Urine field fortification samples were prepared three days prior to harvest (in Porterville), two days prior to harvest (in Fresno), on the day of harvest, and two days following harvest. Triplicate control urine samples were fortified at each event at three fortification levels for 4-nitrophenol analysis. Samples were fortified at 2.0, 10, and 50 ppb (μg/L), representing 2x, 10x, and 50x the LOQ, respectively. The urine field fortification samples were stored and shipped with the actual field samples. No field fortifications were conducted using either 4-NP glucuronide or 4-NP sulfate. The authors noted that "because stabilized (acidified) urine was used for these fortifications, sample handling was only supported from the time actual study samples were acidified in the field. Stability information on non-stabilized (non-acidified) urine regarding the period of sample collection through acidification was reported in another study (Study No. KP-99-17)." All reported urine field fortification recoveries were corrected for the mean recovery of concurrently analyzed 4-NP freshly fortified control samples.

For the Fresno site, recoveries from "exposure" (fortified, placed on blue ice for 24 to 36 hours, then frozen) field fortifications ranged from 58 percent to 127 percent and yielded a mean and standard deviation of 90 percent ± 15 (n=27) for 4-NP. For the Porterville site, recoveries from "exposure"field fortifications yielded a mean and standard deviation of 81 percent ± 11 (n=27) and ranged from 63 percent to 117 percent. The authors noted that the results indicate that 4-NP is stable in acidified urine under the same sample handling and shipping procedures as used for actual study samples.

Table 2 summarizes field-fortified control values obtained at the two test sites. The author chose to correct all urine field fortification recovery values with the mean laboratory recovery values. Tables 6a and 6b (Pages 85 and 87) of the Study Report identify individual recovery values.

Table 2. Field Fortified Recovery Values for 4-Nitrophenol in Urine Samples*

Test Site	4-Nitrophenol Fortification Level	Percent Recovery
Fresno, CA	2 μg/L	97.4 (n=9)
	10 μg/L	89.2 (n=9)
	50 μg/L	84.8 (n=9)
	Overall Average	**90 ± 15 (n=27)**
Porterville, CA	2 μg/L	87.4 (n=9)
	10 μg/L	81.3 (n=9)
	50 μg/L	72.9 (n=9)
	Overall Average	**81 ± 11 (n=27)**

***Corrected for Concurrent Laboratory Recovery**

Methyl parathion/methyl paraoxon (OVS tubes)

OVS tubes were fortified with methyl parathion and methyl paraoxon only on the day of harvest. Duplicate OVS samples were fortified with a single fortification solution containing 0.25 μg each of methyl parathion and methyl paraoxon. At each spiking event, identically fortified sets were either placed immediately in freezer storage ("travel") or were attached to an air sampling pump with air drawn through for the longest interval that the workers were in the field ("exposure"). The field fortification sets were submitted with the field samples and handled in the same manner as the actual field samples. All reported OVS field fortification recoveries were corrected for the mean recovery of concurrently analyzed freshly fortified control samples.

At the Fresno site, overall methyl parathion recoveries for both the "travel" (fortified and immediately frozen) field fortifications and "exposed" fortifications combined yielded a mean and standard deviation of 96 percent ± 6.1 (n=3) and ranged from 89 to 100 percent. Recoveries from "travel" field fortification OVS tube samples yielded a mean of 100 percent (n=2) and ranged from 99 to 100 percent. The recovery from a single "exposed" field fortification OVS tube sample was 89 percent. Overall methyl paraoxon recoveries for both travel and exposure fortifications combined ranged from 92 percent to 94 percent and yielded a mean and standard deviation of 93 percent ± 1.2 (n=3). Recoveries from "travel" field fortification OVS tube samples yielded a mean of 94 percent (n=2) and ranged from 94 to 94 percent. The recovery from a single "exposure" field fortification OVS tube sample was 92 percent.

Overall methyl parathion recoveries for the Porterville site for both the "travel" (fortified and immediately frozen) field fortifications and "exposed" fortifications combined yielded a mean and standard deviation of 83 percent ± 18 (n=4) and ranged from 56 to 94 percent. Recoveries from "travel" field fortification OVS tube samples ranged from 56 to 92 percent and yielded a mean of 74 percent (n=2). Recoveries from "exposure" field fortification OVS tube

samples ranged from 89 to 94 percent and yielded a mean of 92 percent (n=2). Overall methyl paraoxon recoveries for both travel and exposure fortifications combined ranged from 50 percent to 87 percent and yielded a mean and standard deviation of 75 percent ± 17 (n=4). Recoveries from "travel" field fortification OVS tube samples yielded a mean of 68 percent (n=2) and ranged from 50 to 85 percent. Recoveries from "exposure" field fortification OVS tube samples ranged from 79 to 87 percent and yielded a mean of 83 percent (n=2). The authors noted that the results indicate that both methyl parathion and methyl paraoxon are stable in OVS tubes under the same sample handling and shipping procedures as used for actual samples.

Storage Stability Recovery

Stability of 4-NP in urine (conducted on urine contained in Urisafe collection containers, stored on wet ice) during the 24-hour collection period of each sampling event up to 48 hours (to allow for sample volume measurement and subsampling, prior to freezing) was determined in a previously conducted study (Study No. KP-99-17, MRID 45200101). The stability results reported in that study (up to 48 hours) support the period of cold storage pertinent to this study (up to 36 hours). Residues of 4-nitrophenol and its glucuronide and sulfate conjugates were found to be stable in urine during frozen storage for up to 30 days (31 days for 4-NP) as determined in another study (KP-2000-02, MRID 45200101). The stability results reported in that study support the period of frozen storage for worker samples pertinent to this study (up to 30 days).

Calculations

4-Nitrophenol Calculations

Samples were analyzed in distinct analytical sample sets. Each set of urine samples included standards for generation of the calibration curve, one reagent blank, one control sample, three laboratory fortification samples (one 4-NP at the LOQ, and one at a higher level to bracket anticipated residues in the field samples, plus one sample containing 4-NP glucuronide fortification), and up to 12 experimental field samples.

Peak response was converted to concentration units (µg/mL) using a four point standard curve, generating a power curve equation (i.e., $y = ax^b$), where y = peak response, x = concentration, and a, b are variables dependent on data points entered. Next, the concentration in a specific urine sample was calculated using the equation which appears on page 250 of the Study Report. All sample results were corrected using the appropriate reagent blank.

Creatinine Calculations

The results of creatinine analyses were also analyzed in groups, each of which contained one fortified control sample, plus up to forty-two field samples. The authors used the GraphPad Prism software program to generate a standard curve for creatinine concentration (mg/dL) versus absorbance at 520 nm. Raw data were entered into a Microsoft Excel® 97 spreadsheet for

analysis according to the equation appearing on page 256 of the Study Report. The amount (grams) of creatinine produced by a study subject in a 24 hour period was reported.

Methyl Parathion/Methyl Paraoxon Calculations

Each set of OVS tubes typically consisted of standards for generation of the calibration curve, one reagent blank, one control sample, two laboratory fortification samples (one at the LOQ and one at 5xLOQ of each analyte), and up to 16 field samples. Calculations for instrumental analysis were conducted using a validated software application to create a standard curve based on linear regression. The regression functions were used to calculate a best-fit line and to determine concentrations of the analyte found during sample analysis from the calculated best fit line. The equation used for the least squares fit is described on page 258 on the Study Report.

Statistical Methods

Statistical procedures performed on the residue data included calculation of the arithmetic mean and corresponding standard deviation, geometric mean, median, and range. Transformation of urine sample data included converting the gross residue (μg/L and total μg 4-NP/sample) to net residue by first averaging each worker's 4-NP residues from samples collected pre-exposure and then subtracting that average from the 4-NP found in samples collected post-exposure. Both gross and net 4-NP were also normalized to μg 4-NP per kg body weight (by dividing the gross and net residue by the worker's weight) and to μg 4-NP per liter of urine produced (by dividing the gross residue by the liters of urine produced by the worker each day). Net 4-NP residues were also normalized to net 4-NP/70 kg body weight by multiplying the net 4-NP residue/kg body weight by 70. Versar recalculated the residue data by correcting field recoveries below 90 percent for the Porterville site (See Tables 3, 4, and 5).

Results

Results for all 24 hour worker urine samples from all 15 workers from both sites ranged from 2.58 μg/sample to 10.2 μg/sample for pre-exposure samples and from 1.76 μg/sample to 13.1 μg/sample for exposure samples. On the day of exposure, samples ranged from 0.88 to 7.68. Total net normalized 4-NP excreted (expressed as μg/70 kg body weight) from Day 0 through 96 hours after exposure ranged from -0.44 to 40.49 μg/70 kg body weight.

Creatinine measured in each harvester's daily urine samples were fairly consistent across the monitoring period, except for one high value for a worker at the Fresno site.

Results from selected air monitoring, using OVS air monitoring tubes, produced no detectable methyl parathion and methyl paraoxon residues (less than 0.05 μg/sample). According to the authors, the results indicate that inhalation exposure was minimal during harvesting activities. Thus, only urinary 4-NP data are presented in this review.

Table 3. 4-Nitrophenol Residues in Harvester's Post Exposure Urine Samples as Calculated by Elf Atochem North America

Parameters	Sampling Interval = 0-24 hours			
	#Rep	Arith. Mean	Std. Dev.	Geo. Mean
Gross 4-NP (μg/L)	15	3.03	1.93	2.16
Net 4-NP (μg/L)	15	0.410	1.69	[1]
Gross 4-NP (total μg)	15	6.09	2.64	5.54
Net 4-NP (total μg)	15	0.780	2.89	[1]
Gross 4-NP (μg/kg weight)	15	0.0713	0.0285	0.0656
Net 4-NP (μg/kg weight)	15	0.00953	0.0355	[1]
Net 4-NP (μg/70 kg weight)	15	0.667	2.48	[1]
Creatinine (g/24 hr)	15	2.41	0.712	2.3
	Sampling Interval = 24-48 hours			
Gross 4-NP (μg/L)	15	2.77	1.43	2.47
Net 4-NP (μg/L)	15	0.160	1.38	[1]
Gross 4-NP (total μg)	15	5.39	1.71	5.12
Net 4-NP (total μg)	15	0.0811	1.72	[1]
Gross 4-NP (μg/kg weight)	15	0.0641	0.0220	0.0605
Net 4-NP (μg/kg weight)	15	0.00235	0.0224	[1]
Net 4-NP (μg/70 kg weight)	15	0.164	1.57	[1]
Creatinine (g/24 hr)	15	2.13	1.09	1.90
	Sampling Interval = 48-72 hours			
Gross 4-NP (μg/L)	15	2.74	1.85	2.24
Net 4-NP (μg/L)	15	0.124	1.86	[1]
Gross 4-NP (total μg)	15	4.64	2.23	4.24
Net 4-NP (total μg)	15	-2.70	1.39	[1]
Gross 4-NP (μg/kg weight)	15	0.0542	0.0228	0.0502
Net 4-NP (μg/kg weight)	15	-0.00750	0.0271	[1]
Net 4-NP (μg/70 kg weight)	15	-0.525	1.89	[1]
Creatinine (g/24 hr)	15	2.25	0.844	2.11
	Sampling Interval = 72-96 hours			
Gross 4-NP (μg/L)	15	2.87	2.20	2.25
Net 4-NP (μg/L)	15	0.253	2.11	[1]
Gross 4-NP (total μg)	15	5.04	2.26	4.62
Net 4-NP (total μg)	15	-0.275	2.09	[1]
Gross 4-NP (μg/kg weight)	15	0.0592	0.0243	0.0547
Net 4-NP (μg/kg weight)	15	-0.00257	0.0242	[1]
Net 4-NP (μg/70 kg weight)	15	-0.180	1.70	[1]
Creatinine (g/24 hr)	15	2.20	0.750	2.08

Footnotes

Arith. Mean = Arithmetic Mean (average) Geo. Mean = Geometric Mean

Std. Dev. = Standard Deviation Gross 4-NP = Total 4-NP found in sample

Net 4-NP = Total 4-NP found in sample minus the average 4-NP residues from pre-exposure samples.

[1] Geometric means were not calculated due to negative values.

Table 4. 4-Nitrophenol Residues in Harvester's Post Exposure Urine Samples as Calculated by Versar, Inc.*

Parameters	Sampling Interval = 0-24 hours			
	#Rep	Arith. Mean	Std. Dev.	Geo. Mean
Gross 4-NP (μg/L)	15	3.36	2.25	2.83
Net 4-NP (μg/L)	15	0.75	2.04	[1]
Gross 4-NP (total μg)	15	6.76	3.25	6.12
Net 4-NP (total μg)	15	4.14	3.15	[1]
Gross 4-NP (μg/kg weight)	15	0.08	0.03	0.07
Net 4-NP (μg/kg weight)	15	0.05	0.03	[1]
Net 4-NP (μg/70 kg weight)	15	3.34	2.36	[1]
	Sampling Interval = 24-48 hours			
Gross 4-NP (μg/L)	15	3.14	1.82	2.73
Net 4-NP (μg/L)	15	0.52	1.75	[1]
Gross 4-NP (total μg)	15	6.07	2.31	5.64
Net 4-NP (total μg)	15	3.45	2.59	[1]
Gross 4-NP (μg/kg weight)	15	0.07	0.03	0.07
Net 4-NP (μg/kg weight)	15	0.04	0.03	[1]
Net 4-NP (μg/70 kg weight)	15	2.86	2.27	[1]
	Sampling Interval = 48-72 hours			
Gross 4-NP (μg/L)	15	3.14	2.31	2.47
Net 4-NP (μg/L)	15	0.52	2.33	[1]
Gross 4-NP (total μg)	15	5.24	2.87	4.68
Net 4-NP (total μg)	15	2.62	3.05	[1]
Gross 4-NP (μg/kg weight)	15	0.06	0.03	0.06
Net 4-NP (μg/kg weight)	15	0.03	003	[1]
Net 4-NP (μg/70 kg weight)	15	2.10	2.29	[1]
	Sampling Interval = 72-96 hours			
Gross 4-NP (μg/L)	15	3.31	2.77	2.48
Net 4-NP (μg/L)	15	0.70	2.96	[1]
Gross 4-NP (total μg)	15	6.98	7.51	5.08
Net 4-NP (total μg)	15	4.37	7.76	[1]
Gross 4-NP (μg/kg weight)	15	0.08	0.09	0.06
Net 4-NP (μg/kg weight)	15	0.05	0.09	[1]
Net 4-NP (μg/70 kg weight)	15	3.60	6.34	[1]

Footnotes:

Arith. Mean = Arithmetic Mean (average) Geo. Mean = Geometric Mean

Std. Dev. = Standard Deviation Gross 4-NP = Total 4-NP found in sample

Net 4-NP = Total 4-NP found in sample minus the average 4-NP residues from pre-exposure samples.

* 4-NP data from the Porterville site corrected for site specific field recovery (81 percent)

[1] Geometric means were not calculated due to negative values.

Table 5. Total Net 4-Nitrophenol Exposure in Individual Harvester's Urine Samples as Calculated by Versar, Inc.*

Worker Rep/ID	Test Site	Total Net 4-NP µg/ 70 kg body wt. (0 to 96 hours)
1	Fresno, CA	5.98
2	Fresno, CA	9.37
3	Fresno, CA	6.56
4	Fresno, CA	12.60
5	Fresno, CA	9.25
6	Fresno, CA	6.15
7	Fresno, CA	-0.44
8	Fresno, CA	4.50
9	Porterville, CA	20.74
10	Porterville, CA	16.32
11	Porterville, CA	3.55
12	Porterville, CA	5.51
13	Porterville, CA	15.91
14	Porterville, CA	40.49
15	Porterville, CA	22.12

* 4-NP data from the Porterville site corrected for site specific field recovery (81 percent)

Guideline Compliance Review

Compliance with US-EPA-OPPTS's Series 875 - Occupational and Residential Exposure Test Guidelines is critical. The following listing summarizes the major relevant requirements found in OPPTS 875: Part B: 875.2500 Post-application Inhalation Exposure and 875.2600, Post-application Biological Monitoring, and Part C: Quality Assurance/Quality Control.

Guideline 875.2500 (Inhalation Exposure)

- *A sufficient number of replicates should be generated to address the exposure issues associated with the population of interest. Specifically, each study should include a minimum of 15 individuals (replicates) per activity.* This criterion was not met. Only five replicates were monitored at each site of the two sites.

- *An accuracy value of between 70 and 120 percent (average recovery) and a precision value less than or equal to 20 percent (coefficient of variation) demonstrated the analytical environment's capability to perform accurate and precise analysis.* This criterion was met. Concurrent laboratory recovery averaged 103 ± 6.2 percent (N=4).

- *The method should be sufficiently sensitive so that, coupled with the trapping and extraction procedures chosen, it is capable of measuring inhalation exposure to 1 μg/hr.* This criterion was met.

- *Extraction efficiency of the laboratory method will be considered acceptable if the lower limit of the 95 percentile interval is greater than 75 percent, unless otherwise specified by the Agency. At a minimum seven determinations should be made at each fortification to calculate the mean and standard deviation for recovery. Total recovery from field-fortified samples must be above 50 percent.* These criteria were met. Field fortified recovery values averaged 96 ± 6.1 percent (N=3) for the Fresno site and 83 ± 18 (n=4) for the Porterville site all at the same fortification level of 0.25 μg/tube.

- *To ensure that collected material is not lost from the medium during sampling, inhalation monitoring equipments should be tested for breakthrough. It is recommended that at least one test be carried out where the initial trap contains 10X the highest amount of residue expected in the field.* This criterion was partially met. Field fortified samples contained 0.25 μg/tube; most of the time front and back sections of the XAD sorbent were analyzed separately. The LOQ was 0.05 μg/tube.

- *Field-fortified samples should be fortified at the expected residue levels of actual field samples. There should be at least one field-fortified sample per worker per monitoring period for each fortification level.* This criterion was met.

- *If extracts from field samples are to be stored prior to analysis, a documented study of stability is to be made.* This criterion was met. The OVS sir sampling tubes were

analyzed within 33 days of collection, therefore, a freezer storage stability study was not conducted. Stability was also verified by the OVS field fortification samples prepared in the field, that were stored and analyzed along with the exposure samples.

- *For agricultural applications, yards, and gardens, the following information should be reported: pesticide identification (e.g. name, formulation, EPA Reg. No., lot number, type of concentrate container); description of the area, application and equipment data, weather data, work activity monitored, exposure observations (including direction of travel of applicator in relation to wind direction, and any special situation observed that might alter normal exposure, such as splashing concentrate), exposure time.* These criteria were met.

- *All samples to be held in a freezer upon return from field.* This criterion was met.

- *Respiratory exposure to be reported as mean residue per Liter air collected, corrected for losses due to trapping, extraction and storage. Values less than LOQ to be considered to have contained ½ LOQ.* These criteria were met.

- *Total time worked and total quantity of active ingredient handled must be reported. Total quantity of air drawn through each individual sample also to be reported.* These criteria were met.

Guideline 875.2600

- *The Agency requires investigators to submit protocols for review purposes prior to the inception of the study. Adequate pharmacokinetic data must exist to effectively interpret the data.* This criterion was met.

- *The test substance should be a typical end use product of the active ingredient.* This criterion was met.

- *The application rate used in the study should be provided and should be the maximum rate specified on the label. However, monitoring following application at a typical application rate is more appropriate in certain cases.* This criterion was met.

- *Selected sites and seasonal timing of monitoring should be appropriate to the activity.* This criterion was met. The test sites were located in Fresno and Porterville representing two walnut growing regions of California. In 1997, California produced 100 percent of the total U.S. walnut production (USDA).

- *Biomonitoring studies should be carried out concurrently with dislodgeable/transferable residue studies.* A parallel study was conducted where dislodgeable foliar data were collected for "Foliar and Soil Dislodgeable Residue Dissipation of Methyl Parathion Residues Following Applications of Penncap-M® Microencapsulated Insecticide to

Walnuts," MRID # 453592-01 and 454009-01 amended. This study was provided to EPA as a separate submission.

- *A sufficient number of replicates should be generated to address the exposure issues associated with the population of interest. Specifically, each study should include a minimum of 15 individuals (replicates) per activity.* This criterion was met. Fifteen replicates were monitored at two sites: 8 at the Fresno site and 7 at the Porterville site. A third geographic location in Ripon, California was to be included as a test site, however, the commercial grower rescinded on his agreement for use of the orchard to monitor reentry activities.

- *The exposure monitoring period should be of sufficient length to ensure reasonable detectability of residues in biological media (e.g., blood and urine). The exposure period should also be representative of a normal activity.* These criteria were met. Pre-screen 24-hour urine samples were collected up to three weeks before the exposure event. Those subjects with the lowest 4-NP levels were selected for participation in the study. Baseline 24-hour urine samples were collected each day beginning 48 hours before the exposure event, and for 96 hours after the exposure began.

- *Biomonitoring should be conducted using validated methodologies based on the pharmacokinetic properties of the pesticide of concern.* This criterion was met. Justification for collection of urinary 4-NP samples was presented to EPA in a separate study, *"Justification for Use of Urinary Excretion of 4-Nitrophenol for Biomonitoring of Worker Exposure to Methyl Parathion," MRID #449744-01.*

- *Any protective clothing worn by study participants should be identified.* This criterion was met.

- *Urine samples should be collected one day before participating in the postapplication exposure monitoring activities and should continue on the day of postapplication monitoring and for an appropriate time period after these activities have been completed, depending on the excretion kinetics of the compound. The 24-hour sample collection cycle should begin with the first void after beginning work activities and end with the first void on the following morning, continuing this 24-hour cycle on subsequent days.* This criterion was met.

- *Baseline blood samples should be collected prior to exposure. Based on pharmacokinetics, postapplication exposure samples should be collected at the appropriate times before, during, and after exposure.* This criterion was met. Twenty-four hour urine samples were collected for 2 days prior to exposure and for 4 days post exposure.

- *Materials used for sample collection should not interfere with (e.g., absorb) the analytes of interest.* This criterion was met.

- *Creatinine levels should be determined as a way of qualitatively monitoring completeness of urine collection samples. Specific gravity, as another measure of 24-hour sample completeness, should be performed as soon after collection as possible (and before sample storage).* These criteria were partially met. Creatinine levels were determined as well as density and volume before the samples were placed in freezer storage. Specific gravity measurements were not reported in the Study Report.

- *Prior exposures to the test pesticide or structurally related compounds may interfere with study results. For blood, a brief history should be taken relating to known prior exposures to pesticides for at least the last 2 weeks, including reentry into potentially treated fields. For urine, there should be a sufficient time period between such exposures and participation in the study to ensure adequate urinary clearance of the compound and its metabolites, based on pharmacokinetic data.* This criterion was met. The test subjects were prescreened prior to exposure monitoring and the subjects with the lowest PNP background were selected. However, no formal discussion of activities performed by subjects within the last two weeks prior to biomonitoring was provided in the Study Report.

- *Validated analytical methods of sufficient sensitivity are needed. Information on method efficiency and limit of quantitation (LOQ) should be provided.* This criterion was met. The target limit of quantitation (LOQ) for 4-NP in urine was 1.0 μg/L and the target limit of detection (LOD) was 0.3 μg/L. For creatinine in urine, the method sensitivity was 0.6 mg/dL based on instrument resolution of 0.01 absorbance units. For inhalation exposure samples, the limit of quantitation (LOQ) was 0.05 µg/sample for both methyl parathion and methyl paraoxon.

- *Samples should be stored in a manner that will minimize deterioration and loss of analytes between collection and analysis. Biological monitoring samples (e.g., serum, plasma and urine) should be refrigerated or stored frozen prior to analysis. Whole blood should not be frozen. Information on storage stability should be provided.* This criterion was met. Short term storage stability was determined in a previously conducted study (Study No. KP-99-17, MRID 45200101). Also, a long term storage stability study has been submitted to EPA (KP-2000-02, MRID 45200101).

- *Field data should be corrected if any appropriate field fortified, laboratory fortified or storage stability recovery is less than 90 percent.* This criterion was <u>not</u> met. Field fortified recovery values averaged 90 percent ± 15 (n=27) for the Fresno site and 81 percent ± 11 (n=27) for the Porterville site. The field data were not corrected by the study author for the Porterville site, however, these data was corrected for field recovery by Versar.

- *Unless stability of the analyte has been established prior to initiation of the study, three samples of control (nonparticipant) should be fortified with two levels of the biological*

analyte (parent or metabolite(s), whichever is appropriate) for each experimental site. This criterion was met.

- *The amount of chemical found should be reported for each sample, and as a cumulative total for each exposure period. Distributional data should be reported, to the extent possible.* This criterion was met.

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