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OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

September 5, 2001

Memorandum

SUBJECT: Review of "*Occupational Exposure Monitoring of Aerial Mixing/Loading of PENNCAP M® Utilizing Biological Monitoring*"(MRID # 453271-01)

FROM: Renee Sandvig, Environmental Protection Specialist Renee Sandvig 9/5/01
Reregistration Branch II
Health Effects Division (7509C)

THROUGH: Al Nielsen, Branch Senior Scientist Al Nielsen 9/5/01
Reregistration Branch II
Health Effects Division (7509C)

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

DP Barcode: D272805

Pesticide Chemical Codes: 053501

EPA MRID Numbers: 453271-01

Attached is a review of the handler biomonitoring and inhalation data submitted by Cerexagri, Inc. (formerly Elf Atochem North America, Inc.). This review was completed by Versar, Inc. on March 26, 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 meet most of the criteria specified in the U.S. Environmental Protection Agency OPPTS Guidelines, Group A, 875.1300, Applicator Inhalation Exposure -- Outdoor, Group A: 875.1500, Biological Monitoring. The data will be considered in future methyl parathion REDs.

Summary

The purpose of this study was to quantify potential exposure of mixer/loaders handling the restricted use organophosphate insecticide, methyl parathion, at three aerial application facilities. The facilities were located in Greenville, MS; Gila Bend, AZ; and Harquahala, AZ. PENNCAP-M® Microencapsulated Insecticide (a flowable aqueous suspension containing 21.1 percent a.i. and packaged in 2.5 gallon containers) was mixed and pumped into aircraft using commercial equipment. Each test subject mixed and loaded sufficient test substance to support aerial application of 350 acres with an application rate of 1.0 lbs ai/A. The mixer/loaders also performed clean-up activities at all three sites.

Fifteen experienced volunteer mixer/loaders were monitored for the urinary exposure analyses. Urine samples were collected from five subjects at each location and at one location inhalation exposure was also monitored. Methyl parathion exposure was quantified by measuring total 4-nitrophenol and its sulfate and glucuronide conjugates in urine samples (the analytical method hydrolyzes these conjugates to 4-nitrophenol equivalents). The samples were also analyzed for creatinine content. Twenty-four hour urine samples (collected as 12 hour samples) were collected for 48 hours prior through 84 hours after exposure, or 5.5 days total. The workers were housed in a hotel during this period, leaving it only to perform mixing/loading operations on the day of exposure and to eat meals.

Results from personal air monitoring of 5 mixer/loaders at the Gila Bend, AZ site indicated that inhalation exposure was minimal during mixing/loading activities. Normalized net urinary 4-NP levels were variable across the three data-sets. For the two sites at which mixer/loaders wore the personal protective equipment (PPE) required by the product label, the geometric mean urinary 4-NP values rose to more than twice (generally MS) and seven times (Gila Bend, AZ) baseline levels on the day of exposure. Thereafter, urinary excretion of 4-NP declined to below baseline levels by 72 hours after exposure. At the third site, where additional PPE was worn, neither the arithmetic nor the geometric mean urinary 4-NP values exceeded baseline values on the day of exposure, and were either very low or near zero (significantly lower than even pre-screen or baseline values) thereafter.

Conclusions

The study was in compliance with most of the OPPT Series 875 Occupational and Residential Exposure Test Guidelines. The following issues of potential concern were identified:

- It could not be determined from the Study Report if "potential inhaled residue" was calculated using a standard adult male breathing rate during light, moderate, or heavy exertion.

- No tank mix samples were collected or analyzed.

- Creatinine levels were very low on the day after exposure in one worker at the Greenville, MS site, relative to the other workers. The worker, subject #3, had a creatinine level of 0.508 g/24hrs.

- Conditions were windy (1 mph to 15 mph) at two of the test sites for significant portions of the work exposure period.

MEMORANDUM

TO: Renee Sandvig

cc: 1000.001.01 File

FROM: Marit Espevik/Diane Forrest

DATE: March 26, 2001

SUBJECT: Review of "*Occupational Exposure Monitoring of Aerial Mixing/Loading of PENNCAP M® Utilizing Biological Monitoring*"(MRID # 453271-01)

Versar reviewed a study entitled *"Occupational Exposure Monitoring of Aerial Mixing/Loading of PENNCAP M® Utilizing Biological Monitoring,"* 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, Group A, 875.1300, Applicator Inhalation Exposure -- Outdoor, Group A: 875.1500, Biological Monitoring, and Part C: Quality Assurance/Quality Control. The following information may be used to identify the study:

Title:	*Occupational Exposure Monitoring of Aerial Mixing/Loading of PENNCAP M® Utilizing Biological Monitoring:* 462 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
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:	William P. Barney (Author) Aaron Rotondaro (Study Director) Grayson Research, L.L.C. 1040 Grayson Farm Road Creedmoor, NC 27522
Report Date:	February 5, 2001
Identifying Codes:	MRID # 453271-01; Cerexagri Study No. KP-99-15; Morse Project No. ML99-0813-ATO

EXECUTIVE SUMMARY

The purpose of this study was to quantify potential exposure of mixer/loaders handling the restricted use organophosphate insecticide, methyl parathion, at three aerial application facilities. The facilities were located in Greenville, MS; Gila Bend, AZ; and Harquahala, AZ. PENNCAP-M® Microencapsulated Insecticide (a flowable aqueous suspension containing 21.1 percent a.i. and packaged in 2.5 gallon containers) was mixed and pumped into aircraft using commercial equipment. Each test subject mixed and loaded sufficient test substance to support aerial application of 350 acres with an application rate of 1.0 lbs ai/A. The mixer/loaders also performed clean-up activities at all three sites.

Fifteen experienced volunteer mixer/loaders were monitored for the urinary exposure analyses. Urine samples were collected from five subjects at each location and at one location inhalation exposure was also monitored. Methyl parathion exposure was quantified by measuring total 4-nitrophenol and its sulfate and glucuronide conjugates in urine samples (the analytical method hydrolyzes these conjugates to 4-nitrophenol equivalents). The samples were also analyzed for creatinine content. Twenty-four hour urine samples (collected as 12 hour samples) were collected for 48 hours prior through 84 hours after exposure, or 5.5 days total. The workers were housed in a hotel during this period, leaving it only to perform mixing/loading operations on the day of exposure and to eat meals.

The study examined the impact of two different personal protective equipment (PPE) regimes. Mixer/loaders at two test sites wore the personal protective equipment (PPE) prescribed on the product label: long-sleeved shirt and long pants underneath coveralls, socks and rubber boots, neoprene protective gloves, goggles, and dust/mist filtering respirator. At the third test site, however, mixer/loaders wore additional PPE while mixing and loading: a chemical resistant apron and a Tyvek® rain type hat.

Results from personal air monitoring of 5 mixer/loaders at the Gila Bend, AZ site indicated that inhalation exposure was minimal during mixing/loading activities. Normalized net urinary 4-NP levels were variable across the three data-sets. For the two sites at which mixer/loaders wore the personal protective equipment (PPE) required by the product label, the geometric mean urinary 4-NP values rose to more than twice (generally MS) and seven times (Gila Bend, AZ) baseline levels on the day of exposure. Thereafter, urinary excretion of 4-NP declined to below baseline levels by 72 hours after exposure. At the third site, where additional PPE was worn, neither the arithmetic nor the geometric mean urinary 4-NP values exceeded baseline values on the day of exposure, and were either very low or near zero (significantly lower than even pre-screen or baseline values) thereafter.

Total net normalized 4-NP excreted (expressed as μg/ 70 kg body weight) ranged as follows:
(1) Greenville, MS (employing current label PPE): 8.32 to 26.54 μg/kg; (2) Gila Bend, AZ (employing current label PPE): 31.07 to 55.62 μg/kg; and (3) Harquahala Valley, AZ (employing additional PPE): 1.26 to 11.54 μg/kg.

The author assumed first-order kinetics to predict 4-NP dissipation in urine. Residue data collected between 0 and 72 hours from the Greenville, MS and Harquahala, AZ data-sets and from 0 to 84 hours for the Gila Bend, AZ data sets were analyzed using Microsoft® 's Excel 97 software. Regression analysis for 4-NP (net μg/kg) predicted the following half lives: (1) Greenville MS: 17.7 hours ($R^2 = 0.8659$); (2) Gila Bend AZ: 13.8 hours ($R^2 = 0.9508$); and (3) Harquahala Valley AZ: 16.5 hours ($R^2 = 0.1904$).

The study was in compliance with most of the OPPT Series 875 Occupational and Residential Exposure Test Guidelines. The following issues of potential concern were identified:

- Subjects also performed cleanup activities at all three test sites, including: rinsing of the mixing tanks, disposal of empty test substance containers and caps. At the Greenville MS site, subjects also washed the aircraft, but this was not standard practice at the AZ test sites. It could not be determined from the Study Report how much additional exposure time might have been involved in performing these activities.

- No tank mix samples were collected or analyzed.

- It could not be determined from the Study Report if "potential inhaled residue" was calculated using a standard adult male breathing rate during light, moderate, or heavy exertion.

- Although analytical results were reported as both total and net 4-NP per liter, results were not reported as creatinine-corrected urinary concentrations (µg/gram creatinine) as requested by the Agency in its review of the proposed study protocol dated November 1, 1999.

- Creatinine levels were very low on the day after exposure in one worker at the Greenville, MS site, relative to the other workers. The worker, subject #3, had a creatinine level of 0.508 g/24hrs.

- Conditions were windy (1 mph to 15 mph) at two of the test sites for significant portions of the work exposure period.

Study Review

Study Background

The purpose of this study was to monitor urinary excretion of methyl parathion (i.e., O,O-dimethyl O-p-nitrophenylphosphorodithioate, CAS No. 298-00-0) in mixer/loaders. Methyl parathion was formulated as a 21.1 percent product in PENNCAP-M® Microencapsulated Insecticide. In this study, 4-nitrophenol (4-NP), a urinary metabolite of methyl parathion, was used to quantify methyl parathion exposure. Exposure was determined by analysis of 4-nitrophenol and its associated biological glucuronide and sulfate conjugates in 24 hour composite urine samples before, during, and after exposure to PENNCAP-M®. In addition, personal air monitoring samples were collected for methyl parathion and 4-nitrophenol levels in five volunteers at one test site.

Mixer/loaders at three aerial application facilities were selected to participate in this study. The study examined the impact of two different personal protective equipment (PPE) regimes. Mixing and loading of the test substance took place on December 15, 1999 at Greenville, MS, on February 2, 2000 near Gila Bend, AZ, and on March 15, 2000 in Harquahala Valley, AZ. The field phase of the study was directed by Grayson Research, L.L.C of Creedmoor, NC. Sample analysis was conducted between February 29, 2000 and March 24, 2000 by Morse Laboratories, Inc. of Sacramento, CA.

Attestations

The study sponsor waived claims of confidentiality within the scope of FIFRA Section 10 (d)(1)(A), (B), or (C). The study sponsor and author attested that the study was conducted and reported in compliance with EPA Good Laboratory Practice Standards (40 CFR Part 160), with certain exceptions. These were: (1) on site weather data were derived from calibrated, computerized field weather stations, however, the computer and software were not validated; (2) the balance used to weigh test subjects at field sites were not maintained according to GLP requirements; (3) some data were not recorded or corrected in complete compliance with GLP; and (4) analytical standards were not characterized according to GLP. Purities provided by the manufacturers were relied on instead. Quality Assurance Statements were included for the protocol, sampling packaging, field activities, field notebook and report, analytical data and report, and the final submission.

Study Subjects

Twenty-seven volunteers who had one to 25 years of experience mixing/loading pesticides were selected as potential candidates. Pre-screen urine samples were obtained within three weeks of the anticipated study start date. Sixteen workers with the lowest detectable 4-NP levels in a 24-hour pre-screen sample were chosen to participate in the study (five workers at each the Greenville, Mississippi and Gila Bend, Arizona sites and six workers at the Harquahala

Valley, Arizona site). (One of the 16 workers was eliminated at the Arizona site.) The study subjects were "healthy Caucasian, African American or Hispanic males, ranging from 18 to 54 years of age, 64 to 74 inches in height, and 128 to 284.5 lbs in weight." All participants read and signed Informed Consent Forms.

The workers were sequestered in a hotel (except to eat meals) during the entire monitoring period except on the day of exposure (mixing and loading). The workers were required to shower or bathe the morning of or evening before their participation in the study.

Personal Protective Clothing and Equipment

At the Greenville, Mississippi and Gila Bend, Arizona sites, test subjects wore personal protective equipment (PPE) while mixing/loading as prescribed on the product label:

- long-sleeved shirt and long pants underneath coveralls (full body, cotton, Lab Safety);
- socks and rubber boots (Bata Alternative);
- protective gloves (neoprene 8696-10, Lab Safety);
- goggles (plastic, American Allsafe Co. 211 style); and
- dust/mist filtering respirator (Gerson 2737, Type N95).

At the Harquahala Valley, Arizona site, test subjects wore the same PPE as above with the following modifications:

- nitrile, instead of neoprene, protective gloves (Stan Solu, nitrile A-10);
- face shield, instead of goggles (Wilson Protecto Shield M86PCCLU);
- chemical resistant apron (rubber coated cotton); and
- Tyvek® rain type hat.

The authors stated that "the chemical resistant apron was inadvertently left off worker number 11 during the mixing/loading procedure. Worker number 16 (the sixth replicate for this site) was used to replace worker 11." Therefore, only 5 replicates for each site were used in the analysis.

Materials and Work Practices Monitored

A product label for PENNCAP-M® Microencapsulated Insecticide [EPA Reg. No. 4581-393] was not provided for review. However, available literature indicates that this product typically contains a nominal 20.9 percent methyl parathion at 2 lbs. ai/gallon. It is a flowable formulation consisting of a water suspension of polymeric-type microcapsules containing the active ingredient. The formulation is packaged in 2.5 gallon containers. The maximum label use rate for cotton is 1 pound ai per acre (i.e., 4 pints formulated product per acre). In this study, PENNCAP-M® was applied at the maximum labeled application rate for cotton plants.

Each worker performed enough mixing/loading cycles (four to five) to mix enough tank mixtures for 350 acres. Each cycle consisted of mixing the appropriate amount of PENNCAP-M® in the nurse tank and loading the solution into the aircraft. At each of the three sites, each volunteer handled a total of 175 gallons of PENNCAP-M® concentrate.

At the Greenville, MS site, an 80 gallon tank was used to mix PENNCAP-M® with water. The mixing procedure started with 15 gallons of water in the mixing tank and the test substance was then poured into the tank. The test substance containers were rinsed into the mixing tank. The mixture was pumped into the aircraft and the final spray volume was reached by pumping water into the aircraft (an Air Tractor Model AT402 airplane). The exposure duration for each of the five subjects monitored averaged 109 ± 3.8 minutes. During this time, a total of 1,750 gallons of tank mix was prepared per subject in five mixing/loading sessions.

At the Gila Bend and Harquahala Valley, AZ sites, a 150 gallon tank was used to mix water with PENNCAP-M®. The test substance containers were allowed to drain onto a stainless steel mixing screen and into the mix tank. The screen and containers were rinsed and the mixture was pumped into the aircraft. Again, the final spray volume was reached by pumping water into the aircraft (an Ayers Model SR2N airplane.) The exposure duration for each of the five subjects monitored at Gila Bend averaged 90.6 ± 32.8 minutes. [The variability was due to a single replicate taking an unusually long time (i.e., 147 minutes) to perform the work activities; the other four subjects took from 66 to 91 minutes to perform the same task.] During this time, a total of 1,923 gallons of tank mix was prepared per subject in four mixing/loading sessions.

The exposure duration for each of the five subjects monitored at the Harquahala Valley, AZ site averaged 56.3 ± 5.8 minutes. During this time, a total of 1,923 gallons of tank mix was prepared per subject in four mixing/loading sessions. Observations were made and recorded on all mixing and loading events, including start and stop times mixing/loading operations (see Study Report, pages 76-81).

Subjects also performed cleanup activities at all three test sites, including: rinsing of the mixing tanks, disposal of empty test substance containers and caps. At the Greenville MS site, subjects also washed the aircraft, but this was not standard practice at the AZ test sites. The Study Report does not provide information for how much additional exposure time may have been involved in performing these activities.

Meteorology

A summary of the meteorological information may be reviewed on page 61 of the Study Report. Hourly weather data were reported during exposure monitoring, including air temperature, humidity, wind speed, cloud cover, and wind direction. Weather data were recorded at the field sites using either a computerized Campbell Scientific Weather Watch® 200 weather station (Greenville, MS) or a Campbell Scientific Data Logger with Vaisala temperature and relative humidity sensor and RM Young wind speed and direction sensors (Gila Bend Harquahala Valley, AZ).

At the Greenville, MS site, air temperatures ranged from low the 40's to low 50's (Fahrenheit) and the relative humidity ranged from 43 to 74 percent. Windspeeds ranged from 8 mph to 14 mph. At the Gila Bend, AZ site, air temperatures ranged from the mid 30's to mid 70's and the relative humidity ranged from 10 to 45 percent. Windspeeds ranged from less than 1 mph to 15 mph. At the Harquahala Valley, AZ site, air temperatures ranged from mid 50's to mid 80's and the relative humidity ranging from 10 to 55 percent. Windspeeds were somewhat calmer at this site, ranging from less than 1 mph to nearly 8 mph. However, conditions were windy at all three sites for significant portions of the work exposure period.

Sampling

Sampling consisted of biological monitoring (urine analysis for the metabolite 4-NP) and limited personal air monitoring. Deviations from protocol were reported (see Study Report, pages 56 and 57, and 447 through 462).

Urine samples were collected at all test sites for 48 hours prior to exposure monitoring and for 84 hours after monitoring. Baseline urine samples were collected from each worker at 12 hour intervals between 48 hours prior and Day 0 (the day of exposure). Urine samples were also collected at 12 hour intervals from inception of mixing/loading activities (Day 0), and up to 84 hours after exposure activities ended. All urine was collected from each worker during the exposure monitoring period. The workers collected their urine into a single Urisafe® container for each time period. Samples were stored in ice chests with substitute ice during the sampling period. After the urine samples were collected from the workers, the entire sample was weighed, specific gravity was determined, then HCl added at a rate of 10 mL per 1,000 grams of urine. [The specific gravity of each urine sample was determined from a small aliquot before HCl was added and before the urine samples were frozen.] The sample was then agitated and a 100 mL aliquot was measured into a separate container. The total volume for each twelve hour sample was calculated from the weight and specific gravity measurements. Both the large and small samples were stored frozen until shipment.

Air monitoring samples were collected at the Gila Bend, AZ site only "to help define the route of exposure." An SKC pump (Model 224-44XR) with a Bios International flow meter (Model DC-L12K) was attached to a belt around the waist of the worker. The pump air flow rate was calibrated at approximately 2 liters per minute. Tygon® tubing connected the pump inlet valve to the sampling train. The inlet of the sampling train was positioned over the worker's shoulder, by attaching the air sampler to the mixer/loader's collar, to sample in the breathing zone of the worker. The sampling train consisted of a glass fiber filter attached to an OVS sampling tube containing XAD-2 sorbent (140/270). A small piece of the dust/mist filtering respirator was inserted into each OVS tube prior to calibration and removed at the end of the monitoring period.

QA/QC

Sample History

The author provided a comprehensive history of all samples analyzed. Urine samples were collected between November 23 and December 17, 1999, at the Greenville, MS site, between January 18 and February 5, 2000 at the Gila Bend, AZ site, and between February 5 and March 18, 2000 at the Harquahala Valley, AZ site. OVS tubes samples were collected on February 2 at the Gila Bend, AZ site. All sample analysis was conducted between February 29, 2000 and March 24, 2000 by Morse Laboratories, Inc. of Sacramento, CA. The longest sample collection to analysis storage interval was 24 days.

Sample Storage and Shipping

Urine samples were kept in ice chests with substitute ice during the exposure monitoring time periods. After weighing and acidification, the aliquot samples were stored frozen until shipment to the analytical laboratory. Aliquot samples and OVS tubes were shipped on dry ice via Federal Express for overnight delivery to Morse Laboratories, Inc. in Sacramento, CA, and stored in a freezer until analysis. Upon receipt at Morse Laboratories, Inc., frozen urine samples were transferred to a limited-access freezer for storage, where they remained until thawed for subsampling and extraction. Freezer storage temperatures were monitored daily and remained at -20 ± 5°C.

Formulation Sample and Tank Mix Analyses

Formulation samples were analyzed to confirm product purity and concentration. The certified ai content of PENNCAP-M® was 21.1 percent (December 13, 1999). Tank mix samples were not collected or analyzed.

Analytical Methodologies

1. 4-NP in Urine Analyses

The analytical methods referenced in the Study Report for the analysis of 4-NP in urine samples were:

- *Morse Laboratories, Inc. Analytical Method No. Meth-120, Draft (Meth-120K-noSPE.sop), dated December 1, 1999, entitled "Determination of 4-nitrophenol in Urine;"*
- *Morse Laboratories, Inc. Analytical Method No. Meth-120, Draft (Meth-120K-noSPE-toluene.sop), dated December 9,1999, entitled "Determination of 4-nitrophenol in Urine;"*
- *Morse Laboratories, Inc. Analytical Method No. Meth-120, Revision #2 dated December, 1999, entitled "Determination of 4-nitrophenol in Urine."*

4-nitrophenol is a urinary metabolite of methyl parathion. 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. The retention time was approximately 13 minutes.

2. Creatinine (urine) analysis:

Creatinine levels were measured in the urine samples as a qualitative measure of renal function of the 5 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 is excreted as a waste product by the kidney and synthesized in the body at a fairly constant rate. Creatinine's serum concentration depends almost entirely upon its excretion rate by the kidneys, independent of diet. 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.

3. Methyl parathion and 4-nitrophenol (OVS sampling tube) analysis:

The analytical method used for the analysis of methyl parathion and 4-nitrophenol in OVS air sampling tubes 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."* Methyl parathion and 4-nitrophenol 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 4-nitrophenol, and, if needed, purified by solid phase extraction (SPE) before gas chromatographic analysis using either flame photometric detection (FPD) detection (for methyl parathion) or NPD detection (for 4-nitrophenol). The limit of quantitation (LOQ) was 0.05 µg/sample for methyl parathion and 0.5 µg/sample for 4-nitrophenol, where a sample is equivalent to the entire tube or a single section of the tube (whichever is applicable). The method was validated in this study.

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."

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 4-nitrophenol or equivalent.

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 methyl parathion and 0.5 μg/sample for 4-nitrophenol.

Calibration

Calibration curves were generated by injecting constant volumes of derivatized 4-nitrophenol standard solutions. Sample responses greater than those produced by the highest concentration of applicable standard curve required dilution and reinjection. In order to maintain consistent chromatography, dilutions were made with 1.5 percent 1-decanol in toluene. A curve check standard was injected every 4-5 sample injections. Details of the instrument parameters were reported in on page 138-139 (Analytical Phase Report) of the Study Report.

Compositing of Urine Samples

Both field-fortified controls and exposure-related ("field") samples were subsampled in the field to reduce the amount of sample shipped to the laboratory. Field samples required composting per worker and per sampling period in the laboratory to generate 24-hour samples from 12 hour samples. Cerexagri provided a specific procedure for compositing control urine whenever more than one container was used for collection (see page 362, Appendix V of the Study Report). Field samples were never collected in more than two containers. Most samples selected to be controls also required compositing.

Control Samples

There were two different sources for "control" urine samples: (1) derived from workers prior to exposure in this study; and (2) derived by laboratory personnel. Urine samples from Morse Laboratory personnel and workers were screened for use in the study as control samples for procedural quality control (concurrently analyzed controls and fortified controls). 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, most control urine samples were found to contain less than 1.2 μg/L 4-NP except for two samples that contained 1.3 μg/L and 1.9 μg/L.

Concurrent Laboratory Recovery

For urine samples from the Greenville, MS site, overall 4-NP procedural recoveries (including fresh fortifications for field fortification runs) yielded a mean and standard deviation of 81 percent ± 11 (n=7) and ranged from 61 to 92 percent. Overall 4-NP glucuronide procedural recoveries yielded a mean and standard deviation of 95 percent ± 26 (n=7) and ranged from 67 to 135 percent.

For urine samples from the Gila Bend AZ site, overall 4-NP procedural recoveries (including fresh fortifications for field fortification runs) yielded a mean and standard deviation of 87 percent ± 6.5 (n=8), and ranged from 78 to 95 percent. Overall 4-NP glucuronide procedural recoveries yielded a mean and standard deviation of 89 percent ± 17 (n=8), and ranged from 61 to 114 percent.

For urine samples from the Harquahala Valley, AZ site, overall 4-NP procedural recoveries (including fresh fortifications for field fortification runs) yielded a mean and standard deviation of 91 percent ± 11 (n=8) and ranged from 83 to 118 percent. Overall 4-NP glucuronide procedural recoveries yielded a mean and standard deviation of 83 percent ± 13 (n=8) and ranged from 63 to 100 percent.

For air samples from the Gila Bend, AZ site, overall methyl parathion procedural recoveries (including fresh fortifications for field fortification runs) yielded a mean and standard deviation of 94 percent ± 2.8 (n=12), and ranged from 89 to 100 percent. Overall 4-NP procedural recoveries yielded a mean and standard deviation of 82 percent ± 7.3 (n=8), and ranged from 74 to 96 percent.

Field Fortification Recovery

1. Urine Samples

Urine field fortification samples were prepared at three fortification levels for 4-nitrophenol analysis. Samples were fortified at 2.0, 10, and 100 µg/L, representing 2X, 10X, and 100X the LOQ, respectively. The fortification levels chosen corresponded well with the 4-nitrophenol levels measured in the field data. Field fortifications were prepared on day 1, 3, and 5 of biological monitoring using a stock solution of 4-nitrophenol. A single control sample of urine was also prepared at each fortification event. The urine field fortification samples were stored and shipped with the actual field samples. The low and high level (2 and 100 µg/L, respectively) urine field fortifications were not prepared at the Greenville, MS site because the fortification solutions were not received on time. In addition, there were no high level (100 µg/L) urine fortifications on day 5 at the Greenville, MS site, as the high level fortifications were inadvertently fortified with the middle fortification level (10 µg/L). No field fortifications were conducted using either 4-NP glucuronide or 4-NP sulfate.

The authors noted that since "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 was reported in another study (Study No. KP-99-17).]

Table 1 summarizes field-fortified control values obtained at the three test sites. The author chose to correct all urine field fortification recovery values with the mean recovery of concurrently analyzed 4-NP in freshly fortified control samples. Corrected recoveries for 4-nitrophenol averaged: (1) Greenville, MS: *100 percent* ± 11 (range = 79 to 123 percent; n=21); (2) Gila Bend, AZ: *104 percent* ± 8.3 (range = 88 to 118 percent; n=27); and (3) Harquahala Valley, AZ: *110 percent* ± 13 (range = 94 to 148 percent; n=27). Tables 5a, 5b, and 17 (Pages 188-191 and 211) of the study report identify individual recovery values. Since the overall percent field recovery values and the individual fortification levels were all above 90 percent recovery for all three sites, the 4-nitrophenol urine data was not corrected for field recovery.

Table 1. Field Fortified Recovery Values for 4-Nitrophenol in Urine Samples.[a]

Test Site	4-Nitrophenol Fortification Level	Percent Recovery
Greenville, MS	2 µg/L (N=6)	92.3 ± 10.8
	10 µg/L (N=12)	104.7 ± 9.6
	100 µg/L (N=3)	99.3 ± 6.5
	Overall Average (N= 21)	100.4 ± 10.7
Gila Bend, AZ	2 µg/L (N=9)	111.9 ± 4.4
	10 µg/L (N=9)	103.1 ± 7.0
	100 µg/L (N=9)	96.0 ± 3.9
	Overall Average (N=27)	103.7 ± 8.3
Harquahala, AZ	2 µg/L (N=9)	120.4 ± 16.0
	10 µg/L (N=9)	109.4 ± 6.8
	100 µg/L (N=9)	101.6 ± 4.5
	Overall Average (N=27)	110.5 ± 12.7

[a] Corrected for average procedural (laboratory) recovery within the analytical set.

2. Inhalation Exposure Samples

OVS tubes were fortified with methyl parathion reference standard at 0.02 and 10 µg/tube. A second set of OVS tubes were fortified at the same levels and used as travel spikes. The fortification samples were placed directly on top of the glass fiber filter and allowed to dry before the pumps were started. The pumps were set to draw at approximately 2 liters per minute

and allowed to run for the approximate amount of time required to collect one exposure replicate. 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 entire exposure monitoring period ("exposure"). The field fortification sets were submitted with the field samples and handled in the same manner as the actual field samples. No field fortifications were conducted with 4-NP.

All reported field fortification recoveries were corrected for the mean recovery of concurrently analyzed methyl parathion freshly fortified control samples. Overall recoveries for both the "travel" (fortified and immediately frozen) field fortifications and "exposed" fortifications combined yielded a mean and standard deviation of 96 percent ± 6.8 (n=12) and ranged from 89 to 113 percent.

Storage Stability Recovery

Stability of 4-NP in urine (conducted on urine contained in Urisafe collection containers, stored on wet ice) during the 12-hour collection period (24-hour for prescreen samples) of each sampling interval up to 48 hours (to allow for sample volume measurement and subsampling, prior to freezing) was determined in another 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 18 hours).

Residues of 4-NP were found to be stable in urine during frozen storage for up to 31 days (as determined in study No. KP-2000-02, MRID 45204701). The stability results reported in that study support the period of frozen storage pertinent to this study (up to 24 days).

Calculations

Statistical analysis of the residue data was limited to arithmetic and geometric means, median, standard deviation, and regression analysis of arithmetic mean values using first order kinetics. Transformation of urine sample data included converting the gross residue (total μg 4-NP/sample) to net residue by first averaging each workers 4-NP residues from samples collected pre-exposure (2 days before exposure) and then subtracting that average from 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), to μg 4-NP per liter of urine produced (by dividing the gross and net residue by the liters of urine produced by the worker each day), and to μg 4-NP /70 kg body weight by multiplying the net 4-NP residue/kg body weight by 70. (See Tables 2, 3, and 4, below.) Since the overall percent field recovery values and the individual fortification levels were all above 90 percent recovery for all three sites, the 4-nitrophenol urine data was not corrected for field recovery.

Results

Normalized net urinary 4-NP levels varied across the three data-sets. For the two sites where mixer/loaders wore the personal protective equipment (PPE) required by the product label, the geometric mean urinary 4-NP values rose to more than twice the baseline levels at the Mississippi site and up to seven times the baseline levels at the Gila Bend, AZ site on the day of exposure. Thereafter, urinary excretion of 4-NP declined to below baseline levels by 72 hours after exposure. At the third site, where additional PPE was worn, neither the arithmetic nor the geometric mean urinary 4-NP values exceeded baseline levels on the day of exposure, and were either very low or near zero (significantly lower than even pre-screen or baseline values) thereafter. (See Tables 2, 3 and 4).

Total net normalized 4-NP excreted (expressed as μg/ 70 kg body weight) from Day 0 through 84 hours after exposure ranged as follows: (1) Greenville, MS (employing current label PPE): 8.32 to 26.54 μg/kg; (2) Gila Bend, AZ (employing current label PPE): 31.07 to 55.62 μg/kg; and (3) Harquahala Valley, AZ (employing additional PPE): 1.26 to 11.54. (See Table 5).

Creatinine measured in each mixer/loader's daily urine sample were fairly consistent across the 5.5 day monitoring period. However, creatinine levels were very low on the day after exposure in one worker at the Greenville, MS site, relative to the other workers. The worker, subject #3, had a creatinine level of 0.508 Although analytical results were reported as both total and net 4-NP per liter, results were not reported as creatinine-corrected urinary concentrations (µg/ gram creatinine) as requested by the Agency in its review of the proposed study protocol dated November 1, 1999.

The author assumed first-order kinetics to predict 4-NP dissipation in urine. Residue data collected between 0 and 72 hours from the Greenville, MS and Harquahala, AZ data-sets and from 0 to 84 hours for the Gila Bend, AZ data sets were analyzed using Microsoft® 's Excel 97 software. Regression analysis for 4-NP (net μg/kg) predicted the following half lives: (1) Greenville MS: 17.7 hours ($R^2 = 0.8659$); (2) Gila Bend AZ: 13.8 hours ($R^2 = 0.9508$); and (3) Harquahala Valley AZ: 16.5 hours ($R^2 = 0.1904$).

Inhalation exposure monitoring results from 5 workers at the Gila Bend, Arizona site ranged from <0.05 to 0.195 μg/sample for methyl parathion to no detectable residues for 4-NP. For three of the five subjects monitored, the OVS air monitoring tubes had no detectable residues for methyl parathion. Two of the five subjects had residues of 0.0822 and 0.0195 μg/front section and only one subject had 1.25 μg for the back section of the air tube for methyl parathion. According to the authors, the results indicate that inhalation exposure was minimal during mixing/loading activities.

Table 2. 4-Nitrophenol Residues in Mixer/Loaders' Post Exposure Urine Samples - Greenville, MS

Parameters	#Rep	Arith. Mean	Std. Dev.	Geo. Mean
	Sampling Interval = 0-24 hours			
Gross 4-NP (μg/L)	5	7.524	5.171	5.755
Net 4-NP (μg/L)	5	6.045	4.640	4.089
Gross 4-NP (total μg)	5	14.696	6.768	13.471
Net 4-NP (total μg)	5	10.437	5.787	9.176
Gross 4-NP (μg/kg weight)	5	0.175	0.083	0.162
Net 4-NP (μg/kg weight)	5	0.124	0.072	0.110
Net 4-NP (μg/70 kg weight)	5	8.671	5.043	7.705
Creatinine (g/24 hr)	5	1.876	0.578	1.812
	Sampling Interval = 24-48 hours			
Gross 4-NP (μg/L)	5	3.616	1.850	3.189
Net 4-NP (μg/L)	5	2.137	1.763	1.609
Gross 4-NP (total μg)	5	12.108	8.528	10.280
Net 4-NP (total μg)	5	7.849	8.702	5.300
Gross 4-NP (μg/kg weight)	5	0.143	0.101	0.123
Net 4-NP (μg/kg weight)	5	0.092	0.103	0.064
Net 4-NP (μg/70 kg weight)	5	6.464	7.238	4.450
Creatinine (g/24 hr)	5	2.258	1.088	1.908
	Sampling Interval = 48-72 hours			
Gross 4-NP (μg/L)	5	2.858	2.330	2.223
Net 4-NP (μg/L)	5	1.388	1.967	--
Gross 4-NP (total μg)	5	5.630	1.250	5.521
Net 4-NP (total μg)	5	1.587	0.905	--
Gross 4-NP (μg/kg weight)	5	0.067	0.011	0.066
Net 4-NP (μg/kg weight)	5	0.019	0.011	--
Net 4-NP (μg/70 kg weight)	5	1.317	0.768	--
Creatinine (g/24 hr)	5	2.418	0.999	2.266
	Sampling Interval = 72-84 hours			
Gross 4-NP (μg/L)	5	3.296	2.852	2.513
Net 4-NP (μg/L)	5	1.817	2.564	0.596
Gross 4-NP (total μg)	5	2.770	1.157	2.561
Net 4-NP (total μg)	5	0.000	0.000	--
Gross 4-NP (μg/kg weight)	5	0.033	0.015	0.031
Net 4-NP (μg/kg weight)	5	0.000	0.000	--
Net 4-NP (μg/70 kg weight)	5	0.000	0.000	--
Creatinine (g/24 hr)	5	1.306	0.541	1.199

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 = Gross 4-NP - (Average 4-NP found in samples collected at -2 and -1 Day)

Note: If the calculation of a net 4-NP value resulted in a negative number, then the result is expressed as 0.000. The geometric mean is shown as (--) if a zero was a data point in the calculation. Calculations by EXCEL 97 spreadsheet software.

Table 3. 4-Nitrophenol Residues in Mixer/Loaders' Post Exposure Urine Samples - Gila Bend, AZ

Parameters	#Rep	Arith. Mean	Std. Dev.	Geo. Mean
	Sampling Interval = 0-24 hours			
Gross 4-NP (μg/L)	5	20.02	6.843	19.030
Net 4-NP (μg/L)	5	18.058	6.745	16.966
Gross 4-NP (total μg)	5	37.440	13.810	35.204
Net 4-NP (total μg)	5	33.349	12.998	31.115
Gross 4-NP (μg/kg weight)	5	0.449	0.102	0.440
Net 4-NP (μg/kg weight)	5	0.399	0.100	0.389
Net 4-NP (μg/70 kg weight)	5	27.916	7.004	27.229
Creatinine (g/24 hr)	5	1.914	0.472	1.874
	Sampling Interval = 24-48 hours			
Gross 4-NP (μg/L)	5	6.990	1.085	6.923
Net 4-NP (μg/L)	5	5.028	0.675	4.990
Gross 4-NP (total μg)	5	13.144	3.923	12.687
Net 4-NP (total μg)	5	9.053	2.998	8.660
Gross 4-NP (μg/kg weight)	5	0.160	0.025	0.159
Net 4-NP (μg/kg weight)	5	0.110	0.020	0.108
Net 4-NP (μg/70 kg weight)	5	7.686	1.405	7.578
Creatinine (g/24 hr)	5	2.196	0.686	2.119
	Sampling Interval = 48-72 hours			
Gross 4-NP (μg/L)	5	2.432	0.683	2.354
Net 4-NP (μg/L)	5	0.518	0.527	--
Gross 4-NP (total μg)	5	8.904	3.469	8.251
Net 4-NP (total μg)	5	4.813	2.647	3.998
Gross 4-NP (μg/kg weight)	5	0.107	0.030	0.103
Net 4-NP (μg/kg weight)	5	0.056	0.028	0.050
Net 4-NP (μg/70 kg weight)	5	3.946	1.965	3.499
Creatinine (g/24 hr)	5	1.994	0.857	1.849
	Sampling Interval = 72-84 hours			
Gross 4-NP (μg/L)	5	4.766	1.856	4.450
Net 4-NP (μg/L)	5	2.804	2.197	1.818
Gross 4-NP (total μg)	5	4.724	0.723	4.682
Net 4-NP (total μg)	5	0.981	1.212	--
Gross 4-NP (μg/kg weight)	5	0.062	0.022	0.059
Net 4-NP (μg/kg weight)	5	0.015	0.019	--
Net 4-NP (μg/70 kg weight)	5	1.062	1.363	--
Creatinine (g/24 hr)	5	0.997	0.280	0.961

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 = Gross 4-NP - (Average 4-NP found in samples collected at -2 and -1 Day)

Note: If the calculation of a net 4-NP value resulted in a negative number, then the result is expressed as 0.000. The geometric mean is shown as (--) if a zero was a data point in the calculation. Calculations by EXCEL 97 spreadsheet software.

Table 4. 4-Nitrophenol Residues in Mixer/Loaders' Urine Samples - Harquahala, AZ

Parameters	#Rep	Arith. Mean	Std. Dev.	Geo. Mean
	Sampling Interval = 0-24 hours			
Gross 4-NP (μg/L)	5	5.304	1.573	5.110
Net 4-NP (μg/L)	5	3.328	1.017	3.206
Gross 4-NP (total μg)	5	11.678	2.743	11.416
Net 4-NP (total μg)	5	5.537	3.951	4.398
Gross 4-NP (μg/kg weight)	5	0.155	0.042	0.150
Net 4-NP (μg/kg weight)	5	0.075	0.054	0.058
Net 4-NP (μg/70 kg weight)	5	5.216	3.791	4.048
Creatinine (g/24 hr)	5	2.132	0.305	2.115
	Sampling Interval = 24-48 hours			
Gross 4-NP (μg/L)	5	1.211	0.379	1.158
Net 4-NP (μg/L)	5	0.000	0.000	--
Gross 4-NP (total μg)	5	4.912	1.875	4.673
Net 4-NP (total μg)	5	0.000	0.000	--
Gross 4-NP (μg/kg weight)	5	0.065	0.024	0.061
Net 4-NP (μg/kg weight)	5	0.000	0.000	--
Net 4-NP (μg/70 kg weight)	5	0.000	0.000	--
Creatinine (g/24 hr)	5	1.920	0.657	1.842
	Sampling Interval = 48-72 hours			
Gross 4-NP (μg/L)	5	1.322	0.250	1.304
Net 4-NP (μg/L)	5	0.088	0.130	--
Gross 4-NP (total μg)	5	5.960	1.658	5.773
Net 4-NP (total μg)	5	0.735	1.644	--
Gross 4-NP (μg/kg weight)	5	0.079	0.024	1.076
Net 4-NP (μg/kg weight)	5	0.010	0.023	--
Net 4-NP (μg/70 kg weight)	5	0.729	1.631	--
Creatinine (g/24 hr)	5	2.014	0.441	1.975
	Sampling Interval = 72-84 hours			
Gross 4-NP (μg/L)	5	1.494	0.486	1.418
Net 4-NP (μg/L)	5	0.128	0.285	--
Gross 4-NP (total μg)	5	3.056	1.042	2.904
Net 4-NP (total μg)	5	0.000	0.000	--
Gross 4-NP (μg/kg weight)	5	0.041	0.014	0.038
Net 4-NP (μg/kg weight)	5	0.000	0.000	--
Net 4-NP (μg/70 kg weight)	5	0.000	0.000	--
Creatinine (g/24 hr)	5	0.939	0.298	0.904

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 = Gross 4-NP - (Average 4-NP found in samples collected at -2 and -1 Day)

Note: If the calculation of a net 4-NP value resulted in a negative number, then the result is expressed as 0.000. The geometric mean is shown as (--) if a zero was a data point in the calculation. Calculations by EXCEL 97 spreadsheet software.

Table 5. Total Net 4-Nitrophenol Exposure in Individual Mixer/Loader

Worker Rep/ID	PPE Worn	Test Site	Total Net 4-NP µg/ 70 kg body wt. (0 to 84 hours)
1	Long sleeved shirt, long pants, coveralls, socks, rubber boots, goggles, dust/mist respirator, and neoprene gloves.	Greenville, MS	21.20
2		Greenville, MS	12.02
3		Greenville, MS	8.32
4		Greenville, MS	26.54
5		Greenville, MS	14.17
6		Gila Bend, AZ	37.65
7		Gila Bend, AZ	31.07
8		Gila Bend, AZ	46.70
9		Gila Bend, AZ	32.01
10		Gila Bend, AZ	55.62
12	Long sleeved shirt, long pants, coveralls, socks, rubber boots, **face shield**, dust/mist respirator, **nitrile** gloves, **chemical resistant apron**, and **Tyvek rain type hat**.	Harquahala Val., AZ	11.54
13		Harquahala Val., AZ	10.39
14		Harquahala Val., AZ	3.67
15		Harquahala Val., AZ	2.87
16		Harquahala Val., AZ	1.26

Footnotes:

Net 4-NP = Gross 4-NP - (Average 4-NP found in samples collected at -2 and -1 Day)

Bolded PPE are different from or in addition to the label PPE worn at the other two sites.

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 A: 875.1300, Applicator Inhalation Exposure -- Outdoor, Group A: 875.1500, Biological Monitoring, and Part C: Quality Assurance/Quality Control.

Guideline 875.1300

- *For outdoor exposure monitoring at least five replicates at each of at least three sites for each job function (with the exception of pilots) should be monitored.* This criterion was met. Five replicates were monitored at each site.

- *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 94 ± 2.8 percent (N=12).

- *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 ± 6.8 percent (N=12).

- *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 met. Field fortified samples contained 0.2 or 10 μg/tube; most of the time front and back sections of the XAD sorbent were analyzed separately. The LOQ was 0.05 μg/tube.

- *The intake tube of any pump-powered sampler unit should be positioned so that the opening is downward... and as near as possible to the nose level of the test subject.* This criterion was met.

- *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. A short term storage stability test was conducted and the results were reported in the study report. Also, a long term storage stability study has been submitted to EPA (MRID# 443038-05).

- *A storage stability study should include three blanks, and three each low-level and high-level fortifications in the expected range of the field samples for each storage interval tested.* This criterion was met.

- *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.* This criterion was met.

- *Typical end use product of the active ingredient tested.* This criterion was met.

- *Selected sites and seasonal timing of monitoring must be appropriate to the activity.* This criterion was met.

- *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 replicates per activity and preferably 5 replicates (i.e., individuals) for each of three monitoring periods.* This criterion was met. There were five mixer/loaders per test site location.

- *Field data should be corrected if any appropriate recovery is less than 90 percent.* This criterion was met. The overall field recoveries and individual field recoveries for each site were above 90 percent and therefore the data were not corrected for field recoveries.

- *The exposure monitoring period must be of sufficient length to have reasonable delectability of residues in urine, and be representative of a normal activity.* This criterion was met. Each volunteer mixed and loaded sufficient test substance to support aerial application to 350 acres. Biomonitoring samples were collected from 48 hours before through 84 hours after exposure.

- *Dermal and/or inhalation exposure must be monitored by validated methodologies. Biological monitoring is consistent with and supported by pharmacokinetic data accepted by the Agency.* These criteria were met. Limited air monitoring (i.e. 5 replicates at one test site) was conducted at one site to "help define the route of exposure." No dermal exposure monitoring was conducted. Justification for collection of urinary 4-NP samples was presented in a separate study, *"Justification for Use of Urinary Excretion of 4-Nitrophenol for Biomonitoring of Worker Exposure to Methyl Parathion," MRID #449744-01.* This study was not included in the Study Report.

- *Quantity of active ingredient handled and duration of monitoring period reported for each replicate.* This criterion was met.

- *Protective clothing worn by each study participant and location of dosimeters reported.* This criterion was met.

- *Baseline urine samples should be collected at least one day before participating in the post-application exposure monitoring activities and 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.* 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 84 hours after the exposure began. Kinetics observed in the field data indicated a rapid drop off of 4-nitrophenol concentrations within this time period.

- *The 24-hour 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.

- *All urine samples should be logged in at the time of collection. Material used to construct containers used for urine collection should not interfere with (e.g., absorb) the analytes of interest. Light sensitive analytes should be protected from degradation.* It is

not known whether these criteria were met. All urine samples were logged in, however, the other issues were not discussed in the Study Report.

- *Specific gravity, as another measure of 24-hour sample completeness, should be performed as soon after collection as possible (and before sample storage).* This criterion was met.

- *All urine samples should be frozen after the specific gravity is measured.* This criterion was met.

- *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.* This criterion was not met. No formal discussion of activities performed by subjects within the last two weeks prior to biomonitoring was provided. The test subjects were prescreened up to 3 weeks prior to exposure monitoring. Only subjects with the lowest PNP background were selected.

- *Creatinine levels should be determined as a way of qualitatively monitoring completeness of urine collection samples.* This criterion was met.

- *Level of detection and level of quantitation defined.* This criterion was met.

- *Storage of samples consistent with storage stability data.* This criterion was met.

- *Efficiency of extraction in laboratory provided as mean plus or minus one standard deviation. Lower 95 percent confidence limit is not less than 70 percent based on a minimum of seven replications per fortification level or prior Agency approval of extraction methodology provided.* This criterion was met. However, concurrent laboratory and fortified field controls were found to have a great degree of variance. The field fortification recoveries were corrected for the mean recovery of concurrently analyzed methyl parathion freshly fortified laboratory control samples.

- *At least one field fortification sample per worker per monitoring period per fortification level for each matrix. At least one field blank per worker per monitoring period for each matrix.* This criterion was met.