UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND
TOXIC SUBSTANCES

September 5, 2001

Memorandum

SUBJECT: Review of *Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Sweet Corn Hand-Harvesting Following Application of PENNCAP-M® Microencapsulated Insecticide* (MRID No. 452001-01).

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)

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

DP Barcode: D270804

Pesticide Chemical Codes: 053501

EPA MRID Numbers: 452001-01

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 February

12, 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 cotton meet most of the criteria specified in the U.S. Environmental Protection Agency's (US EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines, 875.2600, Biomonitoring Data. The data will be considered in future methyl parathion REDs.

Summary

The purpose of this study was to quantify potential worker exposure due to hand-harvesting of sweet corn following four treatments of the crop with the restricted use, organophosphate insecticide methyl parathion. All applications were made aerially over an eleven day period. PENNCAP-M® Microencapsulated Insecticide was applied at 0.75 lbs active ingredient (ai)/acre, which is less than the maximum label application rate (i.e., 1.0 lbs. ai/A). The insecticide was applied at 5 gallons/acre. The minimum application volume referenced on the product label is 2 gallons/acre.

Four days after the last PENNCAP-M® application, sixteen subjects harvested sweet corn from a 13 Acre test plot during a single work period, which lasted about 5.6 hours (in-field). The test plot was located near Stuart, FL (Martin County). While hand harvesting sweet corn, study subjects wore identical, new clothing. Twenty-four hour urine samples were collected from each worker beginning 2 days prior to hand-harvesting, and for 2 days after hand-harvesting. The workers were housed in a hotel during this period, leaving it only to perform hand-harvesting on the day of exposure and to eat meals. A total of 306 urine samples (i.e., 90 field urine samples and 216 field control urine samples) were analyzed for metabolites of methyl parathion, 4-nitrophenol and its sulfate and glucuronide conjugates. The 90 field samples were also analyzed for creatinine content.

In general, on the day of exposure to treated sweet corn, the average 4-nitrophenol concentration in urine was more than 10 times baseline values. These levels declined quickly on the following day, and returned to baseline values by Day 2 after exposure. On the day of exposure, the range of 4-nitrophenol concentrations was 25.1 to 137 µg/L for 15 of 16 samples; the highest value found was somewhat outside this range (i.e., Subject #1 - 229.1 µg/L).

Conclusions

The study followed the OPPTS Series 875 Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines 875.2600, and Part C & D in most respects. The following issues of potential concern were identified:

C The spray application was not done at the highest label rate and lowest label dilution as required in the guidelines. Methyl parathion was applied four times at a single rate of 0.75 lbs ai/A to the test site. The maximum label rate was 1.0 lbs. ai/A. The application volume was 5 gallons/acre, and the label recommended minimum was 2 gallons/acre.

C 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*." There was only one monitoring period. Also, the study was conducted at a single location, instead of the preferred 3 locations. Two other sites were tested for DFR residues on sweet corn, one in New York and one in California. Considering that Florida has the warmest and wettest climate of the three possible locations, it is not the worst-case location for residue dissipation. The other two sites tested had at least 100 times more residue on the day of the activity (day 4 or 5) than the Florida site. The dislodgeable residues found on the fourth day after the final application at the Florida site were extremely low at 3.6 nanograms/cm^2. However, 16 individuals were monitored at that site.

- Pre-screening, baseline and 2^{nd} day after exposure urine concentrations for one worker, Subject #8, showed consistently higher 4-nitrophenol values in his urine than all the others. The worker's 4-nitrophenol levels at prescreening, baseline and the 2^{nd} day after exposure were 8, 5 and 3 times higher than the average levels on that respective day. The 4-nitrophenol levels were also higher on second day after exposure than the first day after exposure.

- Creatinine levels were very low on the day of exposure in three workers, relative to the other workers. The three workers, subjects #1, #15, and #17, had creatinine levels of 0.396, 0.390 and 0.705 g/24hrs, respectively.

MEMORANDUM

TO: Renee Sandvig cc: 1000.001.01
Margarita Collantes

FROM: Diane Forrest/Patricia Wood

DATE: February 12, 2001

SUBJECT: Review of *Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Sweet Corn Hand-Harvesting Following Application of PENNCAP-M® Microencapsulated Insecticide* (MRID No. 452001-01)

This report reviews *Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Sweet Corn Hand-Harvesting Following Application of PENNCAP-M®,* Microencapsulated Insecticide submitted in support of re-registration requirements for the insecticide active ingredient methyl parathion. The requirements for this study are specified by the U.S. Environmental Protection Agency (US-EPA) in OPPTS Series 875 Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines 875.2600, and Parts C & D. The following information may be used to identify the Study:

Title:	*Biomonitoring Assessment of Worker Exposure to Methyl Parathion During Sweet Corn Hand-Harvesting Following Application of Penncap-M®,* Microencapsulated Insecticide 293 pages
Sponsor:	Cerexagri, Inc. (formerly Elf Atochem North America, Inc.) Agrichemicals Division 2000 Market Street, 21st Floor Philadelphia, PA 19103-3222
Field Phase:	1) W. Thomas Minter (Principal Field Investigator) Florida Pesticide Research, Inc., Oviedo FL 2) Raymond E. Dyson (Aerial Applicator) Southeastern Aerial Crop Service
Analytical Facility:	Richard Reed, III and Gary L. Westberg (Author of Analytical Report) Morse Laboratories, Inc. 1525 Fulton Avenue Sacramento, CA 95825
Author/Study Director and Testing Facility:	Tommy R. Willard American Agricultural Services, Inc. 404 E. Chatham Street Cary, NC 27512
Report Date:	August 23, 2000
Identifying Codes:	MRID No. 452001-01; Study No. KP-99-17; Morse Project No. ML00-0851-ATO; Draft Protocol MRID No. 450017-01

EXECUTIVE SUMMARY

The purpose of this study was to quantify potential worker exposure due to hand-harvesting of sweet corn following four treatments of the crop with the restricted use, organophosphate insecticide methyl parathion. All applications were made aerially over an eleven day period. PENNCAP-M® Microencapsulated Insecticide was applied at 0.75 lbs active ingredient (ai)/Acre, which is less than the maximum label application rate (i.e., 1.0 lbs. ai/A). The insecticide was applied at 5 gallons/acre. The minimum application volume referenced on the product label is 2 gallons/acre.

Four days after the last PENNCAP-M® application, sixteen subjects harvested sweet corn from a 13 Acre test plot during a single work period, which lasted about 5.6 hours (in-field). While hand harvesting sweet corn, study subjects wore identical, new clothing: long-sleeved shirts, undershirt, long pants, socks and underwear. All wore closed shoes, some also wore hats, but none wore gloves. Twenty-four hour urine samples were collected from each worker beginning 2 days prior to hand-harvesting, and for 2 days after hand-harvesting. The workers were housed in a hotel during this period, leaving it only to perform hand-harvesting on the day of exposure and to eat meals. A total of 306 urine samples (i.e., 90 field urine samples and 216 field control urine samples) were analyzed for metabolites of methyl parathion, 4-nitrophenol and its sulfate and glucuronide conjugates. [The conjugates were hydrolyzed by the analytical method and reported as 4-nitrophenol equivalent.] The 90 field samples were also analyzed for creatinine content.

In general, on the day of exposure to treated sweet corn, the average 4-nitrophenol concentration in urine was more than 10 times baseline values. These levels declined quickly on the following day, and returned to baseline values by Day 2 after exposure. On the day of exposure, the range of 4-nitrophenol concentrations was 25.1 to 137 µg/L for 15 of 16 samples; the highest value found was somewhat outside this range (i.e., Subject #1 - 229.1 µg/L).

The study followed the OPPTS Series 875 Occupational and Residential Exposure Test Guidelines, Group B: Postapplication Exposure Monitoring Test Guidelines 875.2600, and Part C & D in most respects. The following issues of potential concern were identified:

- The spray application was not done at the highest label rate and lowest label dilution as required in the guidelines. Methyl parathion was applied four times at a single rate of 0.75 lbs ai/A to the test site. The maximum label rate was 1.0 lbs. ai/A. The application volume was 5 gallons/acre, and the label recommended minimum was 2 gallons/acre.

- 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*." There was only one monitoring period. Also, the study was conducted at a single location, instead of the preferred 3 locations. Two other sites were tested for DFR residues on sweet corn, one in New York and one in California. Considering that Florida has the warmest

and wettest climate of the three possible locations, it is not the worst-case location for residue dissipation. The other two sites tested had at least 100 times more residue on the day of the activity (day 4 or 5) than the Florida site. The dislodgeable residues found on the fourth day after the final application at the Florida site were extremely low at 3.6 nanograms/cm^2. However, 16 individuals were monitored at that site.

- Pre-screening, baseline and 2nd day after exposure urine concentrations for one worker, Subject #8, showed consistently higher 4-nitrophenol values in his urine than all the others. Subject #8 had 4-nitrophenol levels at prescreening, baseline and the 2nd day after exposure that were 8, 5 and 3 times higher than the average levels on that day, respectively. The 4-nitrophenol levels were also higher on second day after exposure than the first day after exposure.

- Creatinine levels were very low on the day of exposure in three workers, relative to the other workers. The three workers, subjects #1, #15, and #17, had creatinine levels of 0.396, 0.390 and 0.705 g/24hrs, respectively.

C The spray equipment was calibrated before the first application, but was not calibrated prior to the other applications. Although tank mix samples were collected, the samples were not analyzed.

STUDY REVIEW

Study Background

The purpose of this study was to quantify potential worker exposure due to hand harvesting sweet corn treated with 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 21.1 percent product in PENNCAP-M® Microencapsulated Insecticide. Four aerial applications were made over an 11 day period. A single episode of hand harvesting was monitored four days after the last application, when the corn was over six feet high.

In this study, methyl parathion exposure was quantified by measuring 4-nitrophenol and its sulfate and glucuronide conjugates in urine samples (the analytical method hydrolyzes these conjugates to 4-nitrophenol equivalents).

Study Subjects

The study subjects were "healthy Hispanic males ranging 59 to 67.5 inches in height and 110 to 157 pounds (50 to 71 kg) in weight with 2 to 10 years of experience as agricultural laborers. All

workers read and signed Informed Consent forms (Spanish translation). The workers were sequestered in a hotel beginning on the morning of 3/28/00 (2 days prior to exposure)... [They] remained in the hotel (except to eat meals) during the entire monitoring period except on the day of exposure (for sweet corn harvesting) on 3/30/00 until they were released on the morning of 4/2/00." The ages of the subjects were not provided in the Study Report.

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 page 268 of the Study Report for a complete list).

Protective Clothing and Work Practices

While hand harvesting sweet corn, study subjects wore identical, new clothing provided by the study coordinator. This consisted of: long-sleeved shirts, undershirt, long pants, socks and underwear. All subjects wore closed shoes, some subjects wore hats, but none wore protective gloves.

Test Site

The test site was located near Stuart, FL (Martin County). The area of the treated plot was approximately 12.67 Acres (i.e., 552 feet wide and 1,000 feet long). The untreated control plot (area unknown) was located about 1 mile from the treated plot, across two dirt roads and an irrigation ditch. [Diagrams can be found on pages 68 and 69 of the Study Report.]

The treated plot consisted of six blocks separated by irrigation ditches, each of which contained 30 rows of sweet corn, spaced 32 inches apart. The soil was sandy. The sweet corn crop (variety *Vail*) had been planted on December 30, 1999. The sweet corn was between 72 inches and 84 inches tall by the time of the last application.

Pesticide Use History

Previously, sweet corn and cucumbers had been grown in rotation on this test plot in 1998 and 1999. Information on pesticides and application rates previously used was reported for the previous two years. The following pesticides had been applied in the past: Dual®, Curbit®, Pounce® 1.5 G, Manzate®, Bravo® 720, and Lannate®. During the study season, seed treatments had been used, and fertilizers were applied a number of times. The following pesticides (application rates unknown) were used prior to the monitoring period: Counter®, Pounce® Bait, and Lannate®.

Materials and Application Methodology

A copy of the product label for PENNCAP-M® Microencapsulated Insecticide [EPA Reg. No. 4581-393] was provided in the Study Report. The PENNCAP-M® contained 20.9 percent methyl parathion and related isomers at 2 lbs. ai/gallon. PENNCAP-M® is a flowable formulation consisting of a water suspension of polymeric-type microcapsules containing the active ingredient. Both the worker reentry time and the preharvest intervals are 4 days (in areas where average annual rainfall is equal to or greater than 25 inches a year, as is the case in Florida). The label rates listed for sweet corn range between 1 and 4 pints/acre (i.e. between 0.5 and 1.0 lbs. ai/A). The target application rate in this study was 0.75 lbs. ai/A.

Four applications were made before exposure monitoring of the hand harvesting operation began. The first three were made 3 days apart, and the last one was made 4 days after the third[1]. The last application was 4 days prior to harvesting. Applications were made using an Air Tractor™ Model AT-602 airplane [ID#N5202X], flying at 155 mph. Ten Micronaire™ AV-3000 nozzles spaced 48 inches apart were used, resulting in a swath width of 85 feet. No overhead irrigation was used. Ditch irrigation was used instead.

The spray equipment was calibrated before the first application, but was not calibrated before the rest of the applications were made. The Study Report states that the airplane carried exactly 67 gallons for each application and used exactly 62 gallons each time.

Work Performed

Sixteen study subjects hand harvested sweet corn by "walking through the field and breaking off the whole ear (unshucked) and tossing it into the collection bin on the packing train as it moved through the field. Work began at approximately 0700 hours and proceeded apparently uninterrupted until the entire treated plot was picked. Work finished at approximately 1240 hours (5.6 hours of in-field exposure)."

Environmental Conditions

On each application day, the following parameters were reported (see page 51 of the Study Report): application time, windspeed and direction, percent cloud cover, percent relative humidity, air temperature, soil temperature, general soil moisture conditions at the surface and subsurface, and foliage moisture conditions.

[1] Penncap® M was applied on: March 15, 18, 21, and 26, in year 2000.

Urine Sample Collection

Study subjects were provided every morning with pre-weighed and coded 3-Liter UriSafe™ urine collection containers and a cooler with blue icepacks. New blue icepacks were provided each evening. Filled UriSafe™ containers were collected the following morning. New coolers, fresh icepacks, and UriSafe™ containers were then provided for the next 24-hour period. Each day's sampling was transported to the field facility for processing and storage.

QA/QC

Sample Storage and Handling

Each day's urine sample was allowed to come to ambient temperature, acidified with hydrochloric acid, weighed, and the approximate volume recorded. The specific gravity was determined by weighing an aliquot of urine. Next, 100 mL aliquots of each acidified sample were placed into labeled amber HPDE bottles. Urine samples were stored frozen at the field facility (Florida Pesticide Research, Inc.) until shipment to Morse Laboratories, Inc. via Federal Express courier service on dry ice. The balance of all the urine samples was shipped to Elf Atochem N.A. via ACDS freezer truck for storage.

Sample History

Sample history information was provided from sample collection through sample analysis (see pages 64-66 and 108-112 of the Study Report). Field urine samples (N=97 samples) were stored from 8 to 30 days prior to analysis. Field-fortified samples (N=54 samples) were stored from 3 to 53 days prior to analysis. Field control samples (N=18 samples) were stored between 34 and 53 days.

Tank Mix Samples

Tank mix samples were collected. However, according to a Protocol Amendment 11 (see page 289 of the Study Report), they were not analyzed because analyses of the samples was not deemed necessary to meet the study objectives.

Analytical Methodology

1. Analysis of 4-Nitrophenol

A proprietary method was used, Morse Laboratories Inc.'s SOP# Meth-120, entitled "*Determination of 4-Nitrophenol in Urine*," Revision #3, dated April 28, 2000. Briefly summarizing the principle of the method, sodium bisulfate and concentrated HCl were added to 8 mL of urine. Acid hydrolysis was performed at 100EC. for 1 hour. A 4.5 mL aliquot of the hydrolyzate was extracted

into toluene. The volume of the extract was concentrated, and derivitized with MTBSTFA (N-(tert-Butyldimethylsilyl)-N-methyltrifluoroacetamide). The derivatized sample was further concentrated, and analyzed for the 4-nitrophenol tert-butyldimethylsilyl derivative using gas chromatography with mass selective detection. The retention time for this analyte was approximately 12.5 minutes. 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. Chromatographic peaks were reasonably sharp; traces tended to be crowded at low 4-nitrophenol levels.

2. Analysis of Creatinine

A proprietary method was used, Morse Laboratories Inc.'s Analytical Method No. Meth-111, entitled "*Quantitative Determination of Creatinine in Urine*," Original Revision, dated June, 1998. Briefly summarizing the principle of this colorimetric method, an aliquot of urine is reacted with an alkaline picric acid reagent in the presence of sodium borate to form an amber-colored creatinine-picrate complex. The concentration of creatinine in the sample is calculated against a known creatinine standard concentration based on absorbance of the resulting complex at 520 nm. The sensitivity of the method is 0.6 mg/dL based on instrument resolution of 0.01 absorbance units. Creatinine was reportedly stable in urine for 3 days at room temperature and for at least 5 days in the refrigerator.

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

For 4-nitrophenol and its conjugates, 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. For creatinine, the method sensitivity was 0.6 mg/dL based on instrument resolution of 0.01 absorbance units.

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 N.A. provided a specific procedure for compositing control urine from 12-hour urine samples to yield 24-hour samples (see page 210 of the Study Report). In the case of control urine obtained by Morse Laboratories from its own staff, compositing was carried out by combining all urine collected.

Concurrent Laboratory Recovery

Urine used for the preparation of concurrent (or procedural) laboratory controls came from 24-hour urine samples obtained "from Morse laboratory personnel and workers [who] were screened for use in the study as control samples for procedural quality controls..." Urine was used only if it contained less than the method LOQ (i.e., 1.0 µg/L), corrected for reagent blank values. Four fortification levels for 4-nitrophenol were chosen: 1 µg/L (N=29); 10 µg/L (N=13); 100 µg/L (N=14);

and 250 µg/L (n=1). Two fortification levels for the glucuronide conjugate were chosen: 2.27 µg/L (N=10) and 22.7 µg/L (N=19).

The overall concurrent (or procedural) laboratory recovery for 4-nitrophenol averaged 95 ± 13 percent (N=60), ranging from 61 to 124 percent. The overall concurrent laboratory recovery for 4-nitrophenol glucuronide conjugate averaged 88 ± 15 percent (N=29), ranging from 64 to 119 percent.

Fortified Field Recovery

Field-fortified samples were prepared three times, that is, on 3/30/00, 3/31/00 and 4/1/00 (i.e., the day study subjects entered the treated field, and the day of exposure and day after the workers had entered the field). The fortification levels were: 0, 2, 10 and 100 parts per billion 4-nitrophenol, and six samples were prepared at each level. No field-fortified recovery samples were prepared using either the glucuronide or the sulfate conjugates of 4-nitrophenol, or creatinine. The overall field fortified recovery averaged 96 ± 9.6 percent (N=54), ranging from 78 to 131 percent. Fortification levels chosen corresponded well to the range of 4-nitrophenol levels found in field data. All field fortification samples were corrected for average procedural (laboratory) recovery within the analytical set. See Table 1 for a summary of the field recoveries at each fortification level. The 4-nitrophenol biomonitoring data was not corrected for field recoveries since they were above 90 percent for all fortification levels.

These samples were prepared using control urine provided by Elf-Atochem. According to Protocol Amendment #1, this urine came from "previous methyl parathion worker exposure studies that has been analyzed for both 4-Nitrophenol (free and conjugated) and creatinine that is currently in freezer storage at Elf-Atochem."

Table 1. Summary of Field Fortification Recoveries*

Test Site	Fortification Level (µg/L)	Recovery* (percent)
Florida	2	101 ± 10.9 (N=18)
	10	96 ± 8.8 (N=18)
	100	92 ± 6.5 (N=18)
	Overall Average	96 ± 9.6 (N=54)

* Corrected for average procedural (laboratory) recovery within the analytical set.

Storage Stability Testing

Two storage stability tests were performed. First, the effect of storing urine samples in coolers was examined using the field fortified controls reviewed in the preceding section. Of the six field-fortified samples, three were "immediately placed in frozen storage" (referred to as "travelers" in the study), and "the other three were placed in a cooler with blue ice to mimic the storage conditions experienced by

the worker-generated urine samples." These latter samples were referred to as "exposed spikes." The latter were kept on blue ice for between 24 and 38.5 hours, then placed in freezer storage. [The longest interval urine samples were stored on blue ice was 36 hours.]

Results from this test yielded a mean of 95 ± 8.6 percent (N=27) for "travel" field-fortified samples (range = 81 to 119 percent). The mean for "exposed" field-fortified controls was 97 ± 11 percent (N=27), ranging from 78 and 131 percent. [These values were corrected for procedural recovery.]

Secondly, the analytical report presents results of a test in which 3 control urine samples were fortified with 10 µg/L 4-nitrophenol and stored in UriSafe™ containers on wet ice for 24 and 48 hours. When corrected for procedural recoveries of 102 percent at 24 hours and 83 percent at 48 hours, the results were that 105 percent and 100 percent recovery of 4-nitrophenol were obtained, at 24 and 48 hours, respectively.

Otherwise, the study author relied on the field-fortified controls for storage stability information. Field urine samples (N=97 samples) were stored from 8 to 30 days prior to analysis. Field-fortified samples (N=54 samples) were stored from 3 to 53 days prior to analysis. Field control samples (N=18 samples) were stored between 34 and 53 days. The analyte appears to have been stable in urine through cooler/freezer storage.

Calculations

General statistical calculations were limited to calculation of the mean, range, and standard deviation using SYSTAT®, version 8.0. Field data were typically corrected using the field blank, but were not corrected for laboratory or field-fortified recovery.

4-Nitrophenol Concentrations

Samples were analyzed in groups, each of which contained a reagent blank, a control sample, three fortified control samples (two containing 4-nitrophenol: 1 at the LOQ, and 1 at a higher level, plus 1 sample containing 4-nitrophenol glucuronide conjugate), and up to 10 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 dependent variables. Next, the concentration in a specific urine sample was calculated using the equation which appears on page 94 of the Study Report, adjusting for dilutions. All sample results were corrected using the appropriate reagent blank.

The study author noted that: "Calculation of [glucuronide] conjugate concentrations applies to the determination of their recoveries only. Both the fortified control samples and their respective control samples were calculated in the same manner..." This involved using, a molecular weight conversion

factor for the p-nitrophenol beta-d-glucuronide conjugate of 2.27, relative to the 4-nitrophenol value of 1.00.

Creatinine Calculations

The results of creatinine analyses were also analyzed in groups, each of which contained one fortified control sample, plus up to 16 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 99 of the Study Report. The amount (grams) of creatinine produced by a study subject in a 24 hour period was reported.

Results

In general, 4-nitrophenol concentrations in urine measured on the day of exposure to treated sweet corn rose to an average value of more than 16 times baseline values, ranging from 2 times to 47 times baseline levels on the day of exposure. The 4-nitrophenol levels declined quickly on the following day, and almost returned to baseline values by the second day after exposure. A regression analysis of the data submitted by the registrant showed a half-life of 0.5 day for 4-Nitrophenol. This calculation was based on 3 uncorrected arithmetic average data points. On the day of exposure, the range of 4-nitrophenol concentrations was 25.1 to 137 µg/L for 15 of 16 samples; the highest value found was somewhat outside this range (i.e., Subject #1 - 229.1 µg/L).

One anomaly was noted. Pre-screening, baseline and 2nd day after exposure urine concentrations for one worker, Subject #8, showed consistently higher 4-nitrophenol values in his urine than all the others. Subject #8 4-nitrophenol levels at prescreening, baseline and the 2nd day after exposure were 8, 5 and 3 times higher than the average levels on that day, respectively. The 4-nitrophenol levels were also higher on second day after exposure than the first day after exposure. Table 2 provides a summary of 4-nitrophenol residue data for Days 0, 1, and 2.

Creatinine levels measured in each day's urine sample from the study subjects were variable. Creatinine levels were very low on the day of exposure in three workers, relative to the other workers. The three workers, subjects #1, #15, and #17, had creatinine levels of 0.396, 0.390 and 0.705 g/24hrs, respectively. The 24-hr creatinine results are shown in Table 2. [Specific gravity and urine weight and volume measurements were made at the field test facility. These data may be found on pages 55 to 60 of the Study Report.]

Table 2. 4-NP Residues in Sweet Corn Hand-Harvester Urine Samples

Parameters	Sampling Interval = 0 Day			
	#Rep	Arith. Mean	Std. Dev.	Geo. Mean
Gross 4-NP (Fg/L)	16	79.6813	48.7872	69.2001
Net 4-NP (Fg/L)	16	74.6813	48.9438	64.2060
Gross 4-NP (total Fg)	16	56.6063	20.6663	53.6535
Net 4-NP (total Fg)	16	50.9963	21.9503	47.3252
Gross 4-NP (Fg/kg weight)	16	0.9124	0.3446	0.8596
Net 4-NP (Fg/kg weight)	16	0.8226	0.3608	0.7582
Net 4-NP (Fg/70 kg weight)	16	57.5820	25.2529	53.0772
Creatinine (g/24 hr)	16	1.4363	0.5238	1.2981
	Sampling Interval = +1 Day			
Gross 4-NP (Fg/L)	16	13.3825	5.0680	12.3983
Net 4-NP (Fg/L)	16	9.2045	5.2044	8.2602
Gross 4-NP (total Fg)	16	17.8063	5.5342	17.0173
Net 4-NP (total Fg)	16	12.7181	6.5277	11.9238
Gross 4-NP (Fg/kg weight)	16	0.2833	0.0835	0.2727
Net 4-NP (Fg/kg weight)	16	0.2011	0.0994	0.1921
Net 4-NP (Fg/70 kg weight)	16	14.0763	6.9563	13.4497
Creatinine (g/24 hr)	16	1.9044	0.3964	1.8648
	Sampling Interval = +2 Day			
Gross 4-NP (Fg/L)	16	7.2494	6.8736	5.6887
Net 4-NP (Fg/L)	16	2.8104	2.1131	2.5897
Gross 4-NP (total Fg)	16	8.8788	5.1006	7.9229
Net 4-NP (total Fg)	16	3.6134	2.8935	3.0321
Gross 4-NP (Fg/kg weight)	16	0.1407	0.0745	0.1269
Net 4-NP (Fg/kg weight)	16	0.0563	0.0434	0.0487
Net 4-NP (Fg/70 kg weight)	16	3.9408	3.0363	3.4077
Creatinine (g/24 hr)	16	1.8588	0.3476	1.8251

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)

Compliance Analysis

The itemized checklist below describes compliance with the major technical aspects of the relevant sections of the OPPTS Series 875 Postapplication Exposure Monitoring Test Guidelines Part B.

- *Typical end use product of the active ingredient used. Where metabolites, breakdown components, or contaminants of pesticide end-use products pose a potential toxicological concern, investigators may need to consider sampling for them on a case-by-case basis.* This criterion was met. This study monitored 4-nitrophenol in urine as a biomarker for methyl parathion exposure. A separate white paper [MRID 449744-01, dated November 18, 1999] documents the rationale for this choice.

- *Selected sites and seasonal timing of monitoring must be appropriate to the activity. The need for studies under different geographical/climatological sites should be considered.* This criterion was only <u>partially</u> met. The study was conducted in a single geographic location (i.e., near Stuart, FL). The seasonal timing appears to be appropriate to the activity monitored.

- *End use product applied by application method and equipment recommended for the crop. Application rate given should be at the least dilution and highest, label permitted, application rate. It is suggested that the product also be applied at a lower application rate. Where multiple applications are recommended, the minimum time interval between applications should be used.* This criterion was <u>not</u> met. Methyl parathion was applied four times each at a rate of 0.75 lbs ai/acre to the test site. The maximum label rate is 1.0 lbs. ai/A. The application volume was 5 gallons/acre, and the label recommended minimum was 2 gallons/acre. The product label does not limit the number of applications, or specify a minimum interval between applications.

- *Applications occurred at time of season that the end-use product is normally used to achieve intended pest control.* This criterion was met. The pesticide was applied to growing sweet corn, at 3-5 day intervals, up until the label-specified pre-harvest interval.

- *Meteorological conditions including temperature, wind speed, daily rainfall, and humidity provided for the duration of the study.* This criterion was met. On each application day, the following parameters were reported (see page 51 of the Study Report): application time, windspeed and direction, percent cloud cover, percent relative humidity, air temperature, soil temperature, general soil moisture conditions at the surface and subsurface, and foliage moisture conditions.

- *Storage stability, method efficiency (residue recovery), and limit of quantitation provided.* These criteria were met.

- *The Agency requires investigators to submit protocols for review purposes prior to the inception of the study*. This criterion was met.

- *Biological monitoring studies must be carried out concurrently with transferable residue studies.* This criterion was met. Dislodgeable foliar data were submitted to US EPA in a separate report.

- *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 not met. There was only one monitoring period. Also, the study was conducted at a single location, instead of the preferred 3 locations. Two other sites were tested for DFR residues on sweet corn, one in New York and one in California. Considering that Florida has the warmest and wettest climate of the three possible locations, it is not the worst-case location for residue dissipation. The other two sites tested had at least 100 times more residue on the day of the activity (day 4 or 5) than the Florida site. The dislodgeable residues found on the fourth day after the final application at the Florida site were extremely low at 3.6 nanograms/cm^2. However, 16 individuals were monitored at that site.

- *The exposure monitoring period must be of sufficient duration to have reasonable detectability of residues in urine, and be representative of a normal activity.* This criterion was met. The exposure episode lasted approximately 5.6 hours. Study subjects entered the treated test site 4 days after the final pesticide treatment. The product label specifies a reentry time of 4 days.

- *Monitoring should be conducted before residues have dissipated beyond the limit of quantitation.* This criterion not was met. The first analysis of the DFR residues from the Florida site showed the residues to be below the LOQ of 0.01 Fg/cm^2. After reanalysis under a different method yielding a lower LOQ of 0.001 Fg/cm^2, the residues on the day of the activity were found to be extremely low at 3.6 nanograms/cm^2.

- *Baseline urine samples should be collected at least one day before participating in the postapplication exposure monitoring activities and continue on the day of postapplication monitoring and for an appropriate time period after the activities have been completed, depending on the excretion kinetics of the compound.* These criteria were met. Pre-screen 24-hour urine samples were collected about 2 weeks before the exposure event. Baseline 24-hour urine samples were collected each day beginning 2 days before the exposure event, through the day of the exposure event, and for 2 days after the exposure event. 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. These issues were not discussed in the Study Report.

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

- *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 partially met. No formal discussion of activities performed by subjects within the last two weeks prior to biomonitoring was provided. However, the study protocol required that "each subject will have had no contact with the prohibited materials listed in Appendix 2 [see page 268 of the Study Review] during the 7 days prior to the day on which he is monitored. In addition, each subject will be sequestered at a hotel convenient to the test site(s) from 2 days prior to the exposure through 3 days after exposure. Finally, each subject will follow the list of personal activity recommendations provided in Appendix 2 from 7 days prior to the beginning of monitoring until the end of monitoring. Compliance with or deviation from these requirements will be documented for each worker."

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

- *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.