UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 5/22/2009

SUBJECT: **DRAFT Chlorpyrifos:** Data Evaluation Record Prepared for the June 2009 Human Studies Review Board Meeting for the Study "Worker Reentry Exposure to Chlorpyrifos In Citrus Treated with Lorsban* 4E Insecticide."

PC Code: 59101
MRID No.: 430627-01
Petition No.: NA
Assessment Type: NA
TXR No.: NA

DP Barcode: D364080
Registration No.: NA
Regulatory Action: Data Evaluation Record
Reregistration Case No.: NA
CAS No.: 2921-88-2

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This study supported the review by the FIFRA Scientific Advisory Panel (SAP) in September, 2008 of HED's evaluation of the toxicity profile for chlorpyrifos. It was included to help demonstrate ways that epidemiology data and data from controlled dosing studies can be linked in the chlorpyrifos risk assessment. The SAP recommended that the Agency refer the pertinent elements of this study to the Human Studies Review Board for their recommendations before deciding to rely on it.

This DER focuses on the elements of the study relevant to the current reassessment of chlorpyrifos toxicity—i.e., on the calculation of absorbed dose in exposed workers based on urinary levels of 3,5,6-trichloro-2-pyridinol (TCP), a recognized metabolite of chlorpyrifos, and on the direct measurement of acetyl cholinesterase inhibition in the same workers.

This study quantified exposures of chlorpyrifos to fifteen occupationally exposed subjects in 1991 and 1992. Subjects worked in citrus groves in Kern and Tulare Counties, California which had been treated with Lorsban* 4E Insecticide. Ten subjects pruned citrus trees two days after they had been treated, and 5 subjects picked fruit 43 days after treatment Although this study was conducted many years ago, the use pattern of chlorpyrifos in tree fruit remains essentially unchanged, so similar activities occur in current agricultural practice.

The investigators used a multi-faceted approach including urinary biomonitoring, measurement of blood cholinesterase activity, passive dosimetry, and corresponding environmental measurements. Urine and blood samples were collected before exposure to establish baseline levels for each subject, and after exposure to capture the kinetics of TCP elimination and anticipated peak cholinesterase changes. Urine samples were collected up to 4 days after exposure and blood samples were collected the day after exposure.

Whole body dosimetry, air monitoring and environmental samples were also collected in this study to evaluate exposures to the workers. But since these data are not directly relevant to this analysis, while a brief summary is provided, no details about these aspects of the study are discussed in this review.

STUDY TYPE: Agricultural Post Application Worker Monitoring (Pruning and Picking Citrus)

PC CODE: 59101

TEST MATERIAL: Lorsban* 4E Insecticide, a liquid formulation containing 40.7% of the active ingredient (ai) chlorpyrifos.

SYNONYMS: Trade name: Lorsban* 4E Insecticide
Chemical name: O,O-Diethyl O-(3,5,6-trichloro-2-pyridyl) phosphorothioate

CITATION: Study Author/Director: Richard C. Honeycutt, Ph.D
Mark A. DeGeare

Title: Worker Reentry Exposure to Chlorpyrifos In Citrus Treated with Lorsban* 4E Insecticide
Report Date: December 10, 1993
Analytical Laboratories: The Dow Chemical Co.
H&ES Analytical Chemistry Laboratory
Building 1803
Midland Michigan 48674
Testing Facility: H.E.R.A.C., Inc. (Hazard Evaluation & Regulatory Affairs Company, Inc.)
3704-B Boren Drive

Greensboro, NC 27407

Identifying Codes: MRID: 430627-01
H.E.R.A.C., Inc. Study No.: 91-102HE
H.E.R.A.C., Inc. Report No.: 93-307
Dow Study No.: DECO-HEH2.2-1-182(125)B

SPONSOR: DowElanco

Executive Summary

Study Design

Fifteen reentry workers, 10 pruners, and 5 harvesters were monitored while reentering three chlorpyrifos-treated test sites (citrus groves) following airblast application in California. Test sites measuring 10-14 acres were used in the study. Two reentry test sites were located in Tulare County and one in Kern County and were chosen as a part of a larger citrus worker exposure study. The test substance, Lorsban 4E Insecticide, is an emulsifiable concentrate containing a nominal 40.7% of the active ingredient (ai) chlorpyrifos. All sites were in proximity to each other. One application of the test substance was made to each treated plot at the maximum label rate of 6 lb ai/acre (A) using airblast sprayers. The location of the test sites was appropriate based on use patterns of the test substance.
Study details are provided in Table 1.

During the reentry event, workers wore briefs and a short sleeve t-shirt (inner dosimeter), long sleeve/long pant coveralls (outer dosimeter), shoes, socks, baseball hat, gloves (cotton for pickers and canvas for pruners), and a canvas protector sleeve (gauntlet) on the upper arm to prevent injury from thorns. Due to the cold weather, the pickers (Site No. 2) also wore a short sleeve shirt and a pair of long pants between the inner and outer dosimeters. All clothing was new. Normal work attire for entry is considered to be long-sleeve shirt, long pants, shoes and socks.

Biological, dermal, and inhalation monitoring of workers was conducted 43 days after the test substance application at Site No. 2 and 2 days after the test substance application at Site Nos. 5 and 6. At Site No. 2 workers were monitored while picking oranges. At Site Nos. 5 and 6 workers were monitored while pruning orange and lemon trees. The work duration for picking and pruning ranged from 5.8 to 6.9 hours. On the day of monitoring, weather conditions were dry at Site No. 2 (pickers) and at Site No. 6 (pruners). At Site No. 5 (pruners), monitoring was conducted under wet conditions. Approximately 0.05 inches of rain fell on the monitoring day at Site No. 5. At Site Nos. 5 and 6, no rainfall occurred prior to the monitoring day. At Site No. 2, rainfall was observed on 4 days after treatment (DAT) (0.12 inch), 5DAT (0.78 inch) and 27 DAT (0.08 inch).

Biological Monitoring

Biological monitoring was conducted by collecting approximate 12-hour composite urine samples from each worker starting from 24-hours prior to the time of entry through 120 hours after entry. Each 12-hour urine sample was analyzed separately for the urinary metabolite 3,5,6-TCP. Urine creatinine levels were analyzed as a way of qualitatively monitoring completeness of urine collection. Additionally, both plasma and red blood cell (RBC) cholinesterase (ChE) activity was monitored prior to the study to establish baseline on Day 1 after the entry.

Passive Dosimetry

Dermal exposures were assessed by analyzing the inner dosimeters (t-shirt and briefs combined), whole-body outer dosimeter (arms, legs, and torso separately), hand washes, head patches, outer work gloves (pickers only), and the protective arm sleeves (i.e. gauntlets). The arm portion of the whole-body outer dosimeter was not analyzed for the pruners. Inhalation exposures were monitored using personal air sampling pumps through a cassette with a pre-filter followed by Chromosorb 102 sorbent. The air flow was set to a rate of 1 liter per minute. Workers were assumed to breathe at 1.5 m^3/hr.

Environmental Sampling (Dislodgeable Foliar Residues or DFR)

This phase of the study was developed to determine the dissipation of DFR (i.e., the amount which can rub off on the skin) of chlorpyrifos applied to the citrus trees at the three sites in California. Duplicate DFR samples were collected from three subplots, prior to and following the application and at 1, 4, 5, 7, 14, 21, 35 and 43 days after the application for Site No. 2, prior to and following the application and at 1, 2, 7, 14, and 40 days after the application for Site No. 5 and prior to and following the application and at 1, 2, 7, 14, 21, and 35 days after the application for Site No. 6.

Table 1. Study Details

Site # (location)	Crop	Application Rate and Regime	Task	Clothing and PPE	Days after Treatment	Number of Monitoring Units	Entry Area (acres)	Hours Worked	Weather
2 (Tulare Co., CA; 80th Ave. and Road #236)	Orange	1 app. At 5.98 lb ai/A	Picking	--Inner: T-shirt and briefs --Middle: Short sleeve shirt and long pants --Outer: Coveralls (long sleeve/long pant) --Gloves --Upper arm sleeve gauntlet --Baseball hat	43	5	1.95 (~30 trees each worker)	5.8[1]	Dry
5 (Tulare Co., CA; 80th Ave. and Road #240)	Orange	1 app. At 5.98 lb ai/A	Pruning	--Inner: T-shirt and briefs --Middle: None --Outer: Coveralls (long sleeve/long pant) --Gloves --Upper arm sleeve gauntlet --Baseball hat	2	5	1.34 (~10 trees each worker)	6 – 6.9[2]	Rain
6 (Kern Co., CA; 3/4 mi west of Hwy 65, South Side of Hart Ave.)	Lemon	1 app. At 5.56 lb ai/A	Pruning	--Inner: T-shirt and briefs --Middle: None --Outer: Coveralls (long sleeve/long pant) --Gloves --Upper arm sleeve gauntlet --Baseball hat	2	5	1.34 (~10 trees each worker)	6.4[3]	Dry

[1]Includes 10 minute lunch break
[2]Two different observations were made as to the time worked.
[3]Includes a 13 minute refreshment break.

Calculation Methods

Daily 3,5,6-TCP levels (µg/day) were calculated by the Agency using six different methods to investigate the sensitivity of the results to the various methods. The correction methods considered by the Agency varied how background levels and completeness of the sample collection are accounted for, and included:

- no corrections for background or creatinine;
- correction for creatinine only by normalizing to a daily creatinine rate of 1.8 g/day (average rate based on literature);
- correction for creatinine only by normalizing to the average daily creatinine rate of each specific worker calculated over the sample collection period;
- correction for background only;
- correction for background and creatinine using the literature average of 1.8 g/day; and
- correction for background and creatinine using worker-specific daily creatinine averages.

The daily 3,5,6-TCP levels were not adjusted for analytical recovery because average recoveries were greater than 90%. Residue values below the limit of detection (LOD) were assigned a value of ½ the LOD.

Total absorbed chlorpyrifos equivalents were calculated by the Agency using a molecular weight conversion factor applied to the sum of the Day 0 up to Day 4 post-exposure 3,5,6-TCP levels (5 days of urine samples) and the application of a urinary excretion factor to account for the fraction of 3,5,6-TCP relative to chlorpyrifos expected to be excreted by Day 5. The molecular weight conversion factor was the ratio of the molecular weight of chlorpyrifos (350) to the molecular weight of 3,5,6-TCP (198). The urinary excretion factor was 0.6124 and was extracted from a pharmacokinetic model developed by Dow (presented p. 23 of this review).

Results

Based on the average of all workers, the maximum 3,5,6-TCP excreted (µg) occurred on either Day 0 or Day 1, depending on the correction method used, for both pickers and pruners. Additionally, average 3,5,6-TCP excretion, in general, declined over the sampling periods and 3,5,6-TCP residues were <LOQ by the last sampling interval in three of the five picker monitoring units and one of the ten pruner monitoring units. On a case by case basis, however, some variation was observed.

Picker Results

The average total absorbed chlorpyrifos for pickers ranged from 24.1 µg (corrected for background only) to 43.1 µg (corrected for creatinine only and using literature standard method). Percent ChE calculated by the Agency ranged from + 5 % to – 7 % (with an average of – 2 %) for plasma ChE and from + 6 % to - 5% (with an average of – 1 %) for RBC ChE.

Pruner Results

For Site No. 5 (wet conditions), the average total absorbed chlorpyrifos for pruners ranged from 136 µg (corrected for background only) to 233 µg (corrected for creatinine only using literature standard method). For Site No. 6 (dry conditions), the average total absorbed chlorpyrifos for pruners ranged from 64.7 µg (corrected for background only) to 174 µg (corrected for creatinine only using literature standard method). The total absorbed chlorpyrifos was higher at Site No. 5 with wet conditions than at Site No. 6 with dry conditions. For all pruner workers, ChE activity calculated by the Agency ranged from + 13% to

- 14% (with an average of – 2 %) for plasma ChE and from + 33% to - 17% (with an average of + 9 %) for RBC ChE.

Statistical Analysis

Descriptive data analysis was performed to evaluate the relationship between worker total chlorpyrifos urinary excretion during the 5-day period following exposure, corrected for background levels of TCP and creatinine, and ChE activity. In general, descriptive analysis failed to identify a relationship between total urinary TCP excretion and either RBC or plasma ChE activity. The inability to identify a relationship, however, should not be interpreted as meaning that the analysis of the study results demonstrated that there is no relationship between urinary TCP excretion and ChE activity. This is because the study was not specifically designed to assess the relationship between the two. As a consequence, there are a number of limitations that may limit the study's power (e.g. ability to identify a relationship between urinary TCP excretion and ChE activity if a relationship does in fact exist). Some of these limitations include:

- It is unclear if measuring ChE levels on the day following exposure is the most appropriate time period to assess ChE activity. The study report provides no rationale for measuring post-exposure ChE levels on the day following exposure.
- The study did not control for factors that may confound the relationship between exposure and ChE levels. One important potential confounder is inter-individual sensitivity to ChE inhibition.
- According to the Study Report, OPP's 875.2600 Guideline indicates that a biological monitoring study should include a minimum of fifteen individuals per activity. Although 15 workers were included in the study, there were only five replicates per study site.
- Although workers were asked to avoid contact with the chlorpyrifos insecticide Lorsban* 4E four days before the start of the study period, several workers had detectable levels of TCP in their urine prior to their re-entry into the treated field. This suggests that some workers may have experienced chlorpyrifos exposures before re-entry, which may have affected their baseline ChE levels.

Issues of concern

Overall, the Agency believes that the results of this study provide adequate information for the purposes of investigating a possible relationship between dose and impacts on cholinesterase activity. However, we did identify the following issues which should be considered in the interpretation of these results.

- **Background Levels in Urine**

Workers were asked not to spray or handle LORSBAN 4E or pick LORSBAN 4E treated fruit for 4 days prior to and after the exposure event, but residues of 3,5,6–TCP were detected in pre-exposure samples collected in the 24-hour period prior to the entry event. Residues ranged from <LOQ to 14.3 ng/g per 12-hour sampling interval. According to the Study Report, the amount of 3,5,6-TCP excreted in the pre-exposure samples equaled between 3 and 16% of the amount excreted over the 5-day post-exposure period. Residues of 3,5,6-TCP were also detected in control urine samples (presumably 12-hour samples) collected from laboratory personnel. 3,5,6-TCP residues in aliquot samples of one laboratory personnel ranged from 68.7 to 71.8 ng/g. In the remaining control samples collected from laboratory personnel, average residues were <LOQ in two samples and ranged from 3.4 ng/g to 5.6 ng/g in three samples. These results indicate possible background levels from the diet and drinking water.

The study author assumed that the pre-study urine represented steady state background excretion of 3,5,6-TCP (i.e., resulting from exposure to chlorpyrifos or 3,5,6-TCP that was unrelated to this study) and therefore, corrected for the pre-exposure levels. The Agency presents the biological monitoring data both corrected for pre-exposure levels and also uncorrected. The study author used the average of the two 12-hour pre-exposure samples, whereas the Agency used the 12-hour sample from immediately before the start of entry.

- **Incomplete Urine Collection**

Urine collection may have been incomplete for some samples based on creatinine rates. The study compared the creatinine rates in the field samples to standard literature rates from Documenta Geigy 1970 (mean of 1.8 g/day, 95% range of 1.1 to 2.5 g/day). The study normalized the sum of the post-exposure residues for each worker to a creatinine rate of 1.8 g/day using the worker's average 24-hour creatinine rate over all days of the study. The Agency performed creatinine correction on the daily 3,5,6-TCP levels using two different methods. One method normalized 3,5,6-TCP levels using a creatinine rate of 1.8 g/day and the other method used each individual worker's average daily creatinine rate. EPA also calculated 3,5,6-TCP excretion without creatinine correction.

- **Laboratory Fortification**

According to the text in the Study Report, concentrations of urinary TCP were corrected for the daily relative recovery of TCP from fortified urine samples. The Agency could not determine if the 3,5,6-TCP concentrations were corrected for the recoveries. Traditionally, EPA does not correct for residues greater than 100%. If the concentrations were corrected for the recoveries, the concentrations would be slightly underestimated; however, only a minimal number of field samples would be affected (less than eight).

- **Worker Specifics**

The Study Report did not provide detailed information on each worker such as gender, weight, age, or years of experience. Based on the names of the workers provided, it is assumed that all workers were male. However, Dow has recently provided additional information to clarify these issues.

- **Number of Monitoring Units**

The prevailing standard of the time based on Agency guidelines recommended 15 monitoring units for each postapplication task. In this study there were only 5 picker monitoring units and 10 pruner monitoring units at the start of the study. For pruner monitoring unit 6 at Site #6, the sample volume at the 48 to 60 hr interval was lost and the sample for the 108 to 120 hr interval was not collected (worker was in a car accident which prevented him from turning in the sample). Therefore, only nine monitoring units overall were included for the calculation of total absorbed chlorpyrifos for pruners.

- **Baseline Blood Samples**

Baseline blood samples were collected from each worker on two occasions 2 to 10 days prior to the entry exposure event. It should be noted however, that the study protocol states that workers were only asked to avoid handling LORSBAN 4E and avoid entering LORSBAN 4E treated areas for 4 days prior to the start of the study. Additionally, in six workers, the plasma and/or RBC cholinesterase (ChE) levels from the two pre-exposure samples were not within 15% of each other. No explanation for this discrepancy is provided in the Study Report. In these cases baseline levels which yield the greatest percent activity reading were calculated.

- **Storage Duration for Urine**

The storage durations of the urine were not provided.

- **Storage Conditions for Blood**

The storage conditions of the blood samples were not provided. For sites 2 and 6 all post exposure samples were analyzed on the day of collection. At Site 5 all post exposure samples were analyzed 2 days after collection, and at Site 2, five of the ten baseline samples were analyzed 2 days after collection. According to the EPA guidelines, whole blood samples should not be stored frozen.

- **Pruner Monitoring Unit 9**

The daily 3,5,6-TCP levels in pruner monitoring unit 9 declined to <LOQ by Day 2 and then increased to maximum levels on Day 3. Based on this data, it appears that this worker could possibly have been exposed to chlorpyrifos on Day 3 (e.g., through diet or drinking water).

- **Specific Gravity**

The specific gravity of each urine sample was not determined; therefore, the volume of urine collected was determined by weighing the sample and assuming a specific gravity of 1.000 for urine. A specific gravity of 1 is slightly less than the lower limit of normal, which is 1.002 to 1.028. A specific gravity of 1.000 is also less than the average density of 1.04419 ± 0.0114 g/mL, which was determined from 20 random samples collected in this study (note that this value is also higher than the upper limit of the normal range). Assuming a specific gravity of 1.000 to determine the sample volume will result in slightly lower sample volumes, however, the difference is insignificant.

Compliance

Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The Study Report states that it meets FIFRA Good Laboratory Practices 40 CFR part 160, with the following exceptions: 1) The weather data collected from NOAA is not known to be produced under GLPs; 2) The collection, analysis, recording and reporting of blood plasma and red blood cell cholinesterase data was not performed under GLPs; 3) The location of Synthesis and Fabrication of the Test Substance and Reference Chemicals is not included in this report and is not in the study file. The data do exist at DowElanco, Indianapolis, Indiana; 4) Some empty test substance containers were discarded at Crumbliss and Horton AG Ply Service; and 5) The Test Substance was not analyzed or characterized prior to the initiation of the study.

Concurrent Dislodgeable Residue Dissipation Study

Guideline or Protocol Followed

The Agency used U.S. EPA OPPTS Harmonized Test Guidelines, Series 875 Occupational and Residential Exposure, Group B 875.2600, Biological Monitoring in the compliance review of the study. A compliance checklist is provided in Appendix A.

I. Materials and Methods

A. Materials:

1. Test Material:

Active ingredient: Chlorpyrifos
Purity: Not Provided
Formulation: Liquid formulation containing a nominal 40.7% ai. The certificate of analysis for the test substance stated that the test substance contained 41.2% ai. The certificate of analysis for the re-analysis of the test substance approximately 7 months later stated that the test substance was stable (% ai was not provided).
Lot/Batch # technical: Not Provided
Lot/Batch # formulation: MM910410-310BB
CAS #(s): 2921-88-2
Other Relevant Information: EPA Registration No. 464-448

2. Relevance of Test Material to Proposed Formulation(s):

The test material appeared to be the same as the product described on the label in the Study Report.

B. Study Design

The study followed H.E.R.A.C., Inc. Protocol No. 91-102HE. For all portions of the study (biological monitoring, dermal monitoring, and inhalation monitoring), there were 20 reported amendments to the study protocol and 81 reported deviations from the study protocol.

1. Site Description:

Test locations: Two test sites were located in Tulare County, California (Site #2 and #5) and one test site was located in Kern County, California (Site # 6). The applications took place on October 23, 1991 (Site #2), March 28, 1992 (Site #5), and April 1, 2992 (Site #6). According to the Study Report, Lorsban 4E is most heavily used in late spring through late summer/fall in Tulare and Kern Counties. However, the Study Report also states that Lorsban 4E applications are most intense in the summer (after pruning). Therefore, the study authors consider the pruner entry exposure worst case since the pruning entry activities were monitored only two days after the application.

Areas sprayed and re-entered: 10 to 14 acres of citrus trees were treated at each site. Only 1 to 2 acres of each citrus grove was entered for post-application exposure monitoring.

Meteorological Data: Air temperature, wind speed and direction, relative humidity, and barometric temperature recordings were collected at each test site on the application and entry days. Also provided in the Study Report are daily air temperature recordings (minimum and maximum) and daily rainfall amounts from NOAA stations in Porterville, CA (Tulare County) for the entire study period in Oxnard, CA for a portion of the study period. Additionally, average monthly temperature and total monthly rainfall recordings were provided for each month between 1982 and 1992 for both Porterville, CA and Oxnard, CA. The distances from the NOAA stations to the test sites were not provided.

The meteorological recordings during the study period were generally within range of the historical conditions. Based on rainfall data from the Porterville, CA NOAA station, the first rainfall occurred 4 days after treatment (4DAT) at Site #2 (0.12 inches). Rainfall also occurred at 5DAT (0.78 inches) and 27DAT (0.08 inches). Rainfall did not occur on the entry day (43DAT). At Site #5, the first rainfall occurred at 2DAT (0.05 inches), which was the monitoring day for pruners. At Site #6, no rainfall occurred between application and entry (2DAT) or on the day of entry. The Study Report did not report if irrigation was used at the sites.

Table 2 provides a summary of the meteorological conditions which existed during the time of applications.

Table 2. Meteorological Conditions at the Time of Applications and Entry[a]

Site #	Date	Air Temperature (°F)	Wind Speed (mph)	Wind Direction	Relative Humidity (%)	Barometric Pressure (inches)
2	10/23/91 (application)	59 to 73	No wind to 8	W, W-NW	50 to 95	Not available
	12/5/91 (picker entry)	41 to 64	No wind to <5	S	34 to 36	Not available
5	3/28/92 (application)	50 to 74	<5 to 5	SE, NE	55 to 60	Not available
	3/30/92 (pruner entry)	54 to 69	<5	SE, NE, S	60 to 100	31
6	4/01/92 (application)	58 to 83	No wind to 6	NW, W, N	30 to 60	28.5 to 29.5
	4/3/92 (pruner entry)	57 to 67	No wind	N/A	58	Not available

a. Conditions are taken from 5 to 7 recording events throughout the day at each site on the day of application and two to three recording events throughout the day at each site for entry.

2. Crop Characteristics:

Crop, variety: Oranges were treated at Site #2 and 5. Lemons were treated at Site #6. Variety was not reported.

Row width, plant spacing: Site #2 – Plant spacing was approximately 22 ft between trees within a row and 21 ft between rows
Site #5 – Plant spacing was approximately 22 ft between trees within a row and between rows
Site #6 – Plant spacing was approximately 14 ft between trees within a row and 24 ft between rows

Stage of growth: The stage of growth was not reported for Site #5 and #6. For Site #2, trees were treated so that fruit could be picked when ripe approximately 35 days later (fruit actually ripened later than this and was picked 42 days after treatment).

3. Application Rates and Regimes:

Application rate(s): One application was made at each test site. The actual application rate was 5.98 lb ai/A for Sites #2 and #5 and 5.56 lb ai/A for Site #6. The maximum label application rate is 6 lb ai/A.

Application Regime: Single applications were made on October 23, 1991 for Site #2, March 28, 1992 for Site #5, and April 1, 1992 for Site #6.

Application Equipment: All applications were made using open cab airblast sprayers equipped with 22 nozzles. The pressure on the airblast sprayer was maintained at about 100-180 psi.

Spray Volume: Approximately 750 gallons water/acre.

Equipment Calibration Procedures: Calibration of the airblast sprayer was performed prior to each treatment. The applicator performed a test run with water and adjustments were made until an application

was performed using a psi between 100 and 180, a speed of 1 to 1.5 MPH (10 to 12 min/0.67 acres), and ~30 gallon left in tank after spray completed. The applicator was then informed that the tractor gear and nozzle parameters that were used in the calibration were to be used during application of Lorsban 4E Insecticide at that particular site.

4. Number and type of workers:

Five workers were monitored at each site. At Site #2, the workers monitored were pickers and at Site #5 and #6 the workers monitored were pruners. Based on the names of the workers, all workers were males. The age of the workers, body weight of the workers, and the years experience of each worker were not provided.

The study protocol states that workers were asked to avoid handling LORSBAN 4E and entering LORSBAN 4E treated areas for 4 days prior to the start of the study.

5. Clothing:

All workers wore 100% cotton t-shirts and briefs (inner dosimeters) underneath one-piece long sleeve/long pant denim coveralls (outer dosimeter). Due to the cold weather, the pickers (Site #2) also wore a short sleeve shirt and a pair of long pants between these layers. All workers also wore new socks, tennis shoes and baseball-style caps. Other personal protective equipment worn by the workers (pickers and pruners) included a canvas protector sleeve (gauntlet) on the upper arm to prevent injury from thorns. The pickers wore white thick work gloves while the pruners wore thick canvas work gloves to protect the hands from thorns. The personal protective equipment (PPE) worn is also listed in Table 2 below.

6. Time Interval(s) for Entry:

The pickers entered Site #2 at 43 days after the application. The pruners entered Site #5 and #6 at 2 days (~48 hrs) after the application. The entry interval for the pickers was scheduled to be 35 days after the application, but the fruit was not ripe enough to be picked at this time (acid/sugar was < 8).

7. Monitoring Units:

Picking: Picking was monitored at one site (#2). Five monitoring units were conducted at the site. Entry tasks were performed for 5.8 hours. This includes a 10 minute lunch break.

The picking activity consisted of each worker picking oranges from about 30 orange trees. The picker performed typical picking activities while standing on ladders, picking from the outside to inside of the tree. Only mature fruit was picked. The pickers used a large shoulder hung canvas bag to place the fruit into. After the bag was full, the oranges were poured into large wooden crates on the ground.

Pruning: Pruning was monitored at two sites (#5 and #6). Five monitoring units were conducted at each site. The entry tasks were performed for 6 or 6.9 hours at Site #5 (there were two different observations made as to time worked at Site #5) and 6.4 hours at Site #6 (this includes a 13 minute lunch break).

The pruning activity consisted of pruning about 10 citrus trees (lemons/oranges). At Site #5, the pruners were inside the orange trees cutting branches from inside to outside. It was raining during this entry monitoring period. At Site #6, the pruners worked from the outside to the inside of the lemon trees due to the presence of large thorns on lemon trees. It was not raining during the entry monitoring at this site.

8. Exposure monitoring methodology:

Urine:

In this study, approximate 12-hr composite urine samples were collected from each worker starting from 24 hours prior to the time of entry (Day -1) through 120 hours after entry (Days 0, 1, 2, 3, and 4). Urine was collected in a plastic urine collection vessel. The study participants were instructed to record, on the card attached to the urine container, the time that each urine collection actually started and ended and if any urine was inadvertently discarded. Each total urine sample was kept at ambient temperature during collection. After the sample was handed over to a H.E.R.A.C., Inc. field technician, the urine sample was processed within one to two days of collection as follows: The urine was kept at ambient temperature during this period. The urine sample was weighed, shaken and two to four 25 mL aliquots were removed with a pipette and each 25 mL aliquot added to a 4 ounce amber bottle. The caps (tef1on lined) were placed on the bottle, wrapped, taped to secure the lid, and each wrapped bottle stored on dry ice in a cooler. The urine samples were shipped on dry ice in a cooler to The Dow Chemical Company. Selected samples were sent from Dow to Pharmaco Analytical Laboratory Inc. for processing and analysis. Samples were kept frozen at -20°C at the laboratory prior to analysis. The number of days between sample collection and analysis was also not provided.

It should be noted that the actual sample collection duration for each 12-hr interval varied and exact durations were not provided in the Study Report. On the pre-exposure day, urine samples from pickers (Site #2) were collected from the morning (starting from the second excretion of the day) until ~3:30 PM to 5:00 PM for the 0 to 12 hr sample and then from the afternoon until the next morning on the day of entry for the 12 to 24 hr sample. From the entry day on, 0 to 12 hr samples were collected from morning (~7:00 AM to 8:00 AM) until the afternoon (~3:30 PM to 5:00 PM) and the 12 to 24 hr samples were collected from afternoon until the next morning. Urine samples from the pruners (Site #5 and #6) on the pre-exposure day were collected from ~8:00 AM until ~6:00 PM for the 0 to 12 hr sample (approximately 10 hours) and from ~6:00 PM to ~5:00 AM for the 12 to 24 hr sample (approximately 11 hours). From the entry day on, pruner samples from Site #5 were collected from the morning (~5:30 AM to 8:00 AM) until the afternoon (~4:30 PM to 6:00 PM) for the 0 to 12 hr samples and from the afternoon until the following morning for the 12 to 24 hr samples. For Site #6. pruner samples were collected from the morning (~5:20 AM to 8:00 AM) until the afternoon (~ 3:00 PM to 7:00 PM) for the 0 to 12 hr samples and from the afternoon until the following morning for the 12 to 24 hr samples.

Blood:

Blood samples were collected from the study participants at three intervals. Samples from pickers were obtained 10 days prior to entry (-10 DAT), -3 DAT, and 1 day after entry (1 DAT). Samples from pruners at Site #5 were obtained on -5 DAT, -2 DAT, and 1 DAT and samples from pruners at Site #6 were obtained on -7 DAT, -4 or -3 DAT, and 1 DAT. The blood samples were sent to Sierra View Outpatient Laboratory, 478 W. Putnam, Porterville California 93257, for analysis. Morinda Medical Group Inc. Porterville, California was responsible for collection, preservation, storage, shipment, and analysis and reporting of results. Storage conditions (i.e. frozen, ambient, etc.) were not provided.

9. Analytical Methodology:

Urine (3,5,6-TCP):

Extraction and Detection method(s):

The 3,5,6-trichioropyridinol (TCP) concentrations in the biological monitoring urine samples were determined using a previously published negative-ion chemical-ionization gas chromatography-mass spectrometry (NCI-GC/MS) method, as well as two slightly modified methods, which also employed NCI-GC/MS. All three methods involved fortification of urine samples with an internal standard, hydrolysis of acid-labile conjugates of TCP, followed by solvent extraction with ethyl ether, derivatization to the t-butyldimethylsilyl ether of TCP and subsequent NCI-GC/MS analysis.

The published method (Method #1) was used for TCP determination for eight 1992 samples (biological monitoring and field spike) that were sent only to the H&ES laboratory at DOW Chemical, and not to the contract laboratory performing the majority of these analyses (Pharmaco Analytical, Richmond, Virginia). The majority of the urine samples from the study were analyzed at Pharmaco Analytical, via a modified version of Method #1. This method (#2) is Pharmaco Analytical Method MS30. Both methods employ the structural isomer 3,5,6-TCP as an internal standard in the TCP analysis. This method differs from Method #1 in the following areas: 1) 1.0 mL urine samples were used vs. 5.0 mL aliquots in method #1; 2) 2.5 mL ether was used in the sample extraction vs. 5.0 mL in method #1; 3) samples were derivatized with 50 µL N-(t- butyldimethylsilyl) -M-methyltrifluoroacetarnide (MTBSTFA) in 1.0 mL toluene/pyridine (95:5, v/v) vs. 100 µL MTBSTFA in 1.0 mL o-xylene in method #1; 4) matrix standards were employed (urine fortified with TCP and 3,5,6-TCP) vs. solvents standards used in Method #1. Selected samples from the study were used to determine the stability of TCP in urine at ambient and elevated (40°C) temperature. These samples were analyzed via a third method, which employed a stable-isotope labelled analog of TCP ($^{13}C_2$-TCP) as an internal standard and did not require evaporation of the extraction solvent.

The NCI-GC/MS conditions used in Method #2 were comparable to those used in Method #1, with the following exceptions: 1) the J&W 1DB-S capillary GC column used was 14m in length, vs. 30m in Method #1; 2) GC injection was split (25:1) vs. 0.2 mm splitless in Method #1; 3) MS selected—ion monitoring dwell time was 50 msec/ion/scan vs. 125 msec/ion/scan in method #1. The NCI-.GC/MS conditions used in Method #3 were comparable to those used in method #1, with only one exception; ions m/z 161 and 165 were monitored for TCP and 1302-TCP, respectively (50-100 msec/ion/scan) vs. ions m/z 161 and 163 monitored both TCP and 3,5,6-TCP (m/z 163 use only for structural confirmation of analytes) in method #1.

Method validation: Method validation spikes (urine fortified with 3,5,6-TCP) had average relative recoveries of 96.7±14.6% (n=24) for Method #1, 92.8±10.1% (n=48) for Method #2, and 105.4±19.8% (n=15) for Method #3.

The LOQ was 1.6 ng/ml for Method #1, 3.0 ng/ml for Method #2, and 1.0 ng/ml for Method #3.

Instrument performance and calibration: A urine calibration curve and blanks were analyzed with each set of samples. Samples were analyzed over the range of 3.00 ng/mL to 1200 ng/mL for 3,5,6-TCP using power least squares regression. The average correlation coefficient was 0.9991 for the 1991 samples (pickers) and 0.9989 for the 1992 samples (pruners). Average back-calculated concentrations of calibration standards were determined for each level of the daily calibration curves. The overall percent coefficient of variation was 7.19% for the 1991 samples (pickers) and 7.62% for the 1992 samples (pruners).

Urine (Creatinine):

Method: Urinary creatinine was measured using a modification of the method described by Fabiny and Ertingshausen which is based on the Jaffe reaction.

Blood (Cholinesterase):

Method: RBC and Plasma Cholinesterase in blood samples were determined using a prescribed method by the Boehringer Mannheim Diagnostics Cholinesterase procedure (Modified Ellman Procedure).

10. Quality Control:

Lab Recovery: Daily study spikes using urine fortified with 3,5,6-TCP were prepared. For Method #1, the average recovery was 126.9±12.4% (n=3). For Method #2, two sets of average relative recoveries were provided, presumably one set for the picker samples and one set for the pruner samples. For one set, the average recovery was 97.3±7.8% (n=28) at 8.8 ng/ml, 98.5±6.0% (n=29) at 60 ng/ml, 105.6±4.8% (n=29) at 750 ng/ml, and 96.8±5.4% (n=6) at 750 ng/ml (dil 10:1). For the other set, average recovery was 95.2±14.7% (n=37) at 8.8 ng/ml, 97.1±14.9% (n=38) at 60 ng/ml, 108.2±13.3% (n=38) at 750 ng/ml, and 97.9±16.8% (n=29) at 750 ng/ml (dil 10:1). For Method 3, the average relative recovery was 103.0±6.0% (n=2) at 51,103 ng/ml,

Field blanks: Control samples were collected from the workers in the 24-hr period prior to entry. 3,5,6-TCP residues were detected in the majority of these pre-exposure urine samples. Residues ranged from <LOQ to 14.3 ng/g per 12-hr sampling interval. Except in four workers, the residues decreased from the 0 to 12 hr interval to the 12 to 24 hr interval. For five of the workers, residues were <LOQ by the 12 to 24 hr interval (the interval immediately before entry).

Control samples (presumably 12-hr samples) were also collected from laboratory personnel. Residues of 3,5,6-TCP in aliquots of one laboratory personnel sample ranged from 68.7 to 71.8 ng/g. It is assumed that laboratory error or other error occurred with these samples and they are not considered further in the review. In the remaining control samples collected from laboratory personnel, average residues were <LOQ in two samples and ranged from 3.4 ng/g to 5.6 ng/g in three samples.

Control samples were also collected and analyzed from 12 volunteers several days prior to the pruning entry day to determine which 10 volunteers should be selected for the pruning entry monitoring. The date of the sampling as well as the results do not appear to have been reported in the Study Report. According to the study protocol, generally, a ratio of creatinine to 3,5,6-TCP of 3.0 will be deemed acceptable for a potential test subject to enter the test.

Field recovery: Field fortification was conducted using control urine from the field workers collected during the 24-hr pre-exposure period and also using control urine from laboratory workers. Samples were fortified at a low and high level (45.9 and 4,593 ng/g for pickers and 43.16 and 4,316 ng/g for pruner). The fortified urine samples were stored and analyzed for 3,5,6-TCP with the other urine specimens. For pickers, the recoveries were 109 ± 7.7% for the low level and 111±5.3% for the high level. For pruners, the recoveries were 116 ± 23% for the low level and 160±29.5% for the high level. Any background residues detected were subtracted out in the calculation of the percent recovery. See Table 3 for a summary of the field fortification recoveries.

The fortification recoveries for the pruners are above the upper end of the generally acceptable range of 70 to 120%. Additionally, the standard deviations are above the generally acceptable value of 20%. The fortification levels also do not in general encompass the residue levels in the field samples. An additional fortification level closer to or at the limit of quantitation would have been more appropriate.

The Registrant and EPA did not correct the field residues for field fortification recoveries.

Table 3. Summary of Field Fortification					
Entry Activity[a]	Fortification Level (ng/ml)	n	Range of Recovery (%)	Average Recovery (%)	Standard Deviation
Pickers	45.9	18	98 – 127	109	7.7
	4593	19	99 – 119	111	5.3
Pruners	43.16	36	79 – 173	116	23.0
	4,316	36	100 – 219	160	29.5

a. The sample IDs for the field fortification samples were not clearly described in the Study Report; therefore, it was difficult to separate out the samples fortified using the lab worker urine and the field worker urine. Additionally, it was difficult to separate out field fortification samples from the two pruner sites (Site #5 and #6).

Formulation: Liquid formulation containing a nominal 40.7% ai. The certificate of analysis for the test substance stated that the test substance contained 41.2% ai (101% of nominal). The certificate of analysis for the re-analysis of the test substance approximately 7 months later stated that the test substance was stable (% ai was not provided).

Tank mix: Tank mix samples were collected from the airblast spray tank in triplicate prior to the final application at each site. Tank samples were taken only after thorough mixing (with agitation) of the Lorsban 4E and water in the spray tank had taken place. At Site #2, recoveries were 102%, 113%, and 114% (average of 109%±6.3%). At Site #5, recoveries were 74%, 78%, and 121% (average recovery of 91%±25.9%). At Site #6, recoveries were 98%, 85%, and 252%. The 252% value was considered an outlier. Not including this value, the average recovery for Site #6 was 92%.

Travel Recovery: Not discussed.

Storage Stability: In addition to the field fortification samples, storage stability was also examined for a variety of scenarios, including urine fortified with 3,5,6-TCP and stored under ambient conditions (24°C and 40°C) for 96 hours and frozen conditions (-10°C) for 6 months. Average recoveries were 98±3% (n=3) at 24°C, 102±6% (n=3) at 40°C, and 110±1% (n=2) at -10°C. Fortification levels were 22 to 50 ng/ml for the ambient samples and 18 to 37 ng/ml for the frozen samples. Additionally, acetonitrile fortified at 10.4 to 1,038 ng/ml and stored for 9 months at 24°C had an average recovery of 100%±4% (n=4).

II. RESULTS AND CALCULATIONS

A. Urine Monitoring

1. Urine Density Measurements

The density was performed on twenty random urine samples by weighing 1 milliliter sample volumes. The mean density for the twenty samples was 1.04419 ± 0.0114 g/mL.

2. Urine Volume Determination

The urine specimens were weighed and the volume of each specimen was calculated from its weight, assuming a specific gravity of 1.0 for the urine. A summary of the volume of urine collected per day per person (sum of 0 to 12 hr and 12 to 24 hr intervals) is reported in Appendix A, Table 1. Overall, urine samples ranging between 297 - 4,025 mL/day of urine were collected per worker. It should be noted that normal specific gravity of urine in an individual ranges from 1.002 to 1.028; therefore, by using a specific gravity of 1.0 to calculate volume from the weight the sample volumes may be slightly underestimated.

3. Urine Creatinine Measurements

The study author assessed completeness of urine collection by analyzing urine samples for creatinine content. The creatinine concentration and urine volumes were used to determine total daily creatinine output. The results were compared to an average daily creatinine excretion rate of 1.8 g/day (95% range of 1.1 to 2.5 g/day) based on standard literature values (Documenta Geigy, 1970). The results were also compared to other samples from the same individual for consistency. The results are shown Appendix A, Table 1. Individual daily creatinine excretion rates ranged from 0.27 to 2.62 g/day and average daily creatinine rates over the course of monitoring for each worker ranged from 0.85 to 1.81 g/day.

4. Daily 3,5,6-TCP In Urine (µg/day) Calculated by the Agency

Daily 3,5,6-TCP levels were calculated for each worker by summing the residues from the 0 to 12 hr and 12 to 24 hr sampling intervals on each day. The following formula (Eq. 1) was used to convert the reported 3,5,6-TCP sample concentration in ng/g to µg:

*3,5,6-TCP (µg) = Sample weight (g) * Sample Concentration (ng/g) * 1 µg/1,000 ng* *(Eq. 1)*

For 3,5,6-TCP residues reported as <LOQ, a value of ½ LOQ was used in the calculations.

Correction Factors

The following corrections factors were assessed: field fortification, workday duration, background, and incomplete urine collection. 3,5,6-TCP residues were not corrected for field fortification recoveries because the recoveries were over 100%. Additionally, a work-day correction factor was not applied; however, one could apply a correction since the actual workday was less than 8 hours for all workers (see Appendix A, Table 2 for details). Corrected daily 3,5,6-TCP levels (µg/day) were calculated by the Agency using six different correction methods to account for steady-state background levels of 3,5,6-TCP (based on pre-exposure levels) and apparent incomplete urine collection (based on creatinine levels). These methods include:

Method 1: No Background or Creatinine Corrections

In this method, daily 3,5,6-TCP levels were not corrected for either background levels from the pre-exposure samples or for potential incomplete urine collection using creatinine excretion rates.

Method 2: Creatinine Only Correction – Using the Literature Average Creatinine Rate of 1.8 g/day

To account for potentially incomplete urine collection, the creatinine excretion in the field samples were compared to an average level of 1.8 g/day referenced in the Study Report (Documenta Geigy, 1970). In this correction method, each worker's daily (24-hour) 3,5,6-TCP level was adjusted if the creatinine level was below 1.8 g/day (Eq. 2):

$$\textit{3,5,6-TCP (µg/day)} = \textit{3,5,6-TCP observed (µg/day)} * \frac{\textit{1.8 g creatinine/day}}{\textit{Observed creatinine rate (g/day)}} \qquad \textit{(Eq. 2)}$$

Daily 3,5,6-TCP levels (µg/day) were not corrected if the corresponding observed daily creatinine level (g/day) was greater than 1.8 g/day.

Method 3: Creatinine Only Correction – Using the Worker-Specific Average Daily Creatinine Rate

In this method, each individual worker's average 24-hour creatinine level over the period of the study was used to correct the worker's 3,5,6-TCP levels when the daily 24-hour creatinine level fell below the worker's average level. (Eq. 3):

$$\textit{3,5,6-TCP (µg/day)} = \textit{3,5,6-TCP observed (µg/day)} * \frac{\textit{Worker-specific average creatinine rate (g/day)}}{\textit{Observed creatinine rate (g/day)}} \quad \textit{(Eq. 3)}$$

Daily 3,5,6-TCP levels (µg/day) were not corrected if the corresponding observed daily creatinine level (g/day) was greater than the worker-specific average daily creatinine level (g/day).

Method 4: Background Correction Only

Although the workers were instructed to avoid exposure to chlorpyrifos for at least 4 days prior to the study, measureable quantities of 3,5,6-TCP were found in pre-study urine specimens. It should be noted that measureable quantities of 3,5,6-TCP were also found in urine specimans collected from unexposed laboratory technicians (see Section I.B.10). The pre-exposure urine levels were considered to represent background and the participants were assumed to have had some unknown steady state exposure to chlorpyrifos. This steady state exposure would be expected to provide some, relatively constant, contribution to the total 3,5,6-TCP excreted during the five days after study exposure. The daily 3,5,6-TCP levels were therefore, each corrected for the 3,5,6-TCP residues detected in the sample from the 12 hr interval prior to the exposure event. The following rules were used in the correction:

1. The background level used was the 3,5,6-TCP level in the 12-hour interval prior to the exposure event, even in the event that this interval had higher residues than the previous 12-hour pre-exposure sampling interval.

2. If the pre-exposure level was <LOQ, the background correction was made using ½ LOQ.

3. If the post-exposure 24-hr 3,5,6-TCP residue (µg/day) was <LOQ, a background correction was not made.

Method 5: Background and Creatinine Correction – Using the Literature Average Creatinine Rate of 1.8 g/day

In this method, background corrected 3,5,6-TCP levels calculated using Method 4 were also corrected using an average daily creatinine rate of 1.8 g/day (see Method 2 above).

Method 6: Background and Creatinine Correction - Using the Worker-Specific Average Daily Creatinine Rate

In this method, background corrected 3,5,6-TCP levels calculated using Method 4 were also corrected using the worker-specific average daily creatinine rates (see Method 3 above).

The results for the individual workers are shown in Appendix A, Table 2 for pickers at Site #2, Appendix A, Table 3 for pruners at Site #5 (wet conditions), and Appendix A, Table 4 for pruners at Site #6 (dry conditions). A summary of the results by post-exposure day is provided in Appendix A, Table 5 for pickers, Appendix A, Table 6 for all pruners combined, Appendix A, Table 7 for pruners at Site #5 only, and Appendix A, Table 8 for pruners at Site # 6 only. Additionally, Figures 1 and 2 (Appendix A) show the decline of 3,5,6-TCP excreted in urine for pickers and pruners, respectively, over the 5 day post-

exposure period and Figures 3 and 4 (Appendix A) show the cumulative 3,5,6-TCP levels over the 5 day post-exposure period.

For pickers and pruners, the maximum average 3,5,6-TCP excreted (µg) occurred on either Day 0 or Day 1, depending on the correction method used. Additionally, average 3,5,6-TCP excretion, in general, declined over the sampling periods and 3,5,6-TCP were <LOQ by the last sampling interval in three of the five picker monitoring units and one of the ten pruner monitoring units. On a case by case basis, however, some variation was observed. For example, in pruner monitoring unit 9, daily 3,5,6-TCP levels declined to <LOQ by Day 2 and then increased to maximum levels on Day 3. Based on these data, it appears that this worker could have been exposed to chlorpyrifos on Day 3.

5. Total Absorbed Chlorpyrifos (µg) Calculated By the Agency

Total absorbed chlorpyrifos (µg) was calculated by EPA for each correction method described above using a Pharmacokinetic Model Used by DowAgroSciences (attached below). The total amount of 3,5,6-TCP excreted over the 5 day exposure period was converted to chlorpyrifos equivalents using a molecular weight conversion factor and then adjusted by the fraction of 3,5,6-TCP relative to chlorpyrifos expected to be excreted by day 5 (0.6124) (see Equation 4).

*Total Absorbed Chlorpyrifos (µg) = (3,5,6-TCP (ug/day) * MWF) / (UEF)* (*Eq. 4)*

Where:

MWF = Molecular Weight Factor - ratio of the molecular weight of chlorpyrifos (350) to the molecular weight of 3,5,6-TCP (198) (unitless)
UEF = Urinary Excretion Factor (0.6124). The urinary excretion factor of 0.7151 corrects for the fact that only approximately 72 percent of the absorbed chlorpyrifos is expected to be excreted as 3,5,6-TCP after about 10 days. The pharmacokinetic model developed by Dow shows that only 85 percent of the 3,5,6-TCP is excreted by day 5. Therefore, 0.7151 * 0.85 = 0.6124, the fraction of 3,5,6-TCP relative to chlorpyrifos expected to be excreted by day 5.

Total absorbed chlorpyrifos (µg) was not calculated for pruner monitoring unit #6 because two of the 12 hour samples were either lost or not collected (48 to 60 hr and 108 to 130 hr samples).

Total absorbed chlorpyrifos (µg) as calculated by the Agency is shown in Appendix A, Table 9 for pickers and Appendix A, Table 10 for pruners. Additionally. total absorbed chlorpyrifos (µg) is shown in Appendix A, Figure 5 (pickers), Figure 6 (all pruners combined), and Figure 7 (pruners at Sites 5 and 6 separately).

For pickers at Site #2, the average total absorbed chlorpyrifos (µg) ranged from 24.1 µg (corrected for background only) to 43.1 µg (corrected for creatinine only using literature average method).

For pruners at Site #5 (wet conditions), the average total chlorpyrifos (µg) absorbed after exposure ranged from 136 µg (corrected for corrected for background only) to 231 µg (corrected for creatinine only using literature average method).

For pickers at Site #6 (dry conditions), the average total chlorpyrifos (µg) absorbed after exposure ranged from 64.7 µg (corrected for corrected for background only) to 174 µg (corrected for creatinine only using literature average method).

Pharmacokinetic Model Used by DowAgroSciences to Estimate the Amount of Chlorpyrifos Absorbed After Exposure

$$Xu(t) = Ka * fXo\ [1/Ka + Exp\ (-Kt)/(K-Ka) - K * exp\ (-Ka * t)\ /\ (Ka*(K-Ka))]$$

Where:

t = time in hours
K =0.0258 = rate constant for elimination, per hr
Ka =0.0308 = rate constant for absorption, per hr
f =0.72 = fraction of absorbed dose excreted as 3,5,6-TCP
Xo = 1

Days	Hours Post Dosing	Ka*f	1/Ka	exp(-Kt)/ (K-Ka)	-K*exp(-Ka*t)/ Ka*(K-Ka)	Cum. Exc. Xut(t)	Int Excr. Xut(t)-Xut(t-1)
	0	0.0222	32.47	-200.00	167.53	0.0000	0.0000
	12	0.0222	32.47	-146.75	115.77	0.0331	0.0331
1	24	0.0222	32.47	-107.67	80.00	0.1064	0.0733
	36	0.0222	32.47	-79.01	55.28	0.1941	0.0877
2	48	0.0222	32.47	-57.97	38.20	0.2820	0.0879
	60	0.0222	32.47	-42.53	26.40	0.3626	0.0806
3	72	0.0222	32.47	-31.21	18.24	0.4329	0.0703
	84	0.0222	32.47	-22.90	12.60	0.4922	0.0593
4	96	0.0222	32.47	-16.80	8.71	0.5412	0.0490
	108	0.0222	32.47	-12.33	6.02	0.5808	0.0396
5	120	0.0222	32.47	-9.05	4.16	0.6124	0.0316
	132	0.0222	32.47	-6.64	2.87	0.6372	0.0248
	133	0.0222	32.47	-6.47	2.79	0.6392	0.0020
6	144	0.0222	32.47	-4.87	1.99	0.6569	0.0197
	156	0.0222	32.47	-3.57	1.37	0.6719	0.0150
7	168	0.0222	32.47	-2.62	0.95	0.6837	0.0118
	180	0.0222	32.47	-1.92	0.66	0.6928	0.0091
8	192	0.0222	32.47	-1.41	0.45	0.6995	0.0067
	204	0.0222	32.47	-1.04	0.31	0.7047	0.0052
9	216	0.0222	32.47	-0.76	0.22	0.7088	0.0041
	228	0.0222	32.47	-0.56	0.15	0.7118	0.0030
10	240	0.0222	32.47	-0.41	0.10	0.7140	0.0022

Values used for calculating chlorpyrifos exposure
0.85 = 0.6124 (amount excreted in 5 days)/ 0.72 (total amount of chlorpyrifos excreted in the urine as TCP)

6. Total Absorbed Chlorpyrifos (µg) Calculated By Study Report

Total chlorpyrifos (µg) absorbed after exposure was calculated by the study using two different methods. In both methods, 3,5,6-TCP was corrected for 1) background chlorpyrifos absorbed using the average chlorpyrifos absorbed from the two 12-hr pre-exposure samples and assuming that the background concentration was steady-state and 2)incomplete urine collection by normalizing the 5-day total 3,5,6-TCP exposure (µg) to an average creatinine rate of 1.8 g/day using worker-specific average daily creatinine rates (g/day).

In the first method (urinary excretion factor method), the amount of chlorpyrifos absorbed was estimated by dividing the cumulative amount of 3,5,6-TCP excreted in the urine over the five post-study days by 0.370. This urinary excretion factor (i.e., 0.370) was based on the kinetics of 3,5,6- TCP in human volunteers given single oral and dermal doses of chlorpyrifos. The urinary excretion factor corrects for the following: a) only 72% of an oral dose of chlorpyrifos was excreted in the urine as 3,5,6-TCP, b) only 91% of the urinary 3,5,6-TCP was expected to be eliminated during the interval 120 hr urine was collected, and c) the difference in molecular weights for 3,5,6-TCP and chlorpyrifos (i.e., 198 and 350.6).

In the second method (kinetic model method), the amount of chlorpyrifos absorbed was estimated by fitting the amount of 3,5,6-TCP excreted in the individual urine specimens to the one compartment

pharmacokinetic model that described the time-course of 3,5,6-TCP in urine of volunteers following application of chlorpyrifos to their forearm (Nolan et al., 1984 referenced in the Study Report). Based on Nolan et al. it was assumed that 72% of the absorbed chlorpyrifos would be excreted in the urine as 3,5,6-TCP. Initial optimizations were performed allowing only the amount of chlorpyrifos absorbed to vary while keeping the absorption (0.0308 hr-1) and elimination (0.0258 hr-1) rate constants at the average value reported by Nolan et al. In subsequent optimizations, the amount of chlorpyrifos absorbed and the absorption rate constant, and then the amount of chlorpyrifos absorbed and both the absorption and elimination rate constants were allowed to vary. This provided three optimized estimates for the amount of chlorpyrifos absorbed. The highest of these three estimates was taken as the estimate from kinetic modeling provided that the optimized absorption and/or elimination rate constants were within 2.576 standard deviation of mean value reported by Nolan et al. Optimization where the absorption, and/or elimination rate differed by more than 2.576 standard deviation from mean rate constants reported by Nolan et al were discarded as biologically implausible. All optimizations were based on the maximum likely hood function and performed using SIMUSOLV*, a computer modeling program that contains integration, optimization, and graphical routines.

Based on the study author's reported calculations for each worker, the average total absorbed chlorpyrifos for pickers as 34.4 µg using the urinary excretion factor method and 52.8 µg kinetic model method. For pruners, the average total chlorpyrifos absorbed after exposure as calculated using the urinary excretion factor method was 447 µg for Site # 5 and 205 µg for Site #6. Using the kinetic model method, the average total absorbed chlorpyrifos was 249 µg for Site # 5 and 160 µg for Site #6

The study author also reported the total absorbed dose (µg/kg/day) for each worker, assuming a body weight of 70 kg.

B. Blood Biological Monitoring

Plasma and RBC Cholinesterase levels

The plasma and RBC cholinesterase (ChE) levels at baseline and following entry are shown in Appendix A, Table 11. The ChE levels in plasma and/or RBC from the two pre-exposure samples (baseline) collected from each worker were within 15% of each other except for 6 workers. According to standard blood cholinesterase testing protocol, the levels for pre-exposure sample #2 must be within ±15% of pre-exposure sample #1 levels, and if not a 3rd sample should be collected and sample #2 and sample #3 data should then be used to calculate the baseline level. It does not appear that there was enough time to analyze a 3rd sample prior to initiation of the study. In a few cases the baseline level that could be calculated using the 2 pre-exposure readings in summary table of the Study Report does not match the baseline level actually reported in the summary table. No explanation for this discrepancy is provided in the Study Report. In these cases both numbers are reported in Appendix A, Table 11 and the % ChE activity presented in Appendix A, Table 11 was calculated using the baseline level which yields the most conservative % ChE activity reading. In all cases, except Pruner 8's plasma ChE activity, the calculated baseline level was used rather than the level reported in the summary table of the Study Report.

The % ChE activity was calculated for each worker using Equation 5.

*% ChE Activity = 1-(pre/post exposure plasma or RBC ChE level / baseline plasma or RBC ChE level) * 100 (Eq. 5)*

For picker entry workers, ChE activity ranged from + 5% to - 7% for plasma ChE and from + 6 % to - 5% for RBC ChE. For pruner entry workers, ChE activity ranged from + 13% to - 14% for plasma ChE and from + 33% to - 17% for RBC ChE.

C. Statistical Analysis of Biological Monitoring Measurements

Descriptive data analysis was performed to evaluate the relationship between worker total chlorpyrifos urinary excretion during the 5-day period following exposure, corrected for background levels of TCP and creatinine, and ChE activity. Figures 1 and 2 provide scatterplots of total TCP excretion and plasma and RBC ChE activity, respectively. These plots suggest that ChE activity is highly variable, since although some workers had decreased ChE levels, other workers had no change or increases in ChE levels. Figure 3 provides a further comparison of RBC and plasma ChE levels before and after workers re-entered the field treated with Lorsban*. As shown, some workers did experience decreases in ChE, but there was not a consistent downward trend across all three sites. However, a notable trend was observed in the plasma ChE levels of the five pruning workers from site #2. In particular, each worker's first baseline plasma ChE measurement was consistently lower than their second baseline plasma ChE measurement and their post-exposure plasma ChE measurement was consistently lower than their second baseline plasma ChE measurement. No explanation of this trend was identified in the Study Report, but one potential explanation is that they were exposed to an organophosphate insecticide that could have lowered their first plasma ChE measurement.

In general, descriptive analysis failed to identify a relationship between total urinary TCP excretion and either RBC or plasma ChE activity. The inability to identify a relationship, however, should not be interpreted as meaning that the analysis of the study results demonstrated that there is no relationship between urinary TCP excretion and ChE activity. This is because the study was not specifically designed to assess the relationship between TCP excretion and ChE activity. As a consequence, there are a number of limitations that may limit the study's power (e.g. ability to identify a relationship between urinary TCP excretion and ChE activity if a relationship does in fact exist). Some of these limitations include:

- It is unclear if measuring ChE levels on the day following exposure is the most appropriate time period to assess ChE activity. The study report provides no rationale for measuring post-exposure ChE levels on the day following exposure.
- The study did not control for factors that may confound the relationship between exposure and ChE levels. One important potential confounder is inter-individual sensitivity to ChE inhibition.
- According to the Study Report, OPP's 875.2600 Guideline indicates that a biological monitoring study should include a minimum of fifteen individual per activity. Although 15 workers were included in the study, there were only five replicates per study site.
- Although workers were asked to avoid contact with the chlorpyrifos insecticide Lorsban© four days before the start of the study period, several workers had detectable levels of TCP in their urine prior to their re-entry into the treated field. This suggests that some workers may have experienced chlorpyrifos exposures before re-entry, which may have affected their baseline ChE levels.

In addition, the descriptive analysis presented in this report may not be the most appropriate method to assess the relationship between TCP excretion and ChE activity. More formal statistical analysis could be conducted to see if there is a statistically significant relationship. This statistical analysis, however, would need to take into account the study design, since repeated measures were taken on individual workers and workers were nested into three groups that experienced chlorpyrifos exposure in different conditions.

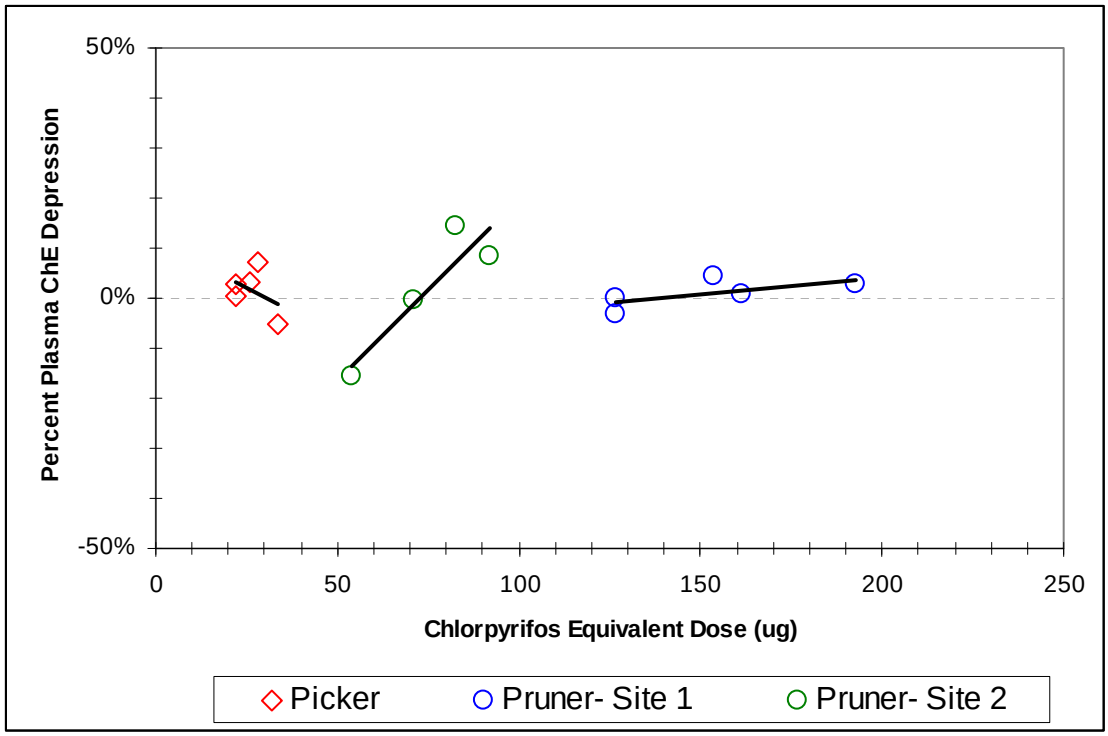


Figure 1: Relationship between plasma ChE activity (%) and chlorpyrifos equivalent dose (ug) based on collection of urine for 5 days following exposure.

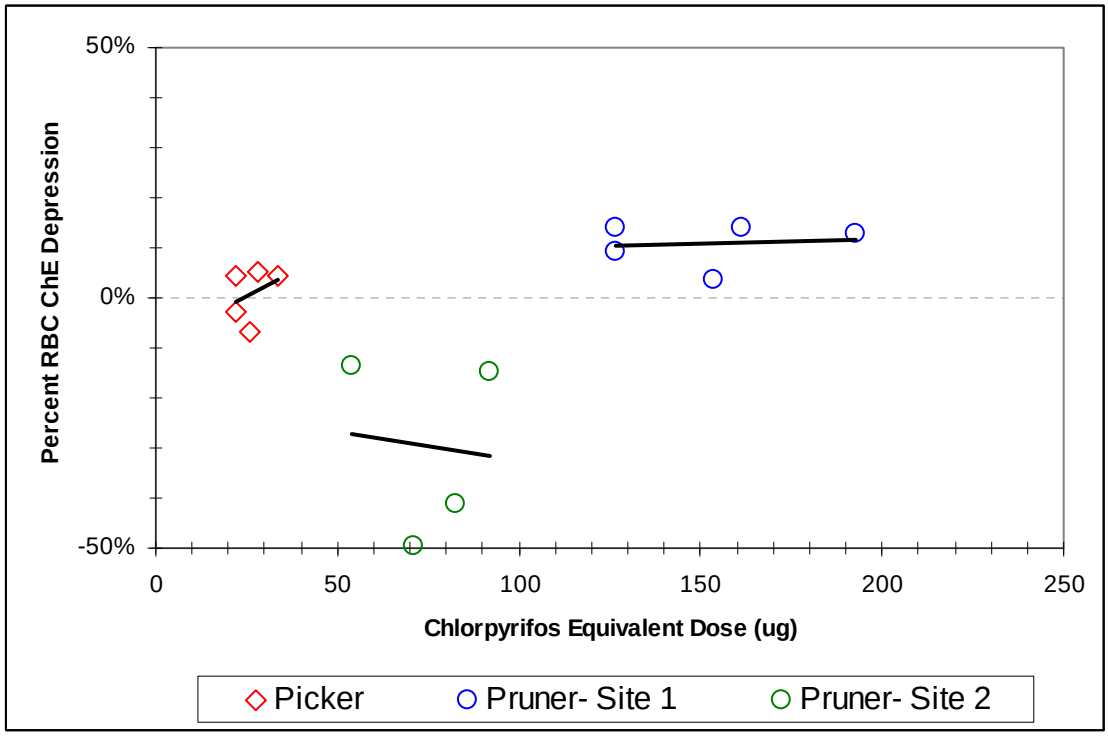


Figure 2: Relationship between red blood cell (RBC) ChE activity (%) and chlorpyrifos equivalent dose (ug) based on collection of urine for 5 days following exposure activity.

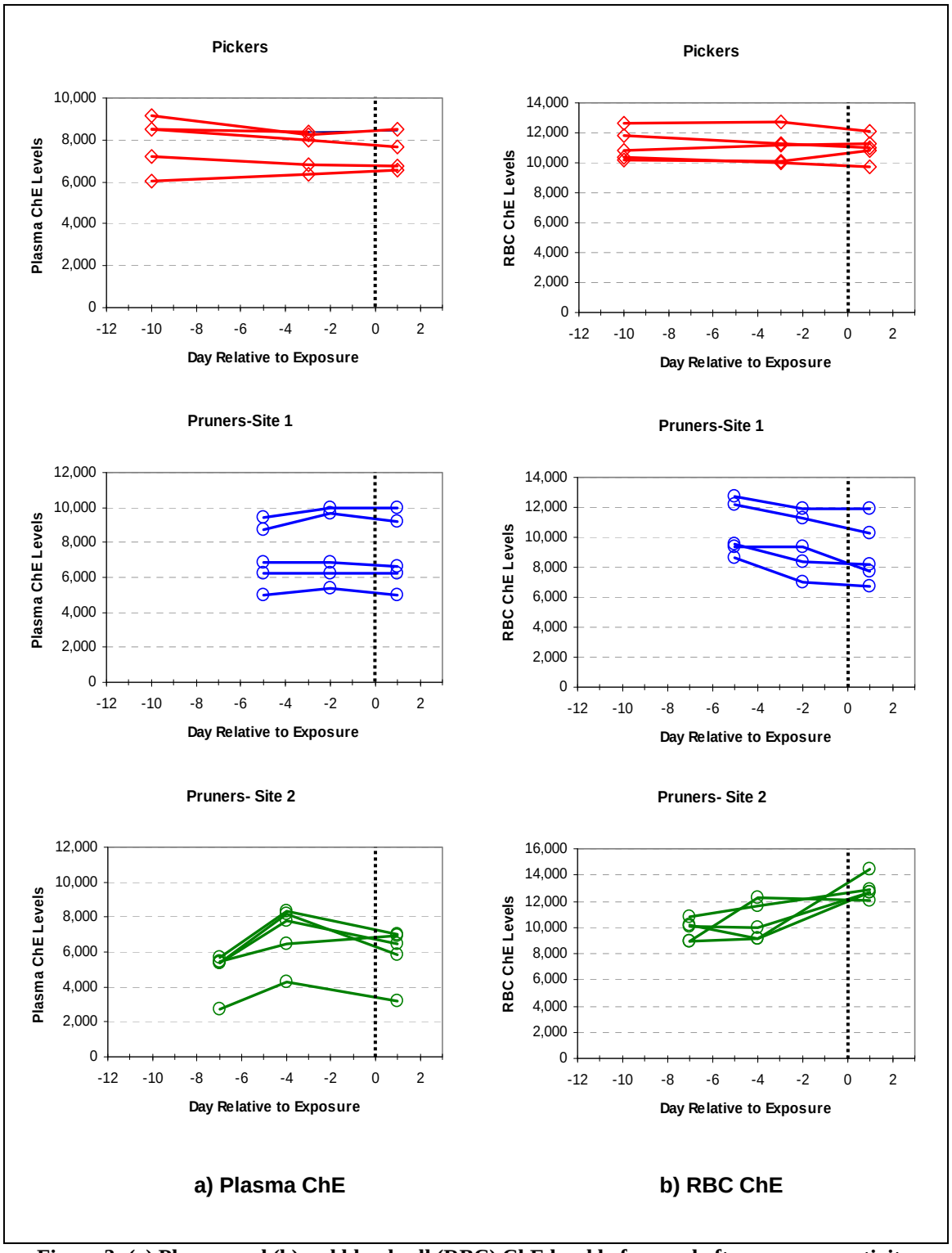


Figure 3: (a) Plasma and (b) red blood cell (RBC) ChE level before and after exposure activity (dashed line indicates day of exposure activity).

Appendix A
Biological Monitoring Results and Compliance Checklist

Table 1. Summary of Daily Urine Volumes (ml) and Creatinine Rates (g/day) in Urine Samples from Workers Collected from the Pre-Exposure Day through Day 4 After Entry

Type of worker (site)	Worker #	Number of days sampled	Urine Volume (ml/day)[1]		Creatinine (g/day)[2, 4]	
			Range	Average ± Standard Deviation	Range	Average ± Standard Deviation
Picker (Site #2)	1	6	716 – 1,369	1,084 ± 248	1.27- 1.56	1.40 ± 0.11
	2	6	825 – 2,781	1,442 ± 700	0.39 - 1.75	1.09 ± 0.61
	3	6	1015 – 494	1,272 ± 188	1.43 - 1.88	1.67 ± 0.18
	4	6	1,392 – 4,025	2,477 ± 951	1.18 - 1.41	1.32 ± 0.08
	5	6	938 – 2,273	1,415 ± 531	1.33 - 2.1	1.66 ± 0.27
Pruner (Site #5)	1	6	297 – 1,018	668 ± 259	0.46 - 1.27	0.91 ± 0.29
	2	6	336 – 1,102	727 ± 266	0.53 - 2.11	1.41 ± 0.58
	3	6	640 – 1,529	1,028 ± 386	0.37 - 1.46	0.94 ± 0.38
	4	6	561 – 1,505	967 ± 331	0.81 - 1.77	1.19 ± 0.44
	5	6	529 – 1,787	1,084 ± 564	1.15 - 2.62	1.81 ± 0.57
Pruner (Site #6)	6	4[3]	495-755	664 ± 116	0.52 - 0.134	0.85 ± 0.38
	7	6	623 – 1,486	972 ± 355	0.3 - 2.3	1.41 ± 0.64
	8	6	487 – 916	706 ± 175	0.75 - 1.37	1.01 ± 0.22
	9	6	645 – 1,898	1,151 ± 453	0.27 - 2.01	1.15 ± 0.63
	10	6	551 – 1,348	1,025 ± 328	0.72 - 1.53	1.20 ± 0.32
Overall					0.3 – 2.62	1.27 ± 0.29 (range 0.85 to 1.81)

[1] The volume of urine was calculated from the weight of the sample and assuming a specific gravity of 1.0.
[2] Creatinine was measured in all urine samples, which were collected over approximate 12 hour intervals starting 24 hours prior to exposure through 4 days after exposure. Daily creatinine (g/day) = 0 to 12 hr creatinine (g/12 hr) + 12 to 24 hr creatinine (g/12 hr).
[3] Only four 24-hr creatinine measurements are available for Pruner #6 because samples were not collected/analyzed at the 48 to 60 hr interval or the 108 to 120 hr intervals. The monitoring unit was excluded from the summary analyses.
[4] According the Study Report, the standard literature values for creatinine in urine average 1.8 g/day with a 95% confidence interval range of 1.1 to 2.5 g/day (Documenta Geigy, 1970).

Table 2. 3,5,6-TCP (µg) in Urine by Individual Pickers

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg/sample) [b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
ICKER #1													
-1 (pre-xposure)	-24 to -12	217	4.2	0.91	1.7	1.35	1.40	--	--	--	--	--	--
	-12 to 0	499	<LOQ	0.75									
0	0 to 12	303	4.7	1.42	6.9	1.56		6.88	7.94	**6.88**	**6.13**	7.07	**6.13**
	12 to 24	620	8.8	5.46									
1	24 to 36	272	10	2.72	6.7	1.39		**6.69**	**8.67**	6.76	5.94	**7.70**	6.00
	36 to 48	779	5.1	3.97									
2	48 to 60	310	3.8	1.18	4.2	1.27		4.22	5.98	4.67	3.47	4.92	3.84
	60 to 72	801	3.8	3.04									
3	72 to 84	783	<LOQ	1.17	2.9	1.34		2.93	3.94	3.07	2.18	2.93	2.29
	84 to 96	586	3.0	1.76									
4	96 to 108	245	5.0	1.23	2.9	1.51		2.86	3.41	2.86	2.11	2.52	2.11
	108 to 120	1089	<LOQ	1.63									
otal of Days 0-4 post-exposure for Picker #1 (n=5 days)								23.6	29.9	24.2	19.8	25.1	20.4
ICKER #2													
-1 (pre-xposure)	-24 to -12	199	7.8	1.55	3.2	0.87	1.09	--	--	--	--	--	--
	-12 to 0	1125	<LOQ	1.69									
0	0 to 12	230	6.7	1.54	6.1	1.75		**6.12**	6.30	6.12	**4.44**	4.56	4.44
	12 to 24	595	7.7	4.58									
1	24 to 36	185	5.7	1.05	2.2	0.39		2.24	10.3	6.25	0.554	2.55	1.54
	36 to 48	791	<LOQ	1.19									

Table 2. 3,5,6-TCP (µg) in Urine by Individual Pickers

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg/sample) [b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
2	48 to 60	330	4.2	1.39	4.1	1.75		4.12	4.23	4.12	2.43	2.50	2.43
	60 to 72	910	3.0	2.73									
3	72 to 84	1378	<LOQ	2.07	4.2	0.47		4.17	**16.0**	**9.66**	4.17[i]	**16.0**	**9.66**
	84 to 96	1403	<LOQ	2.10									
4	96 to 108	345	<LOQ	0.52	2.3	1.30		2.25	3.1	2.25	2.25 [i]	3.12	2.25
	108 to 120	1158	<LOQ	1.74									
Total of Days 0-4 post-exposure for Picker #2 (n=5 days)								18.9	40.0	28.4	13.8	28.7	20.3

Table 2. 3,5,6-TCP (µg) in Urine by Individual Pickers

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg/sample) [b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
ICKER #3													
-1 (pre-exposure)	-24 to -12	426	5.1	2.17	5.4	1.48		--	--	--	--	--	--
	-12 to 0	693	4.7	3.26									
0	0 to 12	281	9.3	2.61	10.2	1.78		10.17	10.3	10.2	6.92	6.99	6.92
	12 to 24	734	10.3	7.56									
1	24 to 36	344	8.8	3.03	10.6	1.88		**10.56**	**10.6**	**10.6**	**7.31**	**7.31**	**7.31**
	36 to 48	1125	6.7	7.54									
2	48 to 60	521	5.6	2.92	8.1	1.65	1.67	8.14	8.88	8.2	4.88	5.33	4.94
	60 to 72	746	7.0	5.22									
3	72 to 84	506	3.9	1.97	5.1	1.43		5.14	6.46	6.0	1.88	2.36	2.19
	84 to 96	988	3.2	3.16									
4	96 to 108	636	3.7	2.35	5.8	1.80		5.77	5.77	5.8	2.51	2.51	2.51
	108 to 120	633	5.4	3.42									
otal of Days 0-4 post-exposure for Picker #3 (n=5 days)								39.8	42.0	40.7	23.5	24.5	23.9
ICKER #4													
-1 (pre-exposure)	-24 to -12	339	6.1	2.07	4.2	1.31	1.3	--	--	--	--	--	--
	-12 to 0	1421	<LOQ	2.13									
0	0 to 12	419	5.1	2.14	8.7	1.33		**8.66**	11.7	**8.66**	**6.52**	8.83	6.52
	12 to 24	973	6.7	6.52									
1	24 to 36	705	<LOQ	1.06	7.8	1.36		7.81	**10.3**	7.81	5.68	7.52	5.68
	36 to 48	2251	3.0	6.75									
2	48 to 60	1979	<LOQ	2.97	7.5	1.41		7.48	9.54	7.48	5.34	6.82	5.34
	60 to 72	683	6.6	4.51									

Table 2. 3,5,6-TCP (µg) in Urine by Individual Pickers

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg/sample) [b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
3	72 to 84	2673	<LOQ	4.01	6.0	1.18		6.04	9.21	6.75	6.04[1]	**9.21**	**6.75**
	84 to 96	1352	<LOQ	2.03									
4	96 to 108	355	3.6	1.28	3.8	1.32		3.85	5.24	3.85	1.71	2.34	1.71
	108 to 120	1712	<LOQ	2.57									
Total of Days 0-4 post-exposure for Picker #4 (n=5 days)								33.8	46.1	34.5	25.3	34.7	26.0

Table 2. 3,5,6-TCP (µg) in Urine by Individual Pickers

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg/sample) [b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
ICKER #5													
-1 (pre-exposure)	-24 to -12	470	3.5	1.65	3.0	2.1	1.66	--	--	--	--	--	--
	-12 to 0	468	3.0	1.40									
0	0 to 12	247	4.6	1.14	8.6	1.64		8.63	9.47	8.72	7.23	7.93	7.30
	12 to 24	707	10.6	7.49									
1	24 to 36	376	8.0	3.01	8.8	1.63		**8.76**	**9.67**	**8.90**	**7.35**	**8.12**	**7.47**
	36 to 48	871	6.6	5.75									
2	48 to 60	614	3.8	2.33	6.6	1.33		6.60	8.93	8.22	5.20	7.03	6.47
	60 to 72	1219	3.5	4.27									
3	72 to 84	1491	<LOQ	2.24	5.6	1.79		5.60	5.63	5.60	4.20	4.22	4.20
	84 to 96	782	4.3	3.36									
4	96 to 108	624	4.4	2.75	6.1	1.45		6.10	7.58	6.97	4.70	5.83	5.37
	108 to 120	622	5.4	3.36									
otal of Days 0-4 post-exposure for Picker #5 (n=5 days)								35.7	41.3	38.4	28.7	33.1	30.8

Footnotes:

Note: LOQ = 3 ng/g. Residues reported as <LOQ were assigned a value of ½ LOQ in all calculations.

a. Sampling intervals are approximate. Actual sampling intervals were not exactly 12 hours in duration. The sampling day started in the morning and continued until the next morning.

b. 3,5,6-TCP (µg) = Sample concentration (ng/g) * Sample weight (g)

c. Creatinine was measured in each 12 hr sample. Daily creatinine excretion is the sum of creatinine measured in both 12 hour samples on one sampling day.

d. 3,5,6-TCP (µg) was not corrected for field fortification recovery because recoveries were >90%.

e. 3,5,6-TCP (µg) was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

f. 3,5,6-TCP (µg) was corrected for background and/or incomplete urine (i.e. creatinine) using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr

interval) was subtracted out of each 24-hr residue. Incomplete urine collection was corrected using two different methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine rate. The "Literature Average" method involves comparing the creatinine rate in each 24-hr residue sample to the literature standard of 1.8 g/day and the "Worker-Specific Average" method involves comparing the creatinine rate in each 24-hr residue sample to the average daily creatinine rate of the specific worker.

g. The sample containing the maximum daily 24-hr excretion of 3,5, 6-TCP over the monitoring period is **bolded**. .

h. Total 3,5,6-TCP (µg) = Sum of Day 0, 1, 2, 3, and 4 levels

i. Because Picker #2 residues on Day 3 and 4 and Picker #4 residues on Day 3 were <LOQ, background residues were not subtracted out.

Table 3. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #5

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg)[b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
Pruner #1													
-1 (pre-exposure)	-24 to -12	385	5.3	2.04	4.8	0.79	0.91	--	--	--	--	--	--
	-12 to 0	311	8.8	2.74									
0	0 to 12	494	10.5	5.19	48.4	1.00		**48.4**	**87.1**	**48.4**	**45.6**	**82.2**	**45.6**
	12 to 24	367	117.7	43.20									
1	24 to 36	194	27.9	5.41	16.5	0.46		16.5	64.7	32.7	13.8	54.0	27.3
	36 to 48	103	108.1	11.13									
2	48 to 60	200	36.1	7.22	17.4	0.82		17.4	38.2	19.3	14.7	32.2	16.3
	60 to 72	277	36.8	10.19									
3	72 to 84	542	17.7	9.59	21.4	1.27		21.4	30.3	21.4	18.6	26.4	18.6
	84 to 96	476	24.7	11.76									
4	96 to 108	202	25.7	5.19	12.1	1.12		12.1	19.4	12.1	9.34	15.0	9.34
	108 to 120	459	15	6.89									
Total of Days 0-4 post-exposure for Pruner #1 (n=5 days)								116	240	134	102	210	117
Pruner #2													
-1 (pre-exposure)	-24 to -12	137	5.9	0.81	1.6	0.53	1.41	--	--	--	--	--	--
	-12 to 0	199	4.2	0.84									
0	0 to 12	360	4.5	1.62	32.9	0.92		32.90	64.4	**50.3**	32.1	**62.7**	**49.0**
	12 to 24	336	93.1	31.28									
1	24 to 36	451	31.1	14.03	35.4	1.83		**35.38**	**63.9**	35.4	**34.5**	34.5	34.5
	36 to 48	651	32.8	21.35									
2	48 to 60	401	40.9	16.40	33.1	1.49		33.13	40.0	33.1	32.3	39.0	32.3

Table 3. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #5													
								3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg)[b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
	60 to 72	406	41.2	16.73									
3	72 to 84	318	29.5	9.38	19.4	1.56		19.37	22.3	19.4	18.5	21.4	18.5
	84 to 96	229	43.6	9.98									
4	96 to 108	530	17.6	9.33	15.4	2.11		15.43	35.4	15.4	14.6	14.6	14.6
	108 to 120	343	17.8	6.11									
Total of Days 0-4 post-exposure for Pruner #2 (n=5 days)								136	226	154	132	172	149

Table 3. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #5

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg)[b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
Pruner #3													
-1 (pre-exposure)	-24 to -12	878	3.7	3.25	5.2	0.83	0.94	--	--	--	--	--	--
	-12 to 0	581	3.3	1.92									
0	0 to 12	1006	10.3	10.36	45.3	1.17		**45.3**	**69.7**	**45.3**	**43.4**	**66.7**	**43.4**
	12 to 24	523	66.8	34.94									
1	24 to 36	410	46.2	18.94	27.9	0.73		27.9	68.7	35.8	26.0	64.0	33.3
	36 to 48	576	15.5	8.93									
2	48 to 60	456	39.8	18.15	29.6	1.46		29.6	36.5	29.6	27.7	34.2	27.7
	60 to 72	442	26	11.49									
3	72 to 84	231	21	4.85	10.0	1.06		10.0	17.0	10.0	8.08	13.7	8.08
	84 to 96	422	12.2	5.15									
4	96 to 108	69	14.3	0.987	1.84	0.37		1.84	9.0	4.7	1.84[i]	8.97	4.67
	108 to 120	571	<LOQ	0.857									
Total of Days 0-4 post-exposure for Pruner #3 (n=5 days)								115	201	125	107	188	117
Pruner #4													
-1 (pre-exposure)	-24 to -12	425	<LOQ	0.64	2.0	0.93	1.2	--	--	--	--	--	--
	-12 to 0	360	3.7	1.33									
0	0 to 12	795	6.3	5.01	30.3	1.73		30.3	31.5	30.3	29.0	30.1	29.0
	12 to 24	710	35.6	25.28									
1	24 to 36	289	67.6	19.54	51.6	0.96		**51.6**	**96.7**	**63.8**	**50.2**	**94.2**	**62.2**
	36 to 48	272	117.7	32.01									
2	48 to 60	448	78.2	35.03	49.4	1.77		49.4	50.2	49.4	48.0	48.9	48.0
	60 to 72	366	39.2	14.35									

Table 3. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #5													
								3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg)[b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
3	72 to 84	709	25.5	18.08	20.3	0.93		20.3	39.2	25.9	18.9	36.6	24.2
	84 to 96	454	4.8	2.18									
4	96 to 108	561	16	8.98	11.3	0.81		11.3	25.1	16.6	10.0	22.2	14.6
	108 to 120	410	5.7	2.34									
Total of Days 0-4 post-exposure for Pruner #4 (n=5 days)								163	243	186	156	232	178

Table 3. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #5

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg)[b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	METHOD 2 Corrected for Creatinine Only (Literature Average)	METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)	METHOD 4 Corrected for Background Only	METHOD 5 Corrected for Background AND Creatinine (Literature Average)	METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)
Pruner #5													
-1 (pre-exposure)	-24 to -12	251	7.5	1.88	4.7	1.15	1.81	--	--	--	--	--	--
	-12 to 0	278	10.1	2.81									
0	0 to 12	662	12.4	8.21	58.3	2.62		**58.3**	**58.3**	**58.3**	**55.5**	**55.5**	**55.5**
	12 to 24	1125	44.5	50.06									
1	24 to 36	883	17.9	15.81	37.1	2.12		37.1	37.1	37.1	34.3	34.3	34.3
	36 to 48	861	24.7	21.27									
2	48 to 60	463	31.3	14.49	20.3	1.30		20.3	28.2	28.4	17.5	24.3	24.5
	60 to 72	148	39.5	5.85									
3	72 to 84	272	26.4	7.18	17.8	1.56		17.8	20.6	20.7	15.0	17.4	17.5
	84 to 96	452	23.6	10.67									
4	96 to 108	325	14.4	4.68	13.0	2.13		13.0	13.0	13.0	10.2	10.2	10.2
	108 to 120	784	10.6	8.31									
Total of Days 0-4 post-exposure for Pruner #5 (n=5 days)								147	157	157	132	142	142

Footnotes:

Note: LOQ = 3 ng/g. Residues reported as <LOQ were assigned a value of ½ LOQ in all calculations.

a. Sampling intervals are approximate. Actual sampling intervals were not exactly 12 hours in duration. The sampling day started in the morning and continued until the next morning.

b. 3,5,6-TCP (µg) = Sample concentration (ng/g) * Sample weight (g)

c. Creatinine was measured in each 12 hr sample. Daily creatinine is the sum of creatinine measured in both 12 hour samples on one sampling day.

d. 3,5,6-TCP (µg) was not corrected for field fortification recovery because recoveries were >90%.

e. 3,5,6-TCP (µg) was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

f. 3,5,6-TCP (µg) was corrected for background and/or incomplete urine (i.e. creatinine) using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr

interval) was subtracted out of each 24-hr residue. Incomplete urine collection was corrected using two different methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine rate. The "Literature Average" method involves comparing the creatinine rate in each 24-hr residue sample to the literature standard of 1.8 g/day and the "Worker-Specific Average" method involves comparing the creatinine rate in each 24-hr residue sample to the average daily creatinine rate of the specific worker.

g. The sample containing the maximum daily 24-hr excretion of 3,5, 6-TCP over the monitoring period is **bolded**. .

h. Total 3,5,6-TCP (µg) = Sum of Day 0, 1, 2, 3, and 4 residues

i. For Pruner monitoring unit #3, the concentration on Day 4 was less than the background concentration, therefore background was not subtracted out.

Table 4. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #6

Day After Entry	Sampling Interval (hr) [a]	Sample Weight (g)	3,5,6-TCP (ng/g)	3,5,6-TCP (µg)[b]	3,5,6-TCP (µg/24 hr)	Daily Creatinine (g/24 hr) [c]	Average Creatinine (g/day)	3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
								METHOD 1 Not Corrected for Background or Creatinine	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
Pruner #6[i]													
-1	-24 to -12	300	<LOQ	0.45	0.7	0.58	0.63	--	--	--	--	--	--
	-12 to 0	195	<LOQ	0.29									
0	0 to 12	200	20.2	4.04	16.7	0.95		16.7	31.6	16.7	16.4	31.0	16.4
	12 to 24	519	24.3	12.61									
1	24 to 36	385	93.8	36.11	49.6	1.34		**49.6**	**66.7**	**49.6**	**49.3**	**66.3**	**49.3**
	36 to 48	370	36.5	13.51									
2	48 to 60	lost	49	NA	NA	0.30		NA	NA	NA	NA	NA	NA
	60 to 72	461	5.5	2.54									
3	72 to 84	472	1.5	0.71	1.4	0.52		1.41	4.90	1.7	1.12	3.88	1.36
	84 to 96	214	3.3	0.71									
4	96 to 108	81	4.5	0.36	NA	0.09		NA	NA	NA	NA	NA	NA
	108 to 120	no sample	NA	NA									
Total of Days 0-4 post-exposure for Pruner #6 (n=5 days)								NA	NA	NA	NA	NA	NA
Pruner #7													
-1	-24 to -12	347	7.6	2.64	4.4	1.56	1.41	--	--	--	--	--	--
	-12 to 0	325	5.3	1.72									
0	0 to 12	335	13.4	4.49	27.6	1.47		**27.6**	33.8	**27.6**	**25.8**	31.7	**25.8**
	12 to 24	410	56.3	23.08									
1	24 to 36	432	25.4	14.83	27.2	1.41		27.2	**34.7**	27.2	25.5	**32.5**	25.5
	36 to 48	584	13.4	12.37									
2	48 to 60	923	<LOQ	0.55	5.5	0.30		5.48	32.9	25.7	3.76	22.5	17.6

Table 4. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #6													
								3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
Day After Entry	**Sampling Interval (hr) [a]**	**Sample Weight (g)**	**3,5,6-TCP (ng/g)**	**3,5,6-TCP (µg)[b]**	**3,5,6-TCP (µg/24 hr)**	**Daily Creatinine (g/24 hr) [c]**	**Average Creatinine (g/day)**	**METHOD 1 Not Corrected for Background or Creatinine**	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
	60 to 72	366	5.2	4.93									
3	72 to 84	948	9.7	5.22	7.9	2.30		7.87	7.87	7.87	6.15	6.15	6.15
	84 to 96	538	9.9	2.65									
4	96 to 108	268	16.4	5.82	11.7	1.41		11.7	14.9	11.7	9.9	12.7	9.9
	108 to 120	355	13.9	5.84									
Total of Days 0-4 post-exposure for Pruner #7 (n=5 days)								79.8	124	100	71.2	106	85.0

Table 4. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #6													
								3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
Day After Entry	**Sampling Interval (hr) [a]**	**Sample Weight (g)**	**3,5,6-TCP (ng/g)**	**3,5,6-TCP (µg)[b]**	**3,5,6-TCP (µg/24 hr)**	**Daily Creatinine (g/24 hr) [c]**	**Average Creatinine (g/day)**	**METHOD 1 Not Corrected for Background or Creatinine**	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
Pruner #8													
-1	-24 to -12	420	5.8	2.44	3.3	0.75	1.01	--	--	--	--	--	--
	-12 to 0	230	3.9	0.90									
0	0 to 12	179	26.3	4.71	22.1	1.01		**22.1**	**39.3**	**22.2**	**21.2**	**37.7**	**21.3**
	12 to 24	308	56.4	17.37									
1	24 to 36	583	16.3	9.50	15.2	0.86		15.2	31.8	17.9	14.3	29.9	16.8
	36 to 48	333	17.1	5.69									
2	48 to 60	159	40.8	6.49	13.0	1.37		13.0	17.1	13.0	12.1	15.9	12.1
	60 to 72	715	9.1	6.51									
3	72 to 84	273	16.8	4.59	8.6	0.96		8.62	16.2	9.1	7.73	14.5	8.16
	84 to 96	271	14.9	4.04									
4	96 to 108	360	14.9	5.36	8.3	1.13		8.29	13.2	8.3	7.39	11.8	7.39
	108 to 120	406	7.2	2.92									
Total of Days 0-4 post-exposure for Pruner #8 (n=5 days)								67.2	118	70.4	62.7	110	65.7
Pruner #9													
-1	-24 to -12	303	9.6	2.91	7.8	1.2	1.15	--	--	--	--	--	--
	-12 to 0	342	14.3	4.89									
0	0 to 12	371	7.3	2.71	12.6	0.82		12.6	49.4	31.6	7.7	17.0	10.9
	12 to 24	653	15.2	9.93									
1	24 to 36	826	12.8	10.57	26.8	1.70		38.2	40.4	38.2	21.9	**23.2**	21.9
	36 to 48	639	25.4	16.23									
2	48 to 60	832	<LOQ	1.25	2.8	0.27		3.00	20.0	12.8	3.00[j]	20.0	12.8
	60 to 72	1066	<LOQ	1.60									

Table 4. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #6													
								3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
Day After Entry	**Sampling Interval (hr) [a]**	**Sample Weight (g)**	**3,5,6-TCP (ng/g)**	**3,5,6-TCP (µg)[b]**	**3,5,6-TCP (µg/24 hr)**	**Daily Creatinine (g/24 hr) [c]**	**Average Creatinine (g/day)**	**METHOD 1 Not Corrected for Background or Creatinine**	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
3	72 to 84	675	22.9	15.46	27.4	2.01		**60.6**	**60.6**	**60.6**	**22.6**	22.6	**22.6**
	84 to 96	318	37.7	11.99									
4	96 to 108	313	15	4.70	11.3	0.91		26.5	52.4	33.5	6.4	12.6	8.05
	108 to 120	570	11.5	6.56									
Total of Days 0-4 post-exposure for Pruner #9 (n=5 days)								141	223	177	62	95.3	76.2

Table 4. 3,5,6-TCP (µg) In Urine by Individual Pruners at Site #6													
								3,5,6-TCP Excreted (µg) [d, e, f, g, h]					
Day After Entry	**Sampling Interval (hr) [a]**	**Sample Weight (g)**	**3,5,6-TCP (ng/g)**	**3,5,6-TCP (µg)[b]**	**3,5,6-TCP (µg/24 hr)**	**Daily Creatinine (g/24 hr) [c]**	**Average Creatinine (g/day)**	**METHOD 1 Not Corrected for Background or Creatinine**	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
Pruner #10													
-1	-24 to -12	794	3	2.38	3.0	1.53	1.20	--	--	--	--	--	--
	-12 to 0	416	<LOQ	0.62									
0	0 to 12	346	8.7	3.01	8.6	0.98		**36.2**	**66.5**	**44.4**	8.02	14.7	9.84
	12 to 24	205	27.5	5.64									
1	24 to 36	407	18.8	7.65	15.7	1.38		34.4	44.9	34.4	**15.0**	**19.6**	**15.0**
	36 to 48	514	15.6	8.02									
2	48 to 60	751	<LOQ	1.13	5.7	1.13		9.30	14.8	9.89	5.11	8.14	5.44
	60 to 72	591	7.8	4.61									
3	72 to 84	171	<LOQ	0.26	6.4	0.72		11.7	29.3	19.5	5.8	14.5	9.67
	84 to 96	604	10.2	6.16									
4	96 to 108	332	10.7	3.55	10.4	1.47		17.4	21.3	17.4	9.7	11.9	9.74
	108 to 120	1016	6.7	6.81									
Total of Days 0-4 post-exposure for Pruner #10 (n=5 days)								109	177	126	43.7	68.9	49.7

Footnotes:

Note: LOQ = 3 ng/g. Residues reported as <LOQ were assigned a value of ½ LOQ in all calculations.

a. Sampling intervals are approximate. Actual sampling intervals were not exactly 12 hours in duration. The sampling day started in the morning and continued until the next morning.

b. 3,5,6-TCP (µg) = Sample concentration (ng/g) * Sample weight (g)

c. Creatinine was measured in each 12 hr sample. Daily creatinine excreted is the sum of creatinine measured in both 12 hour samples on one sampling day.

d. 3,5,6-TCP (µg) was not corrected for field fortification recovery because recoveries were >90%.

e. 3,5,6-TCP (µg) was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

f. 3,5,6-TCP (µg) was corrected for background and/or incomplete urine (i.e. creatinine) using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr

interval) was subtracted out of each 24-hr residue. Incomplete urine collection was corrected using two different methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine rate. The "Literature Average" method involves comparing the creatinine rate in each 24-hr residue sample to the literature standard of 1.8 g/day and the "Worker-Specific Average" method involves comparing the creatinine rate in each 24-hr residue sample to the average daily creatinine rate of the specific worker.

g. The sample containing the maximum daily 24-hr excretion of 3,5, 6-TCP over the monitoring period is **bolded**.

h. Total 3,5,6-TCP (µg) = Sum of Day 0, 1, 2, 3, and 4 residues

i. Total 3,5,6-TCP (µg) was calculated for pruner #6 because samples were lost or not collected at intervals 48 to 60 hr and 108 to 120 hr.

j. Because Picker #9 residues on Day 2 were <LOQ, background residues were not subtracted out.

Table 5. Summary of 3,5,6-TCP (µg) In Urine By Day For Pickers (n=5) at Site #2 [a, b, c, d, e]							
Day After Entry	Statistical Parameter	**METHOD 1** Not Corrected for Background or Creatinine	**METHOD 2** Corrected for Creatinine Only (Literature Average)	**METHOD 3** Corrected for Creatinine Only (Worker-Specific Average)	**METHOD 4** Corrected for Background Only	**METHOD 5** Corrected for Background AND Creatinine (Literature Average)	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
0	Minimum	6.12	6.30	6.12	4.44	4.56	4.44
	Maximum	10.2	11.7	10.2	7.23	8.83	7.30
	Average	**8.09**	9.14	**8.11**	**6.25**	**7.08**	**6.26**
	Standard Deviation	1.60	2.10	1.61	1.09	1.59	1.110
	CV (%)	19.8	22.9	19.9	17.5	22.5	17.7
	Geometric Mean	7.96	8.94	7.98	6.16	6.91	6.17
1	Minimum	2.24	8.67	6.25	0.55	2.55	1.54
	Maximum	10.6	10.6	10.6	7.35	8.12	7.47
	Average	7.21	**9.92**	8.06	5.37	6.64	5.60
	Standard Deviation	3.12	0.775	1.73	2.80	2.30	2.40
	CV (%)	43.3	7.81	21.5	52.1	34.7	42.8
	Geometric Mean	6.41	9.89	7.91	3.98	6.15	4.92
2	Minimum	4.12	4.23	4.12	2.43	2.50	2.43
	Maximum	8.14	9.54	8.24	5.34	7.03	6.47
	Average	6.11	7.51	6.54	4.26	5.32	4.60
	Standard Deviation	1.86	2.30	2.00	1.27	1.82	1.54
	CV (%)	30.4	30.6	30.5	29.7	34.3	33.4
	Geometric Mean	5.87	7.19	6.27	4.09	5.01	4.37
3	Minimum	2.93	3.94	3.07	1.88	2.36	2.19
	Maximum	6.04	16.0	9.7	6.04	15.98	9.66
	Average	4.78	8.24	6.21	3.69	6.94	5.02
	Standard Deviation	1.24	4.72	2.37	1.70	5.73	3.19
	CV (%)	26.0	57.3	38.1	46.0	82.5	63.5
	Geometric Mean	4.63	7.33	5.83	3.37	5.33	4.24
4	Minimum	2.25	3.12	2.25	1.715	2.34	1.71
	Maximum	6.10	7.58	6.97	4.70	5.83	5.37
	Average	4.17	5.02	4.34	2.66	3.26	2.79
	Standard Deviation	1.72	1.83	1.99	1.18	1.47	1.47
	CV (%)	41.2	36.4	45.8	44.3	44.9	52.6
	Geometric Mean	3.87	4.76	3.98	2.49	3.06	2.56
Total	Minimum	18.9	29.9	24.2	13.8	24.5	20.3
	Maximum	39.8	46.1	40.7	28.7	34.7	30.8
	Average	30.4 **(4)** [e]	39.8 **(6)** [e]	33.3 **(5)** [e]	22.2 **(1)** [e]	29.2 **(3)** [e]	24.3 **(2)** [e]
	Standard Deviation	8.75	5.99	6.88	5.67	4.60	4.38
	CV (%)	28.8	15.0	20.7	25.5	15.7	18.0
	Geometric Mean	29.3	39.4	32.7	21.6	29.0	24.0

a. 3,5,6-TCP (µg) in urine was corrected for background and/or potential incomplete urine collection using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr interval) was

subtracted out of each 24-hr residue. Potential incomplete urine collection was addressed using two different correction methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine excretion rate. The "Literature Standard" method involves comparing the creatinine rate in each 24-hr urine sample to the literature standard of 1.8 g/day and the "Worker-Specific" method involves comparing the creatinine rate in each 24-hr urine sample to the individual's average daily creatinine excretion rate.

b. 3,5,6-TCP (µg) excreted was not corrected for field fortification because recoveries were >90%.

c. 3,5,6-TCP (µg) excreted was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

d. The maximum average 24-hr excretion of 3,5,6-TCP over the monitoring period is **bolded**.

e. The average total 3,5,6-TCP (µg) values are ranked in parenthesis from lowest (1) to highest (6).

Table 6. Summary of 3,5,6-TCP In Urine (µg) By Day for Pruners (Site #5 and #6 Combined) [a, b, c, d, e,]							
Day After Entry	Statistical Parameter	**METHOD 1** Not Corrected for Background or Creatinine	**METHOD 2** Corrected for Creatinine Only (Literature Average)	**METHOD 3** Corrected for Creatinine Only (Worker-Specific Average)	**METHOD 4** Corrected for Background Only	**METHOD 5** Corrected for Background AND Creatinine (Literature Average)	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
0	Minimum	12.6	31.5	22.2	7.74	14.7	9.84
	Maximum	58.3	87.1	58.3	55.5	82.2	55.5
	Average	**34.8**	**56**	**39.8**	**29.8**	**44.3**	**32.3**
	Standard Deviation	14.0	18.5	12.2	16.4	23.5	16.8
	CV (%)	40.3	33.4	30.7	55.0	53.1	52.1
	Geometric Mean	32.0	52.7	38.0	24.7	38.2	27.6
1	Minimum	15.2	31.8	17.9	13.8	19.6	15.0
	Maximum	51.6	96.7	63.8	50.2	94.2	62.2
	Average	31.5	53.7	35.8	26.2	42.9	30.1
	Standard Deviation	11.3	21.4	12.24	12.0	23.8	14.0
	CV (%)	35.9	39.9	34.1	45.8	56	46.6
	Geometric Mean	29.5	50.2	34.1	23.9	38.1	27.7
2	Minimum	3.00	14.8	9.89	3.00	8.14	5.44
	Maximum	49.4	50.2	49.4	48.0	48.9	48.0
	Average	20.1	30.9	24.6	18.2	27.2	21.9
	Standard Deviation	15.0	11.8	12.5	15.2	12.5	12.9
	CV (%)	74.7	38.4	50.8	83.1	46.0	59.0
	Geometric Mean	14.8	28.7	21.8	12.5	24.3	18.5
3	Minimum	7.87	7.87	7.87	5.79	6.15	6.15
	Maximum	60.6	60.6	60.6	22.6	36.6	24.2
	Average	19.7	27.0	21.6	13.5	19.2	14.8
	Standard Deviation	16.2	15.6	15.9	6.5	8.8	6.8
	CV (%)	82.1	57.6	73.7	48.4	45.7	46.1
	Geometric Mean	16.1	23.4	17.9	11.9	17.4	13.3
4	Minimum	1.84	9.0	4.7	1.84	8.97	4.67
	Maximum	26.5	52.4	33.5	14.6	22.2	14.6
	Average	13.1	22.6	14.7	8.82	13.3	9.84
	Standard Deviation	6.71	13.7	8.12	3.46	3.83	3.20
	CV (%)	51.4	60.4	55.1	39.2	28.7	32.6
	Geometric Mean	10.9	19.7	13.0	7.9	12.9	9.3
Total	Minimum	67.2	118	70.4	43.7	68.9	50
	Maximum	163	243	186	156	232	178
	Average	119 **(3)** [e]	190 **(6)** [e]	137 **(4)** [e]	96.5 **(1)** [e]	147 **(5)** [e]	109 **(2)** [e]
	Standard Deviation	31.2	48.2	36.6	38.8	56.3	42.7
	CV (%)	26.2	25.4	26.8	40.2	38.3	39.2
	Geometric Mean	115	184	132	89.2	137	101

NOTE: Monitoring unit 6 not included in summary statistics because samples were lost or not collected at intervals 48 to 60 hr and 108 to 120 hr.

a. 3,5,6-TCP (µg) in urine was corrected for background and/or potential incomplete urine collection using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr interval) was subtracted out of each 24-hr residue. Potential incomplete urine collection was addressed using two different correction methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine excretion

rate. The "Literature Standard" method involves comparing the creatinine rate in each 24-hr urine sample to the literature standard of 1.8 g/day and the "Worker-Specific" method involves comparing the creatinine rate in each 24-hr urine sample to the individual's average daily creatinine excretion rate.

b. 3,5,6-TCP (µg) excreted was not corrected for field fortification because recoveries were >90%.

c. 3,5,6-TCP (µg) excreted was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

d. The maximum average 24-hr excretion of 3,5,6-TCP over the monitoring period is **bolded**.

e. The average total 3,5, 6-TCP (µg) values are ranked in parenthesis from lowest (1) to highest (6).

Table 7. Summary of 3,5,6-TCP In Urine (µg) By Day for Pruners By Day at Site #5 Only [a, b, c, d, e]							
Day After Exposure	**Statistical Parameter**	**METHOD 1 Not Corrected for Background or Creatinine**	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)**
Day 0	Minimum	30.3	31.5	30.3	29.0	30.1	29.0
	Maximum	58.3	87.1	58.3	55.5	82.2	55.5
	Average	**43.0**	62.2	**46.5**	**41.1**	59.4	**44.5**
	Standard Deviation	11.5	20.2	10.3	10.7	19.1	9.8
	CV (%)	26.8	32.5	22.1	26.1	32.1	22.0
	Geometric Mean	41.8	59.0	45.5	40.0	56.5	43.5
Day 1	Minimum	16.5	37.1	32.7	13.8	34.3	27.3
	Maximum	51.6	96.7	63.8	50.2	94.2	62.2
	Average	33.7	**66.2**	41.0	31.8	**56.2**	38.3
	Standard Deviation	12.9	21.2	12.88	13.3	24.8	13.65
	CV (%)	38.2	31.9	31.4	42.0	44.1	35.6
	Geometric Mean	31.5	63.3	39.6	29.2	52.1	36.7
Day 2	Minimum	17.4	28.2	19.3	14.7	24.3	16.3
	Maximum	49.4	50.2	49.4	48.0	48.9	48.0
	Average	30.0	38.6	32.0	28.1	35.7	29.8
	Standard Deviation	12.6	7.91	11.0	13.3	9.07	11.8
	CV (%)	42.1	20.5	34.4	47.4	25.4	39.6
	Geometric Mean	28.0	38.0	30.5	25.6	34.8	28.0
Day 3	Minimum	10.0	17.0	10.0	8.08	13.7	8.08
	Maximum	21.4	39.2	25.9	18.9	36.6	24.2
	Average	17.8	25.9	19.5	15.8	23.1	17.4
	Standard Deviation	4.53	8.90	5.83	4.62	8.91	5.82
	CV (%)	25.5	34.4	30.0	29.2	38.6	33.5
	Geometric Mean	17.2	24.7	18.6	15.1	21.8	16.4
Day 4	Minimum	1.84	9.0	4.67	1.84	8.97	4.67
	Maximum	15.4	35.4	16.6	14.6	22.2	14.6
	Average	10.7	20.4	12.4	9.19	14.2	10.7
	Standard Deviation	5.20	10.4	4.67	4.61	5.20	4.16
	CV (%)	48.5	51.1	37.8	50.1	36.6	38.9
	Geometric Mean	8.72	18.2	11.3	7.61	13.5	9.89
Total	Minimum	115	157	125	102	142	117
	Maximum	163	243	186	156	232	178
	Average	135 **(2)** [e]	213 **(6)** [e]	151 **(4)** [e]	126 **(1)** [e]	189 **(5)** [e]	141 **(3)** [e]
	Standard Deviation	20.6	35.5	23.6	21.9	34.7	25.3
	CV (%)	15.2	16.6	15.6	17.4	18.4	18.0
	Geometric Mean	134	211	150	124	186	139

a. 3,5,6-TCP (µg) in urine was corrected for background and/or potential incomplete urine collection using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr interval) was subtracted out of each 24-hr residue. Potential incomplete urine collection was addressed using two different correction methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine excretion rate. The "Literature Standard" method involves comparing the creatinine rate in each 24-hr urine sample to the literature standard of 1.8 g/day

and the "Worker-Specific" method involves comparing the creatinine rate in each 24-hr urine sample to the individual's average daily creatinine excretion rate.

b. 3,5,6-TCP (µg) excreted was not corrected for field fortification because recoveries were >90%.

c. 3,5,6-TCP (µg) excreted was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

d. The maximum average 24-hr excretion of 3,5,6-TCP over the monitoring period is **bolded**.

e. The average total 3,5, 6-TCP (µg) values are ranked in parenthesis from lowest (1) to highest (6).

Table 8. Summary of 3,5,6-TCP In Urine (µg) for Pruners By Day at Site #6 Only [a, b, c, d, e, f]							
Day After Entry	**Statistical Parameter**	**METHOD 1 Not Corrected for Background or Creatinine**	**METHOD 2 Corrected for Creatinine Only (Literature Average)**	**METHOD 3 Corrected for Creatinine Only (Worker-Specific Average)**	**METHOD 4 Corrected for Background Only**	**METHOD 5 Corrected for Background AND Creatinine (Literature Average)**	**METHOD 6 Corrected for Background AND Creatinine (Worker-Specific Average)**
Day 0	Minimum	12.6	33.8	22.2	7.74	14.7	9.84
	Maximum	36.2	66	44.4	25.8	38	25.8
	Average	24.6	**47.2**	**31.4**	15.7	25.3	17.0
	Standard Deviation	9.9	14.4	9.5	9.2	11.2	7.9
	CV (%)	40.1	30.4	30.1	58.8	44.3	46.3
	Geometric Mean	23.0	45.7	30.4	13.6	23.4	15.6
Day 1	Minimum	15.2	31.8	17.9	14.3	19.6	15.0
	Maximum	38.2	44.9	38.2	25.5	32.5	25.5
	Average	**28.7**	38.0	29.4	**19.2**	**26.3**	**19.8**
	Standard Deviation	10.12	5.8	8.93	5.42	5.9	4.76
	CV (%)	35.20	15.4	30.35	28.2	22.6	24.0
	Geometric Mean	27.1	37.6	28.3	18.6	25.8	19.4
Day 2	Minimum	3.00	14.81	9.89	3.00	8.14	5.44
	Maximum	13.0	32.9	25.7	12.1	22.5	17.6
	Average	7.69	21.2	15.3	5.99	16.6	11.99
	Standard Deviation	4.38	8.07	7.06	4.16	6.29	5.01
	CV (%)	57.0	38.1	46.0	69.5	37.8	41.8
	Geometric Mean	6.7	20.2	14.3	5.1	15.5	11.0
Day 3	Minimum	7.9	7.9	7.9	5.8	6.1	6.1
	Maximum	60.6	60.6	60.6	22.6	22.6	22.6
	Average	22.2	28.5	24.3	10.6	14.4	11.6
	Standard Deviation	25.7	23.2	24.8	8.04	6.70	7.42
	CV (%)	115.6	81.3	102.1	76.2	46.5	63.8
	Geometric Mean	14.8	21.8	17.1	8.88	13.1	10.23
Day 4	Minimum	8.29	13.2	8.29	6.36	11.8	7.39
	Maximum	26.5	52.4	33.5	9.94	12.7	9.94
	Average	16.0	25.5	17.7	8.36	12.2	8.78
	Standard Deviation	7.97	18.31	11.20	1.76	0.46	1.25
	CV (%)	49.9	71.9	63.2	21.1	3.76	14.3
	Geometric Mean	14.5	21.6	15.4	8.21	12.2	8.7
Total	Minimum	67.2	118	70.4	43.7	68.9	49.7
	Maximum	141	223	177	71.2	110	85.0
	Average	99.2 **(4)** [e]	160 **(6)** [e]	118 **(5)** [e]	59.8 **(1)** [e]	94.9 **(3)** [e]	69.2 **(2)** [e]
	Standard Deviation	32.9	49.4	45.1	11.5	18.4	15.2
	CV (%)	33.1	30.8	38.1	19.3	19.4	21.9
	Geometric Mean	95.3	155	112	58.9	93.4	67.8

a. 3,5,6-TCP (µg) in urine was corrected for background and/or potential incomplete urine collection using six different methods. These methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr interval) was subtracted out of each 24-hr residue. Potential incomplete urine collection was addressed using two different correction methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine excretion rate. The "Literature Standard" method involves comparing the creatinine rate in each 24-hr urine sample to the literature standard of 1.8 g/day

and the "Worker-Specific" method involves comparing the creatinine rate in each 24-hr urine sample to the individual's average daily creatinine excretion rate.

b. 3,5,6-TCP (µg) excreted was not corrected for field fortification because recoveries were >90%.

c. 3,5,6-TCP (µg) excreted was not corrected for an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

d. The maximum average 24-hr excretion of 3,5,6-TCP over the monitoring period is **bolded**.

e. The average total 3,5, 6-TCP (µg) values are ranked in parenthesis from lowest (1) to highest (6).

f. Total 3,5,6-TCP (µg) was calculated for pruner #6 because samples were lost or not collected at intervals 48 to 60 hr and 108 to 120 hr.

Table 9. Summary of Total Absorbed Chlorpyrifos (µg) for Pickers at Site #2 (n=5)[a]						
Worker #	**METHOD 1** Not Corrected for Background or Creatinine	**METHOD 2** Corrected for Creatinine Only (Literature Average)	**METHOD 3** Corrected for Creatinine Only (Worker-Specific Average)	**METHOD 4** Corrected for Background Only	**METHOD 5** Corrected for Background AND Creatinine (Literature Average)	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
1	25.5	32.4	26.2	21.5	27.2	22.0
2	20.5	43.3	30.8	15.0	31.1	22.0
3	43.1	45.4	44.1	25.4	26.5	25.8
4	36.6	49.9	37.4	27.4	37.6	28.2
5	38.6	44.7	41.6	31.0	35.9	33.4
Minimum	20.5	32.4	26.2	15.0	26.5	22.0
Maximum	43.1	49.9	44.1	31.0	37.6	33.4
Average	32.9 **(4)**[b]	43.1 **(6)**[b]	36.0 **(5)**[b]	24.1 **(1)**[b]	31.7 **(3)**[b]	26.3 **(2)**[b]
Standard Deviation	9.47	6.48	7.45	6.14	4.98	4.74
CV (%)	28.8	15.0	20.7	25.5	15.7	18.0
Geometric Mean	31.7	42.7	35.4	23.4	31.3	26.0

a. Total Absorbed Chlorpyrifos Equivalents (µg) = Total 3,5,6-TCP (µg) excreted (see Tables 5-7) * molecular weight conversion factor (350.6/198.4) * urinary excretion factor of 0.6124.

Additional corrections for background and/or incomplete urine (i.e. creatinine) were also made. These correction methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr interval) was subtracted out of each 24-hr residue. Incomplete urine collection was corrected using two different methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine rate. The "Literature Average" method involves comparing the creatinine rate in each 24-hr residue sample to the literature standard of 1.8 g/day and the "Worker-Specific Average" method involves comparing the creatinine rate in each 24-hr residue sample to the average daily creatinine rate of the specific worker.

Correction for field fortification was not made because recoveries were >90%.Additionally, corrections were not made to normalize to an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

b The average total 3,5,6-TCP (µg) values are ranked in parenthesis from lowest (1) to highest (6).

Table 10. Summary of Total Absorbed Chlorpyrifos (µg) for Pruners at Site #5 and #6 (n=9)[a, b]						
Worker #	**METHOD 1** Not Corrected for Background or Creatinine	**METHOD 2** Corrected for Creatinine Only (Literature Average)	**METHOD 3** Corrected for Creatinine Only (Worker-Specific Average)	**METHOD 4** Corrected for Background Only	**METHOD 5** Corrected for Background AND Creatinine (Literature Average)	**METHOD 6** Corrected for Background AND Creatinine (Worker-Specific Average)
Site #5						
1	125	260	145	111	227	127
2	147	245	166	143	186	161
3	124	217	136	116	203	127
4	176	263	201	169	251	193
5	159	170	170	143	153	154
Site #6						
6	NA	NA	NA	NA	NA	NA
7	86.4	134	108.3	77.0	114	92.1
8	72.7	127	76.3	67.9	119	71.2
9	153	241	191	66.7	103	82.5
10	118	191	136	47.3	74.6	53.8
Overall Statistics (n=9)						
Minimum	72.7	127	76.3	47.3	74.6	53.8
Maximum	176	263	201	169	251	193
Average	129 **(3)** [b]	205 **(6)** [b]	148 **(4)** [b]	105 **(1)** [b]	159 **(5)** [b]	118 **(2)** [b]
Standard Deviation	33.8	52.2	39.7	42.0	60.9	46.3
CV (%)	26.2	25.4	26.8	40.2	38.3	39.2
Geometric Mean	125	199	142	96.6	148	109
Site #5 Only Statistics (n=5)						
Minimum	124	170	136	111	153	127
Maximum	176	263	201	169	251	193
Average	146 **(2)** [b]	231 **(6)** [b]	164 **(4)** [b]	136 **(1)** [b]	204 **(5)** [b]	152 **(3)** [b]
Standard Deviation	22.3	38.4	25.5	23.7	37.5	27.4
CV (%)	15.2	16.6	15.6	17.4	18.4	18.0
Geometric Mean	145	228	162	135	201	150
Site #6 Only Statistics (n=4)						
Minimum	72.7	127	76.3	47.3	74.6	53.8
Maximum	153	241	191	77.0	119	92.1
Average	107 **(4)** [b]	174 **(6)** [b]	128 **(5)** [b]	64.7 **(1)** [b]	103 **(3)** [b]	74.9 **(2)** [b]
Standard Deviation	35.6	53.5	48.8	12.5	19.9	16.4
CV (%)	33.1	30.8	38.1	19.3	19.4	21.9
Geometric Mean	103	168	121	63.7	101	73.4

a. Total Absorbed Chlorpyrifos Equivalents (µg) = Total 3,5,6-TCP (µg) excreted (see Tables 5-7) * molecular weight conversion factor (350.6/198.4) * urinary excretion factor of 0.6124.

Additional corrections for background and/or possible incomplete urine collection were also made. These correction methods are described in detail in Section II (Results). When background corrections were made, the background residue was assumed to be steady state. Thus, the background residue (from the -12 to 0 hr

interval) was subtracted out of each 24-hr residue. Incomplete urine collection was corrected using two different methods, both involving normalizing the 3,5,6-TCP (µg) levels to an average creatinine rate. The "Literature Average" method involves comparing the creatinine rate in each 24-hr urine sample to the literature standard of 1.8 g/day and the "Worker-Specific Average" method involves comparing the creatinine rate in each 24-hr urine sample to the average daily creatinine rate of the specific worker.

Correction for field fortification recovery was not made because recoveries were >90%.Additionally, corrections were not made to normalize to an 8 hour work day. The work day ranged from 5.8 to 6.6 hours (see Table 2).

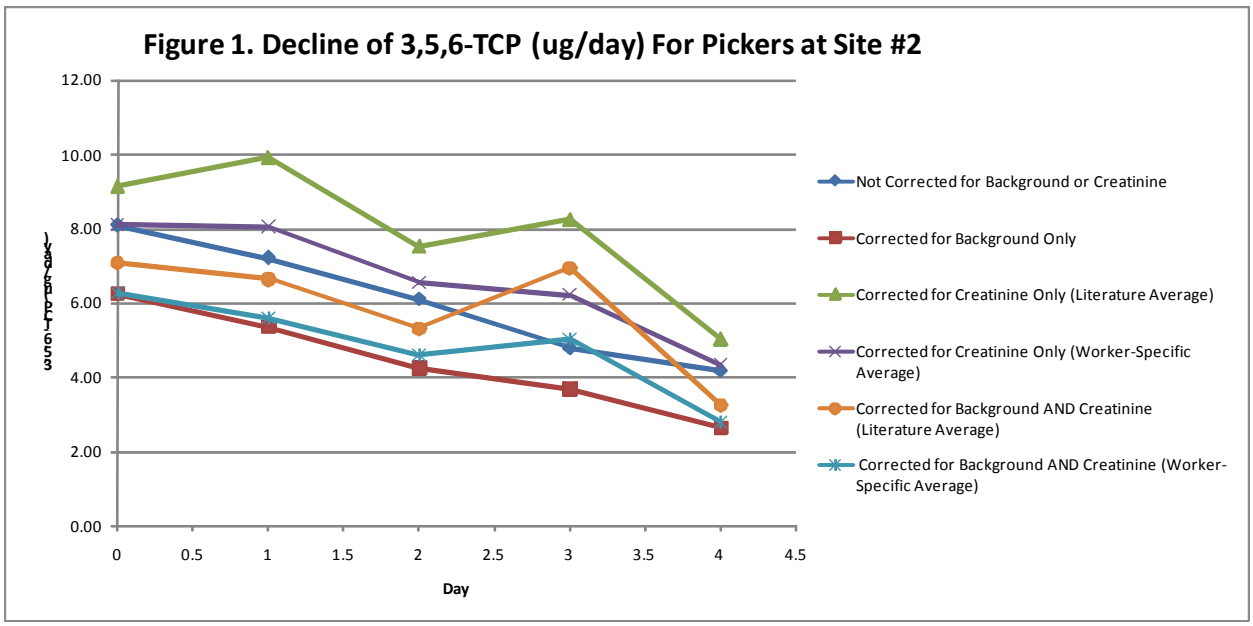
b The average total 3,5,6-TCP (µg) values are ranked in parenthesis from lowest (1) to highest (6).

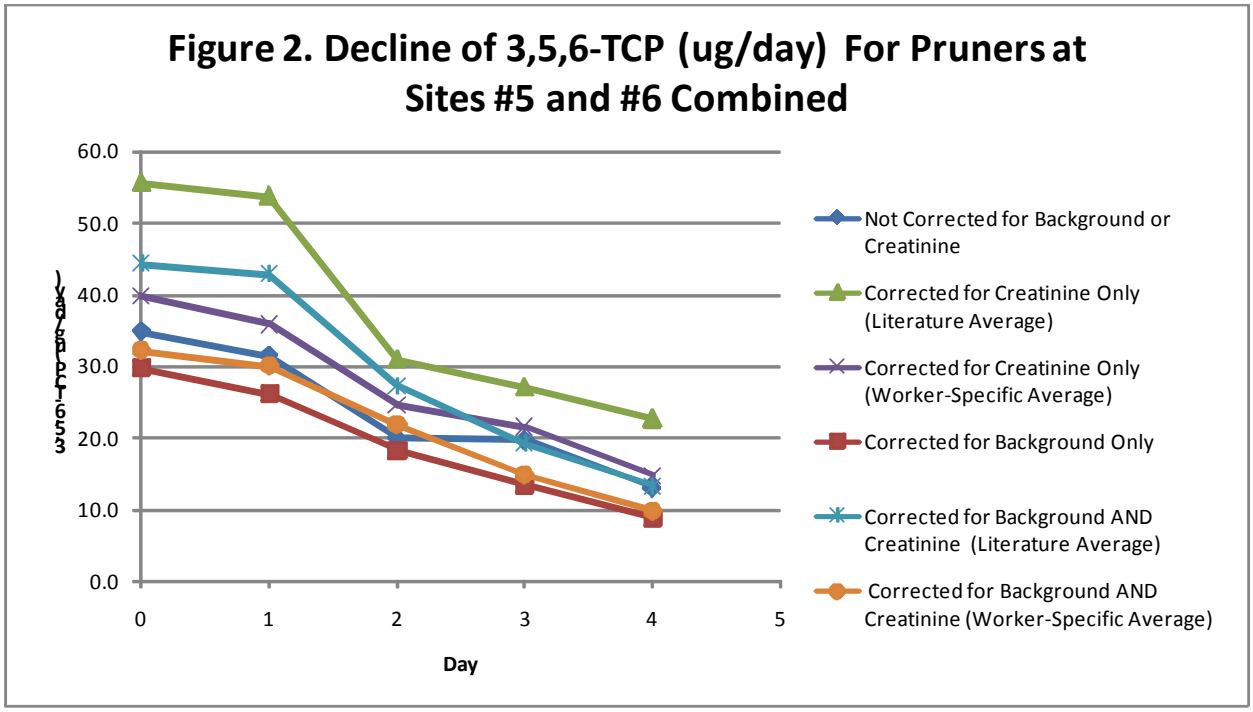
Table 11. Plasma and RBC Cholinesterase Biological Monitoring Data of Workers Entering Chlorpyrifos Treated Citrus Orchards

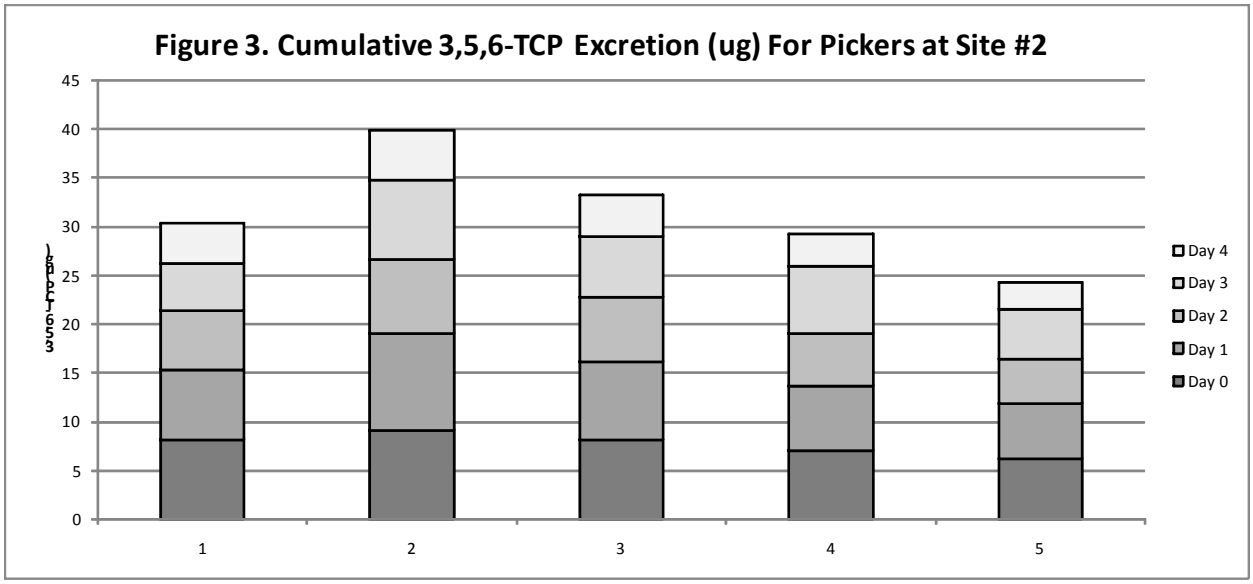
Monitoring unit	Days After Entry	Plasma ChE	Baseline Plasma ChE[a]	% Activity Plasma ChE[c]	RBC ChE	Baseline RBC ChE[a]	% Activity RBC ChE[c]	Maximum 24-hr 3,5,6-TCP (µg)[e] (Sampling Interval)
PICKERS								
Picker 1	-10	8496	8433	(-) < 1%	10388	10178	(-) 5%	6.13 (Day 0)
	-3	8370			9967			
	1	8415			9710			
Picker 2	-10	9177	8715	(-) 3%	10811	10985	(+) 3%	9.66 (Day 3)
	-3	8253			11158			
	1	8481			11307			
Picker 3	-10	7236	7011	(-) 3%	10194	10164	(+) 6%	7.31 (Day 1)
	-3	6786			10134			
	1	6783			10835			
Picker 4	-10	8481	8231	(-) 7%	11834	11553	(-) 5%	6.75 (Day 3)
	-3	7980			11272			
	1	7644			10967			
Picker 5	-10	6066	6216	(+) 5%	12593	12653	(-) 4%	7.47 (Day 1)
	-3	6366			12712			
	1	6540			12102			
PRUNERS								
Pruner 1	-5	8751	9221	(-) <1%	8604	7821[b]	(-) 14%	45.6 (Day 0)
	-2	9690			7038			
	1	9210			6721			
Pruner 2	-5	6243	6243[d] *(6201)*	(-) 1%	9320	9320[d] *(8984)*	(-) 17%	49.0 (Day 0)
	-2	6243			9320			
	1	6195			7711			
Pruner 3	-5	9411	9690	(+) 3%	9576	8977	(-) 9%	43.4 (Day 0)
	-2	9969			8378			
	1	9984			8162			
Pruner 4	-5	6879	6860	(-) 3%	12161	11715	(-) 13%	62.2 (Day 1)
	-2	6840			11269			
	1	6660			10231			
Pruner 5	-5	4998	5204	(-) 4%	12689	12307	(-) 4%	55.5 (Day 0)
	-2	5409			11925			
	1	4974			11872			
Pruner 6	-7	5384	6607[b,d] *(5938)*	(-) 2%	10089	10022	(+) 21%	49.3 (Day 1)
	-4	7830			9955			
	1	6492			12653			
Pruner 7	-7	2734	3505[b,d] *(2973)*	(-) 8%	10757	11201	(+) 13%	25.8 (Day 1)
	-4	4275			11645			
	1	3213			12838			
Pruner 8	-7	5660	7003[b,d] ***(7687)***	(-) 9%	10144	9661	(+) 33%	21.3 (Day 0)
	-4	8346			9178			
	1	7029			14453			
Pruner 9	-7	5412	6800[b,d] *(5622)*	(-) 14%	8890	9000	(+) 29%	22.6 (Day 3)
	-4	8187			9110			
	1	5832			12702			
Pruner 10	-7	5482	5992[b,d] *(6715)*	(+) 13%	8920	10595[b,d] *(12152)*	(+) 12%	15.0 (Day 1)
	-4	6501			12269			
	1	6930			12035			

Note: Blood samples were collected at Morinda Medical Group, Porterville, CA and blood testing occurred at Sierra View Outpatient Laboratory using the modified Ellman Procedure. Dr. James Lessinger and Marcia Penry, RN had oversight responsibility for the blood monitoring procedures.

a. Baseline = sum of two blood samples for Plasma or RBC ChE levels taken on two separate days prior to exposure / 2.
b. According to standard blood cholinesterase testing protocol, the levels for pre-exposure sample #2 must be within ±15% of pre-exposure sample #1 levels, and if not a 3rd sample must be collected and sample #2 and sample #3 data would be used to calculate the baseline level. These samples do not meet that criteria as the second pre-exposure sample is >15% of the first pre-exposure sample. It does not appear that there was enough time to analyze a 3rd sample prior to initiation of the study.
c. % ChE Activity = 1-(post exposure plasma or RBC ChE level / baseline plasma or RBC ChE level) * 100
d. In a few cases the baseline level calculated using the 2 pre-exposure readings taken from the summary table of the Study Report does not match the baseline level actually reported in the summary table. No explanation for this discrepancy is provided in the Report. In these cases the number reported in the Study Report is identified in this table as the number in parentheses and italics. In these cases the % ChE activity presented in this table has been calculated using the baseline level which yields the greatest % ChE activity reading. In all cases, except Pruner 8's plasma ChE activity, we have used the calculated baseline level rather than the level reported in the summary table of the Study Report.
e. The maximum daily 24-hr 3,5,6-TCP (µg) values are reported for correction Method 6, in which 3,5,6-TCP excretion is corrected for background and is normalized to the worker-specific average daily creatinine rates.







Key:

1 = Not Corrected for Background or Creatinine

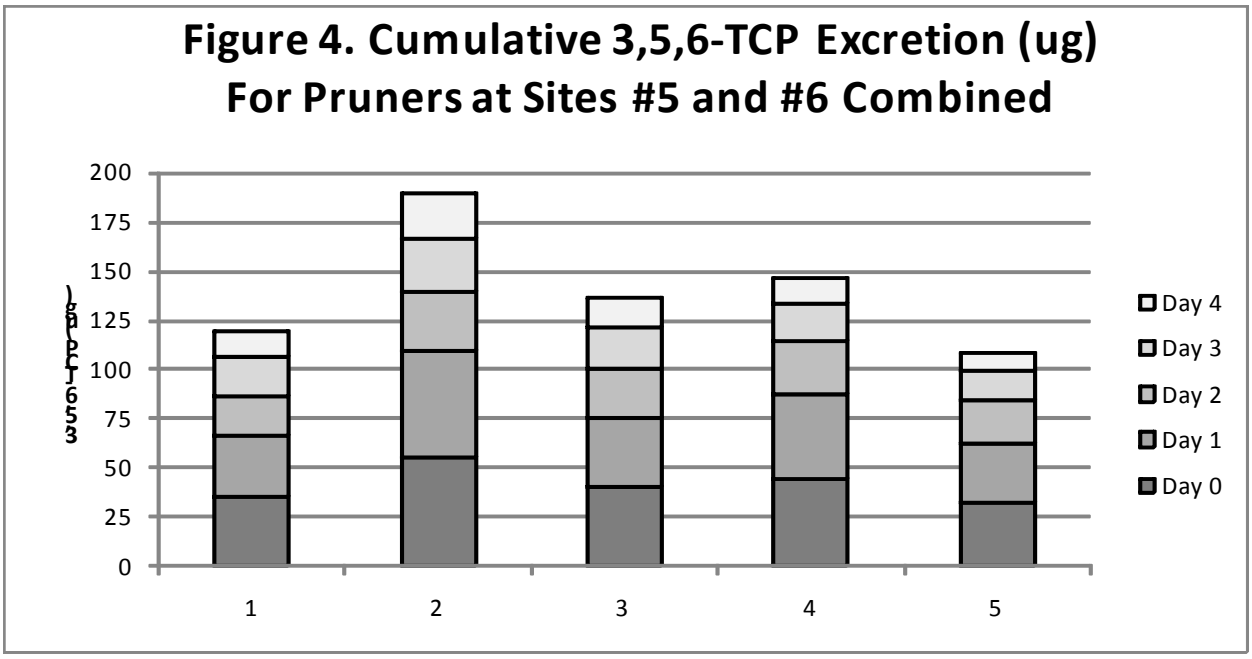
2 = Corrected for Background Only

3 = Corrected for Creatinine Only (Literature Average)

4 = Corrected for Creatinine Only (Worker Specific Average)

5 = Corrected for Background AND Creatinine (Literature Average)

6 = Corrected for Background AND Creatinine (Worker Specific Average)



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6 = Corrected for Background AND Creatinine (Worker Specific Average)

Figure 5. Total Absorbed Chlorpyrifos Equivalents (ug) For Pickers at Site #2

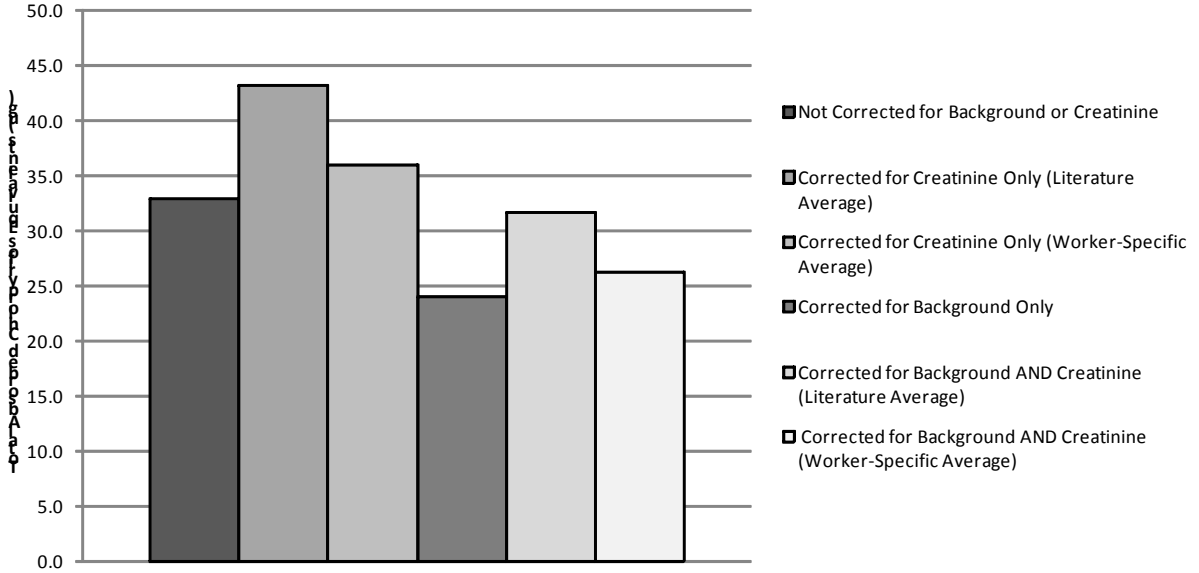
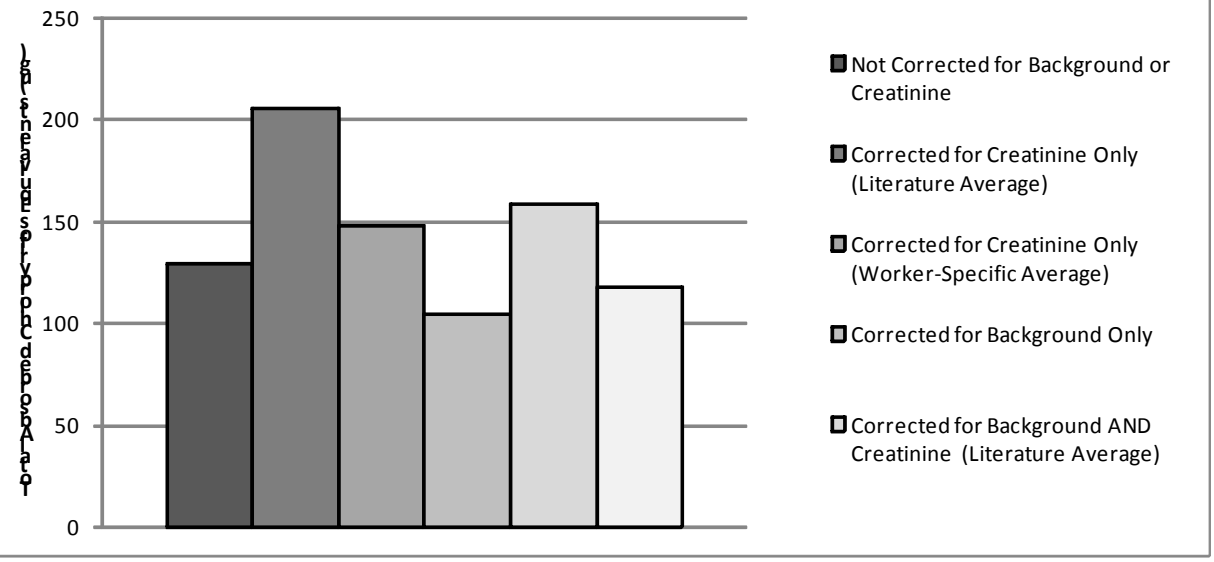
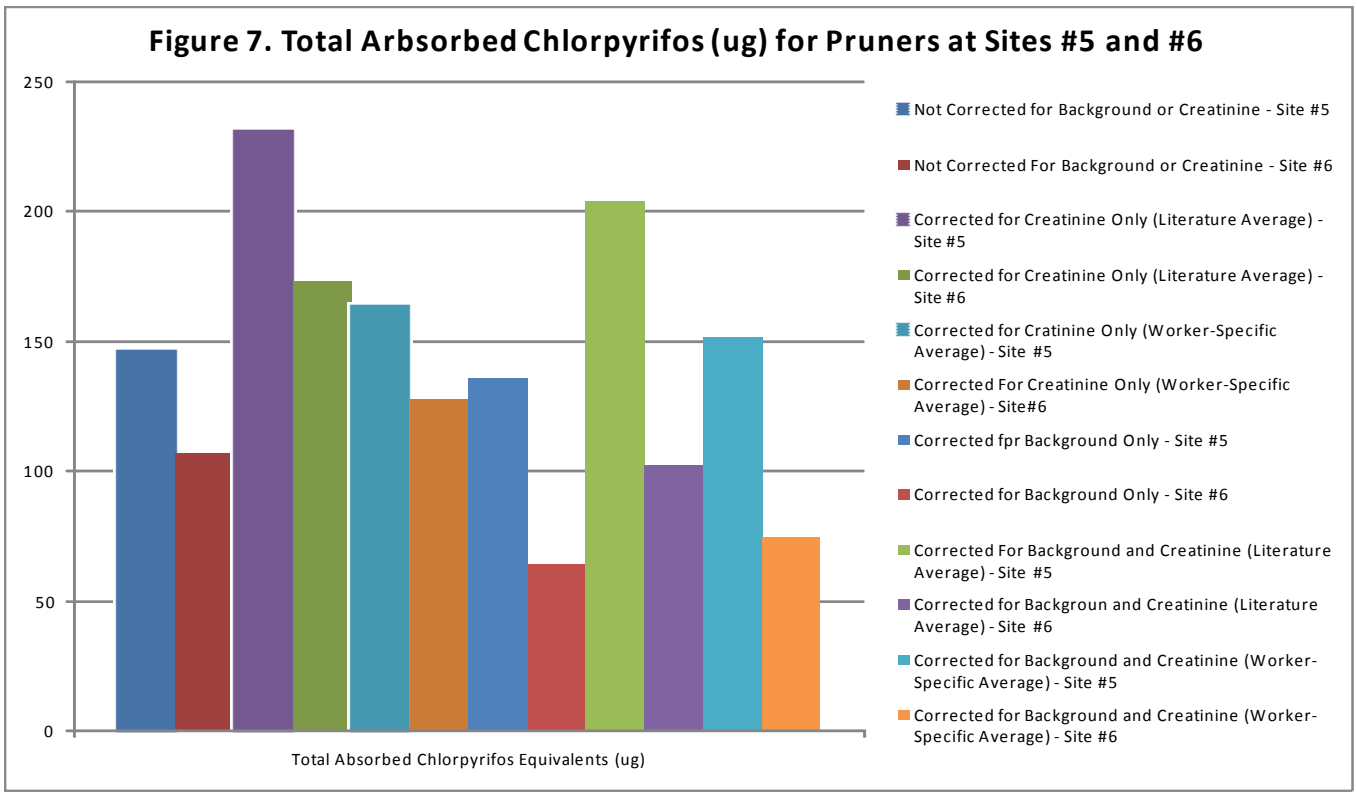


Figure 6. Total Absorbed Chlorpyrifos Equivalents (ug) for Pruners at Sites #5 and #6 Combined





Compliance Checklist - Guideline 875.2600
Biological Monitoring - Postapplication

1. *The Agency requires investigators to submit protocols for review purposes prior to the inception of the study. Adequate pharmacokinetic data must exist to effectively interpret the data.* It is uncertain if the protocol was submitted to EPA prior to inception of the study. Adequate pharmacokinetic data are available.

2. *Expected deviations from GLPs should be presented concurrently with any protocol deviations and their potential study impacts.* This criterion was met. GLP deviations and protocol deviations were reported and their impacts adequately assessed.

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

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

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

6. Biological monitoring studies should be carried out concurrently with dislodgeable residue studies. This criterion was met.

7. A sufficient number of monitoring units should be generated to address the exposure issues associated with the population of interest. Specifically, each study should include a minimum of 15 individuals (monitoring units) per activity. This criterion was not met according to the prevailing standards of the day. Only 5 picker monitoring units and 10 pruner monitoring units were monitored, and one pruner monitoring unit had to be dropped due to incomplete or lost specimen collection. However, this study does provide adequate information for the purposes of investigating a possible relationship between dose and impacts on cholinesterase activity.

8. Test subjects should be regular workers, volunteers trained in the work activities required, or typical homeowners. This criterion was met.

9. The monitored activity should be representative of a typical working day for the specific task in order to capture all related exposure activities. This criterion was met.

10. The exposure monitoring period should be of sufficient length to ensure reasonable detectability of residues in biological media (e.g., blood and urine) consistent with pharmacokinetic data such as excretion profile, duration time, etc. This criterion was met.

11. Biological monitoring should be conducted using methodologies based on the pharmacokinetic properties of the pesticide (parent compound and its metabolites) of concern (e.g., need validated pharmacokinetic models from humans or appropriate animal surrogate and appropriate route of exposure). This criterion was met.

12. Any protective clothing worn by study participants should be identified and should be consistent with the product label. This criterion was partially met. The study identified the personal protective equipment worn by the workers. The workers wore cotton or canvas gloves, baseball type hats, and protective sleeve gauntlets. These articles are not required to be worn according to the label, but are typically worn by the workers when conducting the monitored tasks.

13. If urine monitoring is being conducted, urine samples should be collected one or two days before participating in the postapplication exposure monitoring activities and should continue on the day of postapplication monitoring and for an appropriate time period after these activities have been completed, depending on the excretion kinetics of the compound. The 24-hour sample collection cycle should begin with the first void after beginning work activities and end with the first void on the following morning, continuing this 24-hour cycle on subsequent days. This criterion was met. Samples were collected in approximate 12 hour increments starting one day before participating in the exposure monitoring activity. The actual sample duration for each sample varied and was not specifically reported.

14. If blood monitoring is being conducted, baseline blood samples should be collected from each individual prior to exposure. Based on pharmacokinetics, postapplication exposure samples should be collected at the appropriate times before, during, and after exposure. This criterion was met. Two baseline samples were collected 2 to 10 days prior to the exposure event. It should be noted however, that the study protocol states that workers were only asked to avoid handling LORSBAN 4E and entering LORSBAN 4E treated areas for 4 days prior to the start of the study.

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

16. Creatinine levels should be determined as a way of qualitatively monitoring completeness of urine collection samples. Specific gravity, as another measure of 24-hour sample completeness, should be performed as soon after collection as possible (and before sample storage). These criteria were partially met. Creatinine was measured in each sample. Specific gravity was not measured in each sample. Density was measured in 20 random samples by weighing 1 ml samples. The average density was reported as 1.04419±0.0114 g/mL. The study author used a specific gravity of 1.000 in all calculations.

17. Prior exposures to the test pesticide or structurally related compounds may interfere with study results. A brief history should be taken from each participant relating to known prior exposures to pesticides for at least the last 2 weeks, including reentry into potentially treated fields. For urine monitoring, there should also be a sufficient time period between such exposures and participation in the study to ensure adequate urinary clearance of the compound and its metabolites, based on pharmacokinetic data. It is uncertain if the criterion was met. The Study protocol states that each worker would be asked not to spray or handle LORSBAN 4E or pick LORSBAN 4E treated fruit for four days prior to and for four days following the day of the test. All workers had 3,5,6-TCP residues in their pre-exposure urine samples; however, the levels were similar to levels in the control samples collected from laboratory technicians and also similar to the residues in the Day 4 post-exposure samples. The Study author assumed that the pre-exposure levels were steady state and the analytical report states that 3,5,6-TCP is common in urine samples due to the widespread use of chlorpyrifos. Additionally, for the pruners, urine samples were monitored in 12 workers prior to the start of the study (date unknown) and 10 of these workers were selected for the study based on the results.

18. Validated analytical methods for the biological analyte (parent compound and its metabolites) of sufficient sensitivity are needed. Information on method efficiency and limit of quantitation (LOQ) should be provided. This criterion was met.

19. Samples should be stored in a manner that will minimize deterioration and loss of analytes between collection and analysis. Biological monitoring samples (e.g., serum, plasma and urine) should be refrigerated or stored frozen prior to analysis. Whole blood should not be frozen. Information on storage stability should be provided. These criterion were met for urine. Urine samples were stored ambient for up to two days prior to processing and then stored frozen until analysis. Ambient storage stability data were provided and recoveries were acceptable. Storage conditions of the blood were not reported.

20. Data should be corrected if any appropriate field fortified, laboratory fortified or storage stability recovery is less than 90 percent. This criterion is not applicable. Average field fortification recoveries were greater than 90%. Data were not corrected for field or laboratory recoveries.

21. Unless stability of the analyte has been established prior to initiation of the study, three samples of control (nonparticipant) should be fortified with two levels of the biological analyte (parent or metabolite(s), whichever is appropriate) for each experimental site. This criterion was met. Fortifications were made using control urine of unexposed laboratory technicians and also using the pre-exposure urine from the pickers and pruners.

22. Each subject's absorbed dose should be expressed in terms of body weight using his/her own measured value, and as a cumulative total for each exposure period. The arithmetic mean, range, standard deviation, and coefficient of variation should be calculated from the results of all individuals. Geometric mean, range and standard deviation may be calculated if the results are shown to be log-normally distributed. Other distributional data should be reported, to the extent possible (e.g.,

percentiles). These criteria were partially met. The body weight of the workers was not provided. Absorbed dose was expressed using a body weight of 70 kg in the Study Report.