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WASHINGTON, D.C. 20460

**OFFICE OF  
PREVENTION, PESTICIDES  
AND TOXIC SUBSTANCES**

**April 29, 1999**

**MEMORANDUM**

**SUBJECT:** Review of *Evaluation of Workers' Exposure to Chlorpyrifos During the Use of Dursban® TC Termiticide Concentrate for Post-Construction Termiticide Applications*, - MRID No. 44729402  
PC Code # 059101 ; DP Barcode 255669

**FROM:** Gary Bangs  
Reregistration Branch 3  
Health Effects Division (7509C)

**TO:** Mark Hartman, Chemical Review Manager  
Special Review and Reregistration Division (7508C)

and

Debbie Smegal, Risk Assessor  
Reregistration Branch 3  
Health Effects Division (7509C)

**THRU:** Steve Knizner, Branch Senior Scientist  
Reregistration Branch 3  
Health Effects Division (7509C)

## EXECUTIVE SUMMARY

### Evaluation of Workers' Exposure to Chlorpyrifos During the Use of Dursban® TC Termiticide Concentrate for Post-Construction Termiticide Applications, - MRID 44729402

This study was designed to quantify potential pesticide applicator inhalation, dermal, and biological exposure to chlorpyrifos, the active ingredient (ai) in the termiticide Dursban TC (43.9% ai). Post-construction treatments were applied to various construction styles of residential housing (i.e., slab-on-grade, basement, crawlspace and combinations thereof) in Virginia, Alabama, and Georgia. The applicators applied termiticide at a rate of approximately 4 gallons of ~1 percent a.i. dilution (range 0.71-1.24%) per 10 linear feet to an average of 124 gallons per structure (range 40-325 gallons). Mixer/loader/applicator exposures during actual structural work using hand held spray gun or injection rod were monitored by passive dosimetry and limited biomonitoring of volunteer pesticide control operators (pco). During applications, the pcos wore the label-required protection, including a cotton coverall, chemically resistant nitrile gloves, a hat, protective eyewear and a half-facepiece respirator (if working in confined spaces). During mixing/loading, subjects wore *additional* PPE: chemically resistant footwear and an extra coverall or a chemically resistant apron. There were a total of 15 replicates but only 9 different volunteers, from 3 companies in three cities. [The authors of the study state there a 9 different volunteers, but there are only 7 unique body weights recorded, with one weight recorded 5 times]. The study was conducted in compliance with most, but not all, OPPTS guidelines, and the report was well-written and fairly well-organized. The biomonitoring was very limited (5 replicates) and mixing/loading exposures were not measured separately from application exposures. In spite of the discrepancies noted, the relatively good correlation between the biomonitoring and passive dosimetry make this data useful for determining worker exposure during application of chlorpyrifos.

Higher inhalation exposures were encountered in basement and crawlspace applications than during slab treatments. The author's values were based on an inhalation rate of 25 L/min, not the 29 L/min for moderate activity used by HED, based upon the Exposure Factors Handbook. The overall potential inhalation intakes, corrected to HED's standard inhalation rate of 29 L/min, averaged 1.48  $\mu\text{g}/\text{kg}$  normalized body weight (70 kg), and ranged from 0.17 to 3.18  $\mu\text{g}/\text{kg}$  normalized body weight (N=14). The mean value is based on data from 14 replicates because the fifteenth replicate had an unusually high dermal exposure resulting from an accident with a broken hose. Average inhalation dose/hour (average 6.62 hours worked) was 15  $\mu\text{g}/\text{hr}$ , with a range of 1.67 to 25.84  $\mu\text{g}/\text{hr}$ .

During crawlspace treatments, workers experienced the greatest amount of dermal exposure to the head/neck (~48 percent of the dermal exposure on average). During slab and basement treatments, workers experienced the highest levels of dermal exposure to the legs (~63 percent and ~51 percent respectively on average). During basement treatments, exposure to the hands was greatest (~23 percent of total dermal exposure on average), however the number of application replicates was low (N=3). The average dermal dose (N=14) based on passive dosimetry was 3.28  $\mu\text{g}/\text{kg}$  BW with a range of 0.45 to 13.85  $\mu\text{g}/\text{kg}$  BW, and excluding the 49.9  $\mu\text{g}/\text{kg}$  exposure due to one replicate being sprayed by a broken hose. These values utilize the HED dermal absorption factor of three percent recommended at the time of this review, while the study authors used one percent.

The total mean dose, calculated by addition of average inhalation and absorbed dermal doses, was estimated to be 4.76  $\mu\text{g}/\text{kg}$  normalized BW (70 kg; N=14; range: 0.82 to 16.7  $\mu\text{g}/\text{kg}$  BW), with inhalation representing 31 percent and dermal representing 69 percent of total dose measured via passive dosimetry. Total estimated exposure (dermal and inhalation) for the 15th replicate was 50.50  $\mu\text{g}/\text{kg}$  BW, which may be considered a worst-case exposure.

Total mean absorbed chlorpyrifos dose measured via the biological monitoring of five workers in Georgia slightly higher than (4.31 vs. 3.24  $\mu\text{g}/\text{kg}$  BW ) the total absorbed chlorpyrifos calculated as the sum of 3 percent of total potential dermal dose (measured via passive dosimetry) and potential inhalation exposure for the same 5 replicates. Total absorbed dose was estimated directly by biomonitoring of the chlorpyrifos metabolite 3,5,6-trichloropyridinol (TCP) in the urine samples of five volunteer applicators at the Georgia location (it is unclear why the fifth replicate had the same weight as another, unless one volunteer was monitored for 2 days). The volunteers were told to avoid chlorpyrifos exposure for ten days before the exposure application and for five days after the exposure. Each applicator collected all the urine voided on the day before application, the day of application, and for four consecutive days after initial exposure. The urine was collected at 12-hour intervals. The first day's collection was used as the baseline for correcting exposure calculations. The baseline chlorpyrifos ranged from 0.39 to 3.4  $\mu\text{g}/\text{kg}$  actual body weight. The difference in estimated absorbed dose levels between biomonitoring and passive dosimetry may be due to various factors, including: incidental oral exposure to chlorpyrifos; field spike recovery from coveralls was consistently low (mean = 22 percent), so losses may not have been fully accounted for, or; subjects participating in biological monitoring experienced exposure to chlorpyrifos outside the study setting.

In at least three cases (replicates AL03, GA13, GA14), significantly more ai was reportedly applied than was handled, and the study report does not explain how that is possible (i.e., did the applicators use other, previously prepared solution in addition to their own). In order to analyze the unit dose per pound ai handled, the average of the pounds "handled" and "applied" was utilized. A range of unit dose based on passive dosimetry was obtained by applying the mean exposure of the 14 replicates to the high (22.8 lb), low (4.0 lb), and mean (10.72 lb) amount of material handled. This provided a range of exposure from 14.6 to 83.3  $\mu\text{g}/\text{lb}$  ai, with a mean of 31.1  $\mu\text{g}/\text{lb}$  ai. The mean exposure based on the five biomonitored volunteers was 47.6  $\mu\text{g}/\text{lb}$  ai.

Several deficiencies were noted. Field spike recoveries for denim coveralls (22%) and underwear dosimeters (61%) were consistently low. In addition, the authors noticed differences between the first sample set and the other eight which seemed significant. The first set was collected during cloudy and cooler conditions. Based on their own field study, the authors conclude that chlorpyrifos recoveries from denim coveralls were reduced due to direct exposure to sun and heat, and the recovery values were a function of time. Therefore, in the case of denim coveralls, due to the wide variability between field recovery data sets on the different days of sampling, different field spike recovery factors were applied to correct each day of monitoring.

## **Review of "Evaluation of Workers' Exposure to Chlorpyrifos During the Use of Dursban® TC Termiticide Concentrate for Post-Construction Termiticide Applications"**

### **Study Background**

The study was submitted in support of the registration requirements for the insecticide, Dursban® TC. The requirements for this study were specified by the USEPA, under OPPTS Series 875 Group A (875.1000-1500 guidelines for indoor/outdoor dermal and inhalation exposure and biomonitoring) of the Pesticide Assessment Guidelines. The study was conducted by Global Environmental Chemistry Laboratory, Dow AgroSciences LLC, and submitted to EPA on October 9, 1998 (original) and December 22, 1998 (amended). The authors of the study are D. E. Barnekow and B.A. Shurdut.

Chlorpyrifos (0,0-diethyl-0-(3,5,6-trichloropyridinyl) phosphorothioate) is a chlorinated organophosphate insecticide. It is the active ingredient (43.9 percent) in Dursban TC, a termiticide registered for use as follows: in pre- and post-construction soil treatment around and under building foundations; injected into infested and damaged wood and hollow concrete block or masonry voids; to protect utility poles and fence posts; and to control a wide variety of wood infesting insects (e.g., carpenter ants, carpenter bees, mites, ticks, powderpost beetles, etc.) in interior living areas, outside surfaces and around buildings. In Guam, Hawaii, and other Pacific islands, the product may also be used as a preventative treatment for underground utility cable and conduit.

Dursban TC is formulated as an emulsifiable concentrate. It is generally diluted in water to yield a concentration between 0.25 percent and 2 percent, although the maximum concentration solution used in treating residential construction is 1 percent. The diluted product is applied using injection rods or coarse, low-pressure sprays. It may also be applied to wall voids, filled porches, chimney bases, and soil under slabs using foam generating equipment.

### **Test Sites**

This study was conducted at fifteen residential structures located in Alabama, Virginia and Georgia between June and August, 1997. The treated properties were of various construction-types: crawlspace (N=2), combination slab/crawls (N=4), basement (N=2), crawl/basement (N=1) and slab (N=6). Treated foundation perimeters ranged from 126 linear feet to 443 linear feet (mean = 199 linear feet).

## Materials and Application Methodology

### Equipment & Method:

Equipment used was essentially the same at all fifteen test-sites, consisting of truck mounted plastic mixing tanks (50 to 200 gallons, depending on location), fitted with low-horsepower gasoline-powered mixing pumps, and hand-held spray guns or T-bars equipped with either short injection rods (8 to 12 inches) or long injection rods (36 to 84 inches). Spray pressures reportedly ranged between 25 and 90 psi. However, it was also noted that none of the trucks had flow meters, and only half had pressure gauges. Treatment methods varied with construction style, as follows:

*Slabs* - drilled every 8 to 18 inches along perimeter walls (either interior or through exterior wall at an angle to reach under the slab).

*Crawlspace* - drilled each void of those foundation blocks just above the footings, from the inside of space

*All structures*- trenched or rodded around the exterior; drilled holes were sealed after application.

### Application Rate:

Only one structure was treated per day. All treatments were post-construction treatments made in accordance with the specimen label. The applicators applied termiticide at a rate of approximately 4 gallons of ~1 percent a.i. dilution per 10 linear feet per foot of depth. However, none of the rigs had flow meters and only half had pressure gauges. The average volume applied per structure was 124 gallons of 1 percent Dursban TC (range: 40 to 325 gallons). Total weight of active ingredient applied ranged between 3.6 and 33.5 lbs. chlorpyrifos. Not all of the active ingredient that was prepared was applied. In at least three cases (AL03, GA13, GA14), significantly more ai was reportedly applied than was handled, and the study report does not explain these discrepancies. In the study report Tables 3 and 4 (pages 46 and 47 of the study) the authors indicate where more than one tank of solution was mixed, but the data in these two tables for volume and amount ai applied do not. Some applicators may have used other, previously prepared solution in addition to their own, but this is not stated or shown in Tables 3 and 4. Therefore, the Agency has chosen to take the average of the indicated amounts "handled" and "applied" for use in estimations of exposure.

### **Protective Clothing**

During applications, applicators wore a cotton coverall, chemically resistant nitrile gloves, a hat, and a half-facepiece respirator (if working in confined spaces). However, the specific type of respirator and filter cartridge were not specified. Although not stated, protective eyewear is also worn in all of the photographs in the study report. During mixing/loading, subjects wore *additional* PPE: All wore chemically resistant footwear (rubber boots with overalls outside of the

boots). Eight subjects wore a second coverall. Seven subjects wore a chemically resistant apron.

### **Meteorological Conditions**

Applications were made on June 23-25, 1997 in Lynchburg, VA, on July 8-10, 1997 in Marietta, GA, and on June 16-18 and August 25, 1997 in Decatur, AL. Data reported included: date, time of day, temperature, relative humidity, wind velocity, wind direction, and atmospheric conditions. Ambient outdoor temperatures reported ranged between 64.1°F (late August - Decatur, GA) to 101.5°F (late June - Lynchburg, VA). Relative humidities ranged between 20 percent and 82 percent. One rain event was reported. The source of the meteorological data was not reported.

### **Sampling**

In each state, five application replicates were evaluated (overall N=15). Worker exposure was assessed using air monitoring, passive dermal dosimetry, and biological monitoring techniques. However, the fifteen replicates reflected only nine actual applicator subjects. The authors stated that:

"Several of the applicators participating in this study were evaluated more than once. All of the applicators participated in three or less replicates. As a result, a total of nine different applicators from three different companies and three locations were monitored. Each of the five volunteers in the biomonitoring phase of the study were limited to participation in only one replicate."

It is confusing that although the study states clearly that nine different people were monitored, *only seven different weights* are presented in the data. Among the five biomonitoring replicates, two of the weights are exactly the same.

Air sampling: Sampling was conducted using 37 mm mixed cellulose ester filter (0.8  $\mu\text{m}$  pore size) "...connected via glass funnel and rubber tubing..." to a 99 mg Chromosorb 102 tube (2 sections). Air flow reportedly averaged 1.5 liters/minute, and sampling was conducted in the breathing zone for between four and eight hours. Pre- and post-calibration of the pumps was performed using a rotameter. The authors note problems with pump shutdowns. [However, the authors state that duplicate air samples were collected to provide back-up samples in case of pump shut-downs.] Sampling media (N=15 filters and N=15 tubes) were extracted in hexane and analyzed according to a proprietary GC-ECD method. A copy of the method was included in an Appendix to the study. The authors stated that chlorpyrifos was well resolved from the solvent peak without any significant interference. Samples of GC traces and example data calculations were also included in an Appendix to the study report.

Dermal exposure to the hands: Surface deposition on hands was evaluated by collecting samples of handwashings. Each applicator/replicate was subject to multiple handwashing sampling events, i.e., before eating, drinking, smoking, using the bathroom. Soap solution (Emcol 4500) was employed, followed by a rinse. Combined washings and rinses were extracted in isoctane

and NaCl, and two 5-ml aliquots analyzed per sample (N=15 samples; N=30 aliquots). Samples were stored and shipped on ice to the analytical laboratory, stored in the freezer, and analyzed by GC-ECD.

Dermal exposure to other body parts: Surface deposition on the rest of the body (i.e., arms, legs, torso front, torso back, and head/neck) was evaluated using passive dosimetry (i.e., denim coveralls, long underwear, socks and head patches). Total dermal exposure values for each replicate (N=15) reported included hand exposure.

Biological samples: All aspects of these samples, collection methodology, sample analysis, sample storage, QA/QC, and results are discussed together in a subsequent section of this review.

### **Sample Storage and Handling**

Air sampling media, handwashing samples, and sectioned cotton dosimetry or clothing were stored in capped 8 oz glass jars and kept on dry ice during storage and shipment to the analytical laboratory. Samples were kept frozen until analysis.

### **Quality Assurance & Control**

Tank Mix Analysis: The nominal concentration of 18 separate tank mixes was verified and actual percent concentrations were found to range between 0.71 percent a.i. and 1.24 percent a.i. with a mean concentration of 1.0 percent ai. The desired target rate was 1 percent ai, which is the maximum rate of application for residential structures.

### Laboratory Method Validation

Method validation work was conducted in a separate referenced study<sup>1</sup>, which is unpublished and was not provided for review. A summary of the results of the unpublished validation report follows, as discussed in the text of the study under review:

1. Air samples: At a 0.04  $\mu\text{g}$  fortification level, filter recoveries averaged 103 percent +/- 2.2 percent and Chromosorb tube recoveries averaged 88.9 percent +/- 9.0 percent. Validated range was 0.013  $\mu\text{g}$  to 0.5  $\mu\text{g}$  for both filters and tubes.

Limit of detection - 0.013  $\mu\text{g}$  Limit of quantitation - 0.04  $\mu\text{g}$ .

2. Cotton Coverall samples: At a 4.0  $\mu\text{g}$  fortification level, recoveries averaged 110.1 percent +/- 6.8 percent. The validated method range was 1.3 to 10,000  $\mu\text{g}$ .

Limit of detection - 1.3  $\mu\text{g}$

Limit of quantitation - 4.0  $\mu\text{g}$ .

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<sup>1</sup> Saunders DG, Powers FL, Lardie TS. (1998). Validation of methods for determination of chlorpyrifos in inhalation dosimeters, dermal dosimeters, and hand wash solutions from user exposure studies with Dursban TC. Unpublished report of Dow AgroSciences LLC, HEA96154.



3. Cotton T-Shirt (underwear): At the 0.4  $\mu\text{g}$  fortification level, recoveries averaged 79.6 percent +/-2.5 percent. The validated method range was 0.13 to 2,000  $\mu\text{g}$ .

Limit of detection - 0.13  $\mu\text{g}$       Limit of quantitation - 0.4  $\mu\text{g}$ .

4. Hand Washes: At the 2.0  $\mu\text{g}$  fortification level, recoveries averaged 116.1 percent +/- 8.6 percent. The validated method range was 0.7 to 25,000  $\mu\text{g}$ .

Limit of detection - 0.7  $\mu\text{g}$       Limit of quantitation - 2.0  $\mu\text{g}$ .

### Laboratory Recovery Values for Spiked Matrices

Table 1 summarizes lab spike recovery values obtained in this study for each specific sampling matrix. Matrix spikes were prepared in the laboratory and included with each field sample set analyzed to evaluate the performance of the analytical method and as a control for potential sample handling losses in the laboratory. The recovery values obtained were used to correct sampling data, and validated method performance. Note that the report does not identify how much chlorpyrifos was used to prepare a given matrix spike.

**Table 1. Laboratory Recovery of Chlorpyrifos from Matrix Spikes**

<b>Matrix</b>	<b>Average Lab Spike Recovery<sup>1</sup></b>
Filters	109% +/- 9.5%
Chromosorb Tubes	95% +/-5.6%
Denim Coverall Dosimeters	112% +/- 10%
Underwear Dosimeters	89% +/-6.3%
Hand Washes	115% +/- 10.0%

<sup>1</sup> See Tables F-1 and F-2 in the study report. N=10 samples for filters and tubes; N=12 samples for hand washes; N=18 for coveralls; N=20 for underwear.

### Storage Stability and Field Control Spikes

Field blanks (N=1), storage stability (N=2) and field control spikes (N=2) were prepared and included with each of nine sample sets (i.e., overall N=18 for storage stability and field control spikes). Spikes were prepared in the field, over a 78-day period, under a variety of environmental conditions. [Note: Dursban TC was applied over a 27 day period.] Appendix F (Tables F3 through F7) summarizes results for each of the matrices, corrected for laboratory recovery. Field blanks were uniformly non detect. Field frozen storage and shipping did not result in significant loss of sample. Therefore, monitoring data were not corrected for storage

losses. When field spike recovery data were <100 percent, the average recovery was used to correct the monitoring data. Table 2 includes a summary of these data.

**Table 2. Storage Stability and Field Control Spikes**

<b>Matrix/ Chlorpyrifos Fortification Level</b>	<b>Average Storage Stability Recovery<sup>1</sup></b>	<b>Average Field Spike Recovery<sup>1</sup></b>
Filters - 0.5 µg	99% range: (101% - 117%)	80.1 +/- 8.7% range: (66% - 92%)
Chromosorb Tubes - 0.5 µg	89% range: (64% - 107%)	99.4% +/-8.6% range: (91% - 113%)
Denim Coverall Dosimeters - 50 µg per 400 cm <sup>2</sup>	98% range: (80% - 117%)	<b>22%</b> range: (11% - 55%)
Underwear Dosimeters - 8 µg per 400 cm <sup>2</sup>	105% range: (99% - 108%)	<b>60.8% +/- 4.6%</b> range: (51% - 66%)
Hand Washes - 20 µg	NA	101% +/-5.1% range: (94% - 107%)

<sup>1</sup> N = 18 for filters and tubes, handwashes, underwear, and coveralls; all values have been corrected for method recovery.

Recoveries for denim coveralls and underwear dosimeters were consistently low. In addition, the authors noticed differences between the first sample set and the other eight which seemed significant. The first set was collected during cloudy and cooler conditions. Therefore, the authors embarked on a study of the influence of time on field spike recovery from the coveralls. Four fortification levels and three time points were used. Little detail is provided in the study on these results, which seem to have become part of the method validation study cited earlier in this review, but what data was reported is summarized in Table 3. The authors' overall conclusion was that chlorpyrifos recoveries from denim coveralls were reduced due to direct exposure to sun and heat, and the recovery values were a function of time. Therefore in the case of denim coveralls, due to the wide variability between field recovery data sets on the different days of sampling, different field spike recovery factors were applied to correct each day of monitoring.

**Table 3. Chlorpyrifos Recovery from Denim Coveralls as a Function of Time**

<b>Chlorpyrifos Fortification Level</b>	<b>Average Recovery After 4 Hours<sup>1</sup></b>	<b>Average Recovery After 8 Hours<sup>1</sup></b>
50 µg	33%	21%
500 µg	33%	21%
5,000 µg	33%	21%
50,000 µg	86%	74%

<sup>1</sup> Many study details are unknown (e.g., number of replicates unknown, standard deviation unknown, a range of temperatures applied (i.e., 69.8° to 95.0° F.) These data were reportedly included in a method validation study previously cited in this review.

## **Inhalation Exposure and Passive Dermal Dosimetry Data - Results**

### General

In order to distinguish differences between inhalation and dermal exposure associated with different application techniques and construction types, exposure data were reported two ways: 1) by route of exposure (inhalation, or dermal - either total or by individual body part); and 2) by structure type.

### Recovery Correction Factors

Exposure data were corrected as follows: 1) all values were corrected for laboratory handling losses (see Table 1 for values used), 2) none of the data were corrected for storage stability losses, in spite of documented losses in some of the samples (see Table 2), 3) depending on the matrix, field spike recovery values were sometimes applied. However, it should be noted that there were no spiked field recovery or laboratory recovery values reported for socks or head patches. Field spike recovery values used are summarized below:

*Air sampling media* - correction factor used was 99.4 percent

*Hand-washings* - data were not corrected

*Coveralls* - different field recovery factors applied for each day's sample collected  
(i.e., 11-55%, average  $22 \pm 13\%$ )

*Underwear* - correction factor used was 61 percent

### Inhalation Exposure

Five replicates (chlorpyrifos filter + tube) from each of the three sites were reported. Sampling times for the 15 replicates ranged between 224 and 534 minutes (median = 389 minutes; mean = 397 minutes).

*Analytical results ( $\mu\text{g}$  chlorpyrifos found in filter + tube):* range: 0.61  $\mu\text{g}$  to 15.96  $\mu\text{g}$  (N=15); mean = 4.97  $\mu\text{g}$ .

*Air concentrations measured:* range: 0.96  $\mu\text{g}/\text{m}^3$  to 29.53  $\mu\text{g}/\text{m}^3$ .

*Average potential inhalation dose:* 1.48  $\mu\text{g}/\text{kg}$  normalized body weight (70 kg), and ranged from 0.17 to 4.7  $\mu\text{g}/\text{kg}$  normalized body weight (N=14, See Table 4).

### Dermal Exposure

Five replicates from each of the three sites were reported. Samples were analyzed from the following six body parts: underwear arms, underwear legs, underwear torso front, underwear torso back, socks, and head patches. Head/neck exposure was estimated using an assumption of 1,300  $\text{cm}^2$  surface area (Series 875 Group A guidelines), and the following formula:

$$\text{Head/neck Exposure} = [\text{Head patch } (\mu\text{g}) / 200 \text{ cm}^2] * 1,300 \text{ cm}^2$$

In addition, hand rinses were reported. [Note that arm and leg exposure in the five replicates from GA "were estimated from an overall penetration factor determined from the other 10 replicates"]. The results were reported individually. Total potential dermal exposure was calculated as the sum of head/neck exposure, underwear arms, underwear legs, underwear torso front and back, and socks.

*Total Potential Dermal Exposure:* range: 1,047  $\mu\text{g}$  to 32,312  $\mu\text{g}$  (N=14);  
(See Table 4) median = 4,814  $\mu\text{g}$ ; mean = 7,653  $\mu\text{g}$ .

[Note: averages calculated after excluding one replicate (AL04) who was sprayed by a broken hose]

Overall, the fraction of the average total potential dermal exposure attributable to the head/neck was 34 percent, while 31 percent was found on the legs, 13 percent was found on the arms, 8 percent was found on the torso front, and hand exposure was 4 percent (despite workers wearing chemical resistant gloves). Torso back and socks were 3 percent and 2 percent, respectively.

As shown in Table 4, the total mean dose, excluding replicate AL04, calculated by addition of average inhalation and absorbed dermal doses, was estimated to be 4.76  $\mu\text{g}/\text{kg}$  normalized BW (70 kg; N=14; range: 0.82 to 16.7  $\mu\text{g}/\text{kg}$  BW), based on an overall average potential inhalation dose of 1.48  $\mu\text{g}/\text{kg}$  BW (31 percent of total dose) and an overall average potential dermal dose of 3.28  $\mu\text{g}/\text{kg}$  BW (69 percent of total dose) measured via passive dosimetry. These values utilize the HED dermal absorption factor of three percent recommended at the time of this review, while the study authors used one percent. The mean value is based on data from 14 replicates because the fifteenth replicate (AL04) had an unusually high dermal exposure resulting from an accident with a broken hose (see Table 4).

As shown on Table 5, the passive dosimetry data were analyzed by the reviewers and used to estimate dermal and inhalation unit exposures ( $\mu\text{g}/\text{lb ai}$ ) based on the average worker-specific amount handled (lb ai) per day, and the worker-specific total dermal or inhalation exposure based on the dosimetry measurements. Table 8 shows that, without the replicate AL04, who was accidentally sprayed with Dursban because of a broken hose, the results are more consistent, with a standard deviation close to the mean for exposure. The mean dermal and inhalation unit exposures were used to calculate the total dermal and inhalation doses for three scenarios (average, minimum and maximum) based on the range of chlorpyrifos (lb ai) handled by the PCOs during the 15 replicates. As shown on Table 5, the amount (lb ai) handled per worker varied significantly and ranged from 4.0 to 22.75 lb ai, with a mean of 11.0 lb ai.

**Table 4: Chlorpyrifos Passive Dosimetry Exposure Data and Dose Calculation**

Replicate #	Potential Dermal Exposure ( $\mu\text{g}$ )	Absorbed Dermal Dose ( $\mu\text{g}/\text{kg}$ ) <sup>1,3</sup>	Airborne Exposure ( $\mu\text{g}$ ) <sup>2</sup>	Inhalation Dose ( $\mu\text{g}/\text{kg}$ ) <sup>3,4</sup>	Dermal + Inhalation Dose ( $\mu\text{g}/\text{kg}$ )
AL01	32312.00	13.85	199.00	2.84	16.69
AL02	1288.00	0.55	18.90	0.27	0.82
AL03	1047.00	0.45	39.80	0.57	1.02
AL04	116371.00	49.87	43.70	0.62	50.50
AL05	20403.00	8.74	190.60	2.72	11.47
VA06	3055.00	1.31	66.40	0.95	2.26
VA07	2243.00	0.96	330.60	4.72	5.68
VA08	1303.00	0.56	93.40	1.33	1.89
VA09	7192.00	3.08	128.70	1.84	4.92
VA10	5842.00	2.50	222.40	3.18	5.68
GA11	8678.00	3.72	25.60	0.37	4.08
GA12	7540.00	3.23	28.20	0.40	3.63
GA13	9084.00	3.89	11.80	0.17	4.06
GA14	2794.00	1.20	26.80	0.38	1.58
GA15	4357.00	1.87	67.40	0.96	2.83
Mean Value	14900.60	6.39	99.55	1.42	7.81
Geometric Mean	5797.35	2.48	63.60	0.91	4.09
Mean Value [Without AL04] <sup>5</sup>	7652.71	3.28	103.54	1.48	4.76

<sup>1</sup> Values based on 3% dermal absorption / 70 kg normalized body weight

<sup>2</sup> Total airborne exposure sample adjusted for standardized 29 L/min inhalation rate \* exposure time

<sup>3</sup> The data is lognormally distributed using Shapiro-Wilks Test

<sup>4</sup> Inhalation exposure / 70 kg normalized body weight

<sup>5</sup> Mean value for each category recalculated without data for replicate AL04, who was accidentally overexposed to diluted Dursban TC when the hose broke and he was sprayed with product. Data for AL04 is included in the table as an example of accidentally high exposure.

**Table 5: Chlorpyrifos Dosage by Pounds AI Handled and Length of Time of Operation**

Replicate#	Avg Lb AI Used	Hours Worked	Linear Feet <sup>1</sup>	Absorbed Dermal Dose ( $\mu\text{g}/\text{kg}/\text{lb ai}$ ) <sup>2</sup>	Absorbed Dermal Dose ( $\mu\text{g}/\text{hr}$ ) <sup>3</sup>	Inhalation Dose ( $\mu\text{g}/\text{kg}/\text{lb ai}$ ) <sup>4</sup>	Inhalation Dose ( $\mu\text{g}/\text{hr}$ ) <sup>5</sup>
AL01	22.75	7.70	274.00	6.09	1258.91	0.12	25.84
AL02	16.25	6.42	170.00	0.34	60.22	0.02	2.95
AL03	14.25	7.95	194.00	0.31	39.51	0.04	5.01
AL04	15.25	6.52	142.00	32.70	5357.23	0.04	6.71
AL05	32.70	5.25	443.00	2.67	1165.89	0.08	36.30
VA06	6.85	5.48	188.00	1.91	167.14	0.14	12.11
VA07	7.85	6.43	296.00	1.22	104.60	0.60	51.39
VA08	4.65	5.03	108.00	1.20	77.66	0.29	18.56
VA09	6.65	3.73	199.00	4.64	577.93	0.28	34.47
VA10	6.25	7.82	126.00	4.01	224.21	0.51	28.45
GA11	6.05	8.03	170.00	6.15	324.07	0.06	3.19
GA12	12.25	8.90	158.00	2.64	254.16	0.03	3.17
GA13	4.55	7.05	128.00	8.56	386.55	0.04	1.67
GA14	4.00	5.00	190.00	2.99	167.64	0.10	5.36
GA15	5.00	7.92	200.00	3.73	165.11	0.19	8.51
<b>Mean Value</b>	11.02	6.62	199.07	5.28	688.72	0.17	16.25
<b>Std Deviation</b>	7.86	1.42	81.67	7.66	1299.69	0.17	14.97
<b>GeoMean</b>	8.93	6.45	186.18	2.78	269.67	0.10	9.86
<b>Mean Value Without AL04<sup>6</sup></b>	10.72	6.62	203.14	3.32	355.26	0.18	16.93

<sup>1</sup> Linear feet of structure that had product applied

<sup>2</sup> Values based on 3% dermal absorption / 70 kg normalized body weight Inhalation exposure / 70 kg normalized body weight

<sup>3</sup> Values based on 3% dermal absorption / hours of application

<sup>4</sup> Total airborne exposure sample adjusted for standardized 29 L/min inhalation rate \* exposure time / 70 kg body weight

<sup>5</sup> Total airborne exposure sample adjusted for standardized 29 L/min inhalation rate \* exposure time / hours of application

<sup>6</sup> Mean value for each category recalculated without data for replicate AL04, who was accidentally overexposed to diluted Dursban TC when the hose broke and he was sprayed with product. Data for AL04 is included in the table as an example of accidentally high exposure.

## Biological Data (Urine samples)

Total absorbed dose was estimated directly by biomonitoring of the chlorpyrifos metabolite 3,5,6-trichloropyridinol (TCP) in the urine samples of five volunteer applicators at the Georgia location. Each applicator collected all the urine voided on the day before application, the day of application, and for four consecutive days after initial exposure. The urine was collected as 12-hour samples. The first day of collection, which was 1 day prior to application, reflected background levels. Urinary creatinine levels were analyzed to validate completeness of urine collection. The urine samples were collected in brown plastic jugs and kept cool on blue ice until collection from the volunteers. The urine's volume was measured and aliquots were placed in the freezer until analysis. The subjects had been asked to abstain from any exposure to chlorpyrifos products for 10 days prior to the first (background) samples being collected and analyzed. The study report does not specify if the volunteers were also instructed to avoid exposure during and after the day of exposure.

### QA/QC

Fortified urine samples (20 µg - 3,5,6-TCP/mL) were prepared using the first urine specimen from volunteers prior to any study-related Dursban TC applications, and from an unexposed person's urine. Recoveries for fortified urines ranged between 91.4 percent and 99.0 percent per set, or 81.4 percent to 104.3 percent per individual sample. For unexposed persons' urine, recovery averaged 94.8 +/-6.4 percent. Additional laboratory recovery samples were processed with each sample set analyzed. At 2.0 ng/mL and 200 ng/mL fortification, average recovery was 93.4 percent +/-6.7 percent.

Daily TCP levels found in urine for each volunteer were corrected for recovery using a control specimen background recovery value specific to that individual volunteer (i.e., 3,5,6-TCP levels found on the day prior to Dursban TC application). Total 3,5,6-TCP excreted per day was corrected by subtracting the individual's background level. One individual (replicate GA14) manifested a high background level of 3,5,6-TCP, possibly indicating an exposure to chlorpyrifos sometime in the previous 10 day period.

The study authors estimated the amount of chlorpyrifos absorbed by the following formula (the fraction (0.6124) 3,5,6-TCP excreted has been adjusted for the fifth day of 10 for total excretion; the fraction used by the study authors was 0.7151):

$$\text{Absorbed Dose (ug/kg BW)} = \frac{(\text{3,5,6-TCP excreted } \mu\text{g/kg} - \text{Bkgd } \mu\text{g/kg})}{(0.6124 \text{ fraction } \underline{\text{3,5,6-TCP}} \text{ excreted in 5 days})} * \frac{(\text{MW chlorpyrifos (350)})}{(\text{MW } \underline{\text{3,5,6-TCP}} \text{ (198)})}$$

This urinary excretion factor of 0.7151 corrects for the fact that only ~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 3,5,6-TCP relative to chlorpyrifos expected to be excreted by day 5. Table 6 summarizes the total amount of 3,5,6-TCP excreted for the 5 day

monitoring period in ug and the estimated total absorbed dose in  $\mu\text{g}/\text{kg}$  BW, corrected using the HED pharmacokinetic model (Appendix A).

Total absorbed chlorpyrifos measured via biological monitoring was slightly higher than total absorbed chlorpyrifos calculated as the sum of 3 percent of total potential dermal dose (measured via passive dosimetry) and potential inhalation exposure (see Table 7). Total absorbed dose was estimated directly by biomonitoring of the chlorpyrifos metabolite 3,5,6-trichloropyridinol (TCP) in the urine samples of four volunteer applicators at the Georgia location (the fifth replicate was one volunteer monitored for 2 days). Each applicator collected all the urine voided on the day before application, the day of application, and for four consecutive days after initial exposure. The urine was collected at 12-hour intervals. There may be several reasons for the difference in estimated absorbed dose levels between biomonitoring and passive dosimetry, including: field spike recovery from coveralls was consistently low (mean = 22 percent) although corrected for the mean recovery rate, or; oral exposures were not accounted for by passive dosimetry, or; subjects participating in biological monitoring experienced exposure to chlorpyrifos outside the study setting.

**Table 6. Total Urinary 3,5,6-TCP Excreted and Calculated Absorbed Chlorpyrifos Dose**

Subject Identifier	Background Chlorpyrifos ( $\mu\text{g}/\text{kg}$ ) Detected <sup>1</sup>	5 Day Total Urinary 3,5,6 - TCP Excreted in $\mu\text{g}$ (corrected for bkgd)	Corrected Absorbed Chlorpyrifos Dose ( $\mu\text{g}/\text{kg}$ BW) <sup>2,3</sup>
GA-11 (BW - 108.86 kg)	0.39	206.06	5.46
GA-12 (BW = 108.86 kg)	0.50	79.40	2.11
GA-13 (BW = 80.72 kg)	0.62	27.11	0.86
GA-14 (BW = 77.1 kg)	3.44	23.66	0.89
GA-15 (BW = 88.90 kg)	0.55	370.55	12.03
MEAN	1.1	141.46	4.27

<sup>1</sup> Background chlorpyrifos ( $\mu\text{g}/\text{kg}$ ) =  $\frac{(3,5,6\text{-TCP prestudy excretion})}{0.72 \text{ (fraction excreted in urine as TCP)}} * \frac{(MW \text{ chlorpyrifos (350)})}{(MW 3,5,6\text{-TCP (198)})}$

<sup>2</sup>The 5 day absorbed dose has been corrected for the fraction of oral dose expected to be excreted in 5 days as 3,5,6-TCP (61 percent) based on the Dow pharmacokinetic model (Appendix 1). The corrected absorbed dose was calculated using the formula:

$$\text{Absorbed Dose (ug/kg BW)} = \frac{(3,5,6\text{-TCP excreted } \mu\text{g/kg} - \text{Bkgd ug/kg})}{(0.6124 \text{ fraction } 3,5,6\text{-TCP excreted in 5 days})} * \frac{(MW \text{ chlorpyrifos (350)})}{(MW 3,5,6\text{-TCP (198)})}$$

<sup>3</sup> The data is lognormally distributed using Shapiro-Wilks Test

Table 7 summarizes the estimated total absorbed dermal and inhalation doses calculated from biomonitoring and passive dosimetry data and the unit dose per pound ai applied for the five biomonitored volunteers.



**Table 7: Estimated Absorbed Chlorpyrifos Dose in Five Dursban TC Applicators**

Replicate ID	Calculated Absorbed Chlorpyrifos Dose <sup>1</sup> (Biomonitoring) $\mu\text{g}/\text{kg}$	Calculated Absorbed Chlorpyrifos Dose (Biomonitoring) $\mu\text{g}/\text{kg}$ (70 kg) / Average # AI Applied	Absorbed Chlorpyrifos Dose (Passive Dosimetry) <sup>2</sup> $\mu\text{g}/\text{kg}$ (70 kg)	Absorbed Chlorpyrifos Dose (Passive Dosimetry) $\mu\text{g}/\text{kg}$ (70 kg) / Avg # AI Applied
GA-11	5.51	$5.51/6.05 = 0.91$	4.08	$4.08/6.05 = 0.67$
GA-12	2.12	$2.12/12.25 = 0.17$	3.63	$3.63/12.25 = 0.30$
GA-13	0.87	$0.87/4.55 = 0.19$	4.06	$4.06/4.55 = 0.89$
GA-14	0.89	$0.89/4.00 = 4.49$	1.58	$1.58/4.0 = 0.40$
GA-15	12.13	$12.13/5.00 = 2.43$	2.83	$2.83/5.0 = 0.57$
MEAN	4.31	$4.31/6.37 = 0.68$	3.24	0.51

<sup>1</sup>See Table 6

<sup>2</sup>See Table 5

### Compliance

Compliance with OPPTS 875 Group A Occupational and Residential Exposure Guidelines (US-EPA, 1995) is critical. The itemized checklist below is based on the "Checklist for Applicator Monitoring Data" and describes compliance with the major technical aspects of the appropriate OPPTS Series 875 Group A guidance. Additional data gaps not covered by the checklist are also presented below:

- *Typical end use product of the active ingredient tested.* The product tested was used as a termiticide on post-construction building foundations, consistent with the product label provided.
- *End use product handled and applied using recommended equipment, application rates, and typical work practices.* These criteria were partially met. Only half the application equipment was fitted with a pressure gauge and none had flow-meters. Therefore, it is difficult to tell whether product was consistently applied at the proper rate specified by the product label. Mean product concentration was equal to maximum label rate of 1.0% (0.71-1.24%).
- *For outdoor exposure monitoring, at least five replicates at each of at least three sites for each job function with the exception of pilots should be monitored.* These criteria were partially met. Mixer/loader and application exposures were not separated at any of the three sites, nor were outdoor and indoor exposures clearly distinguishable (see

below). Also, although five replicates were collected at each of the three sites, these reflect nine, not fifteen, study subjects (and of the nine, only seven unique body weights were recorded). Several of the applicators were evaluated more than once; all applicators participated in three or fewer replicates. Those subjects who participated in biological monitoring (at a single site in GA) supposedly participated in only one replicate each, but replicates GA11 and GA12 had identical body weights.

- *For indoor exposure monitoring at least five replicates at each of at least three sites for each job function must be monitored.* The criterion was partially met. The basement applications likely reflect indoor work at the three basement sites, one of which also had a crawlspace. It is likely that some replicates (i.e., crawlspace applications) reflect a mixture of outdoor and indoor inhalation exposures. This issue was not addressed in the study. No application data sheets were included which could help untangle what fraction of an inhalation exposure sample reflected outdoor versus indoor exposure.
- *Monitoring period is sufficient to collect measurable residues, but not excessive so that residue loss occurs.* This criterion was met. Total mixing, loading, preparation, application and clean up time averaged 6.62 hours (3.73-8.9).
- *Dermal and/or inhalation exposure must be monitored by validated methodologies.* This criterion was partially met. Unpublished validation data for the sampling and analytical methodologies were only summarized - actual validation data were not available for review. However, the sampling and analytical methods used seem to have been appropriate.
- *Quantity of active ingredient handled and duration of monitoring period reported for each replicate.* These criteria were met. However, in at least three cases (AL03, GA13, GA14), significantly more ai was reportedly applied than was handled, and the study report does not explain how that is possible (i.e., did the applicators use other, previously prepared solution in addition to their own).
- *Clothing worn by each study participant and location of dosimeters reported.* These criteria were partially met. The report listed PPE and location of dosimeters, but the gloves and eye protection worn in the photographs were not listed in the report.
- *Quantitative level of detection is at least 1  $\mu\text{g}/\text{cm}^2$ .* This criterion was partially met. LOD and LOQ values were reported (as  $\mu\text{g}$ ) for four sample matrices from a previously performed Dow AgroSciences method validation study (unpublished). LOD and LOQ values for two other matrices analyzed in the study (i.e., socks and head patches) were not reported.
- *Storage of samples consistent with storage stability data.* This criterion was partially met. Storage stability data were submitted for four sample matrices, but were not available for socks and head patches. Storage stabilities ranged between 64 percent and 117 percent. Exposure data were not corrected for storage stability.

- *Efficiency of extraction in a laboratory provided as mean plus or minus one standard deviation. Lower 95 percent confidence limit is not less than 70 percent based on a minimum of seven replications per fortification level or prior Agency approval of extraction methodology provided.* The criterion was met. Laboratory recovery for all matrices ranged from 89.1 percent +/-6.3 percent and 115.2 percent +/-10.0 percent. Laboratory recovery from socks and head patches was not reported.
- *At least one field fortification sample per worker per monitoring period per fortification level for each matrix. At least one field blank per worker per monitoring period for each matrix.* These criteria were met.

### Potential Problems/ Items of Note

- Dates of sample extraction and analysis were not provided in this study.
- The fifteen replicates reflected only nine actual applicator subjects. The authors stated that:

"Several of the applicators participating in this study were evaluated more than once. All of the applicators participated in three or less replicates. As a result, a total of nine different applicators from three different companies and three locations were monitored. Each of the five volunteers in the biomonitoring phase of the study were limited to participation in only one replicate."

It is confusing that although the study states clearly that *nine* different people were monitored, *only seven different weights* are presented in the data.

- Field spikes were reportedly prepared in the field, over a 78-day period, under a variety of environmental conditions. However, the applications of Dursban TC occurred over a 27 day period.
- None of the exposure data were corrected for storage stability losses, but the lowest storage stability average was 89%, so this should have little effect on the data (see Table 2).
- There were no spiked field recovery or laboratory recovery values reported for socks or head patches.
- Data Reporting Discrepancy: In the study report, there is a mismatch between the "estimated total dermal doses" reported in Table 8 (the five GA replicates), and what should be the same values carried over to Table 10. Values in Table 10 do not match those in Table 8, and the discrepancy is not explained. However, in Table 10, the

estimated total dose (potential inhalation dose  $\mu\text{g}/\text{kg BW}$  + 1 percent of estimated amount dermally absorbed) was at least calculated using the higher numbers.

- Field Spike Recovery - Dosimetry: Very low recovery values were reported from denim cotton coveralls (mean = 22 percent) and cotton long underwear (mean = 60 percent). The authors studied this problem and demonstrated the effect of heat and sunlight on recovery of field spikes.
- Clothing Penetration Data: The authors report penetration of chlorpyrifos through coveralls to underwear/dosimetry below. There were 15 replicates for the torso back and front, but only 10 replicates for the legs and arms (i.e., five replicates in GA did not wear long-underwear covering legs and arms beneath their coveralls). Results were as follows:
  - Average penetration through *torso back* coveralls was: 3.9 percent +/-6.6 percent; (N=15).
  - Average penetration through *arms* coveralls was: 3.3 percent +/-2.6 percent; (N=10).
  - Average penetration through *legs* coveralls was: 2.0 percent +/-2.5 percent; (N=10).
  - Average penetration through *torso front* coveralls was: 1.4 percent +/-1.5 percent; (N=15).

In summary, the study completed in support of the regulatory requirements for chlorpyrifos met most of the criteria contained in Series 875 Group A guidelines. The following issues were noted: (1) storage stability data was not presented for all matrices; (2) exposures were not broken out into separate job functions (i.e., mixer/loader and applicator); (3) there were no field spike recovery data or laboratory recovery values reported for socks of head patches; (4) biomonitoring data was very limited; and (5) there were data reporting discrepancies, including numbers of replicates (one was omitted from analysis due to a very high exposure incident).

## Reference

Nolan, R.J., Rick D.L., Freshour, N.L., Saunders J.H. 1984. Chlorpyrifos: Pharmacokinetics in Human Volunteers. *Toxicol. Appl. Pharmacol.* 73:8-15.

**APPENDIX**

**APPENDIX A**  
**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	<i>Ka</i> * <i>f</i>	1/ <i>Ka</i>	<i>exp</i> (- <i>Kt</i> )/( <i>K</i> - <i>Ka</i> )	- <i>K</i> * <i>exp</i> (- <i>Ka</i> * <i>t</i> )/ <i>Ka</i> *( <i>K</i> - <i>Ka</i> )	Cum. Exc. <i>Xut</i> ( <i>t</i> )	Int Excr. <i>Xut</i> ( <i>t</i> )- <i>Xut</i> ( <i>t</i> -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)