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

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JUN 17 1995
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MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: **REVIEW OF STUDY MEASURING ENVIRONMENTAL LEVELS OF AND EXPOSURE TO CHLORPYRIFOS FOLLOWING LAWN CARE TREATMENT**

TO: Linda Propst
PM 73
Reregistration Branch
Special Review and Reregistration Division (7508W)

FROM: David Jaquith
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Occupational and Residential Exposure Branch
Health Effects Division (7509C)

THRU: Larry Dorsey, Chief
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Health Effects Division (7509C)

Please find below the OREB review of ....

DP Barcode: D197713 Pesticide Chemical Code: 059101

EPA Reg. No.: 464-571

Deferral to:

PHED: N/A

1.0 INTRODUCTION

DowElanco has submitted a study measuring environmental levels of chlorpyrifos and exposures of individuals to the insecticide following treatment of turf. The study was conducted to evaluate the potential exposures of individuals to the insecticide as a result of performing activities on residential or recreational turf following application of this material. The study was submitted in response to a Data Call In notice (DCI) issued on September 18, 1991. A protocol was received by the Agency and comments were provided by OREB in October 1992 (1). Dursban Turf Insecticide is an emulsifiable concentrate containing 45 percent chlorpyrifos as the active ingredient (4 lbs ai per gallon). The maximum label rate (for grubs) is 3 fluid ounces of concentrate per 1000 ft^2. Most applications occur at approximately 1/4 of this concentration.

2.0 CONCLUSIONS

OREB has reviewed a study estimating the amount of chlorpyrifos that would be absorbed by individuals performing typical homeowner activities on a lawn treated with Dursban Turf Insecticide (DTI). The material was applied to the turf at the maximum label rate of 3 ounces of DTI per 1000 ft^2, an application rate usually used for grubs. Air concentrations, total residues on aluminum foil coupons, and dislodgeable residues were determined for intervals of up to 48 hours post-application. A drag sled, described in Appendix A, was used to estimate dislodgeable residues. Rinses were used to monitor exposures of the hands. These are considered indirect measurements, requiring additional information and/or assumptions to estimate exposure.

Eight volunteers performed activities intended to mimic a child walking/running, sleeping, crawling, and sitting on the turf. The subjects performed the activities for a period of four hours, beginning when the turf had dried, four hours after application. Absorption of chlorpyrifos was determined by monitoring the amount of the metabolite 3,5,6-trichloro-2-pyridinol (3,5,6-TCP) excreted in the urine over a six-day period following exposure. The mean exposure, corrected for background exposure to the chlorpyrifos was 6.1 μg per kg with a range of 2.5 to 12.2 μg per kg. This method directly measures internal dose. In order to extrapolate these exposures to estimate the potential exposures of children, the registrant estimated the respiratory exposure contribution and subtracted it from the total exposure, yielding an estimate of dermal exposure. The estimates of exposure via the dermal route were then adjusted to account for surface area and pressure differences between adults and children. Oral exposure via hand to mouth activity was estimated by assuming that all of the pesticide removed by hand rinse was available for ingestion. The estimates of exposure of the eight volunteers, using both biomonitoring and extrapolating for child exposure using indirect measurement, are presented in Table 1.

A number of uncertainties are associated with exposure monitoring in the residential environment: 1) It is not known how well the activities conducted during this study relate to activity patterns of the general population; 2) The correlation between residues dislodged by

the drag sled and those removed by contact with human skin has not been established at this time; 3) Hand/oral exposure may in fact be somewhat different from that estimated by using the assumption that all of the residue measured by the hand wash technique is available for oral exposure. The actual contribution from that route is unknown and may be more or less than estimated. Each of the factors needed to extrapolate the indirect measurements to account for child exposure contains some error. Combination of these errors from various factors and assumptions contributes to the total error in the exposure assessments. It is OREBs view that the biomonitoring data, with the addition of the hand rinse residues provides the best estimate of the exposures of children and that children performing the same activities would receive approximately the same exposures as adults **on a mg per kg basis**. Uncertainties associated with these estimates include possible differences in dermal absorption and age-related differences in metabolism of chlorpyrifos. In lieu of extensive data addressing the above uncertainties, OREB considers this study to provide a reasonable estimate of the potential exposure of individuals, both adults and children, to chlorpyrifos following spray application to turf.

A number of environmental measurements were also collected during the study. Analysis of aluminum foil coupons (positive controls) over a 48 hour period indicated that an average of 22.5 percent of the material dissipated from these surfaces within that time. There was no clear evidence of decline in the dislodgeable residues during the first 24 hours, possibly due to the variation between the five samples at each pressure. Dislodgeable residues after 48 hours were lower than those at 24 hours. A t test of the 24 vs. 48 hour samples (pooled for each pressure used) indicated a highly significant ($p < 0.01$) difference between the intervals. This supports the idea that dislodgeable residues fall rapidly after treatment and is consistent with the results of a study found in the scientific literature (2) in which dislodgeable residues declined from 632 $\mu g/ft^2$ of leaf surface (0.68 $\mu g/cm^2$) one hour after treatment to 19 $\mu g/ft^2$ (0.02 $\mu g/cm^2$) after 2 days. Direct comparison of the two studies is not possible because of differences in study design. However they both indicate similar trends in dislodgeable residue behavior.

As expected, air concentrations peaked within 2-4 hours after application and continued to decline for the remainder of next 48 hours. The concentrations measured after 48 hours were 3.64 μg per m^3 and 1.93 μg per m^3 at heights of 15 inches and 60 inches, respectively.

3.0 DESCRIPTION OF STUDY

3.1 Treatment

Dursban Turf Insecticide (DTI) was applied to a 200 ft x 200 ft area of turf using conventional lawn-care application equipment. The grass was approximately 3 to 4 inches in height. Two gallons of DTI were mixed with 348 gallons of water to prepare enough 0.29 percent spray to treat approximately 2 acres of turf. Since the total treatment area was 40000 ft^2 the total amount applied was approximately 160 gallons of the finished spray. Assay of the spray tank indicated a concentration of 0.3 percent. The material was applied

to the turf at the maximum label rate of 3 ounces of DTI per 1000 ft^2 (for grubs). Approximately 190 gallons of spray mix was left in the tank after application. Application was made at 9:00 AM and the spray was allowed to dry for 4 hours. The turf plot was divided in half, forming two 100 ft x 200 ft subplots. One half was used for physicochemical evaluation and the second for the activity pattern portion of the study.

3.2 Physicochemical Measurements

Several investigations were conducted In the physicochemical (PC) portion of the plot. Ten areas were designated in the PC subplot. Two aluminum foil coupons attached to gauze pads (3 in x 3 in) were placed in each of these areas before application. All twenty of these coupons were removed immediately after application to determine deposition ($\mu g/ft^2$). The gauze backing served to trap any material that might run off the smooth aluminum foil surface. A diagram of the test area is presented in Figure 1. The mini-areas are presented in Figure 2. The gauze/aluminum coupons were stored in amber glass bottles and stored on ice for shipment to the laboratory. These samples were kept frozen until analysis.

Drag sampling areas were established in each of the ten areas to be used to determine transfer coefficients. Dislodgeable (Transferrable) residues were determined by the use of the Dow drag system ("Dow sled", described in Appendix A.). The system has been used to determine dislodgeable residues on carpet surfaces in previous submissions (3). The system uses a lead weight on a 3" x 3 " plywood block. For this study two weights were used; one to imitate the pressure from a 10 kg child, and a second intended to imitate an adult female weighing approximately 60 kg. A drag sample was collected from each of the ten mini-areas 4 hours after application (after the spray had dried) and at intervals of 8, 12, 24, and 48 hours after the treatment. Five of these samples were collected using high pressure and 5 with low pressure at each interval. A diagram of the mini area used for drag sampling is presented in Figure 2. The drag lanes were guided with a plywood grating 48 inches in length. Each drag sample consisted of a single pass over the treated area. Denim was used to imitate human skin. Each drag coupon was rolled up and store in vial on dry ice until analysis.

Air sampling was conducted at the center of the interface between the two 20,000 ft^2 subplots. Samples were collected at heights of 15 inches and 60 inches, reflecting the breathing zones of a child and an adult, respectively. Air concentrations of chlorpyrifos were determined by drawing air through sampling cassettes at a rate of one liter per minute using calibrated high speed Flow-Lite pumps for approximately one hour. The sampling cassettes consisted of cellulose membrane filters (GN-4) backed up by tubes containing Chromosorb 102 to trap any vapors. During the 4-hour activity period (described below) a time weighted average (TWA) was determined for all participants at both heights using a separate sampler. Sampling tubes and cassettes were stored on dry ice for shipment to the analytical laboratory where they were stored frozen until analysis.

Positive controls were prepared by spiking a known amount of the chlorpyrifos formulation

Table 1. Estimates of the Exposures of Adults and Children Performing Activities on Turf Treated with a 0.29 Percent Chlorpyrifos Spray.

Subject	Exposure (μg/kg)								
		Adult				Child			
	Biomonitoring	Inhalation	Dermal	Hand/Oral	Total	Inhalation	Dermal	Hand/Oral	Total
1	2.5	0.46	2.0	1.22	3.7	1.14	2.0	1.76	4.9
2	6.9	0.53	6.4	1.38	8.3	1.14	6.2	2.99	10.4
3	9.7	0.55	9.2	0.37	10.1	1.14	3.5	0.45	5.1
4	5.3	0.61	4.7	0.52	5.8	1.14	6.2	0.99	8.4
5	4.4	0.63	3.8	0.73	5.1	1.14	4.9	1.33	7.3
6	3.0	0.60	2.4	0.48	3.5	1.14	3.2	0.92	5.3
7	8.7	0.59	8.1	0.18	8.9	1.14	11.2	0.36	12.7
8	4.6	0.55	4.1	0.35	5.0	1.14	7.9	0.43	9.5
Mean	**5.6**	**0.60**	**5.1**	**0.7**	**6.3**		**5.6**	**1.2**	**8.0**
Std. Dev.	**2.6**	**0.10**	**2.6**	**0.4**	**2.5**		**2.9**	**0.9**	**2.8**
Maximum	**9.7**	**0.60**	**9.2**	**1.4**	**10.1**		**11.2**	**3.0**	**12.7**
Minimum	**2.5**	**0.50**	**2.0**	**0.2**	**3.5**		**2.0**	**0.4**	**4.9**

DIAGRAM 1

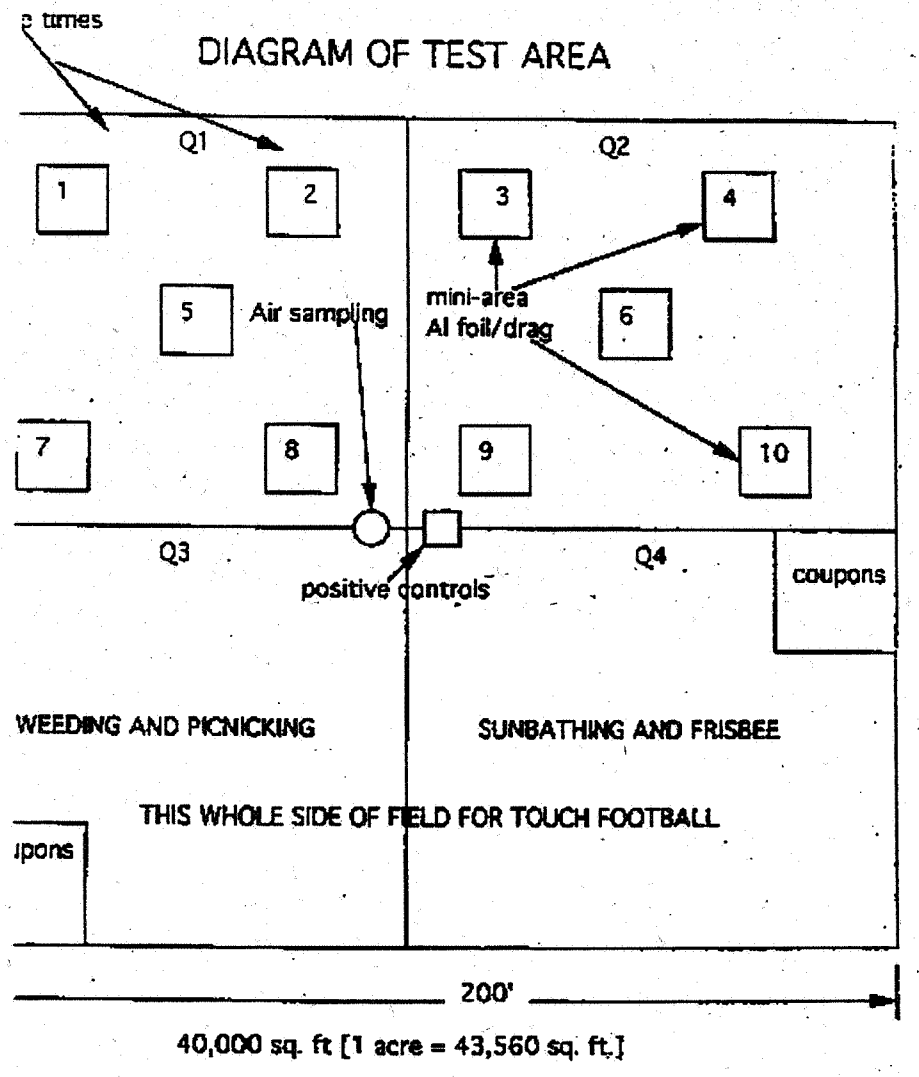
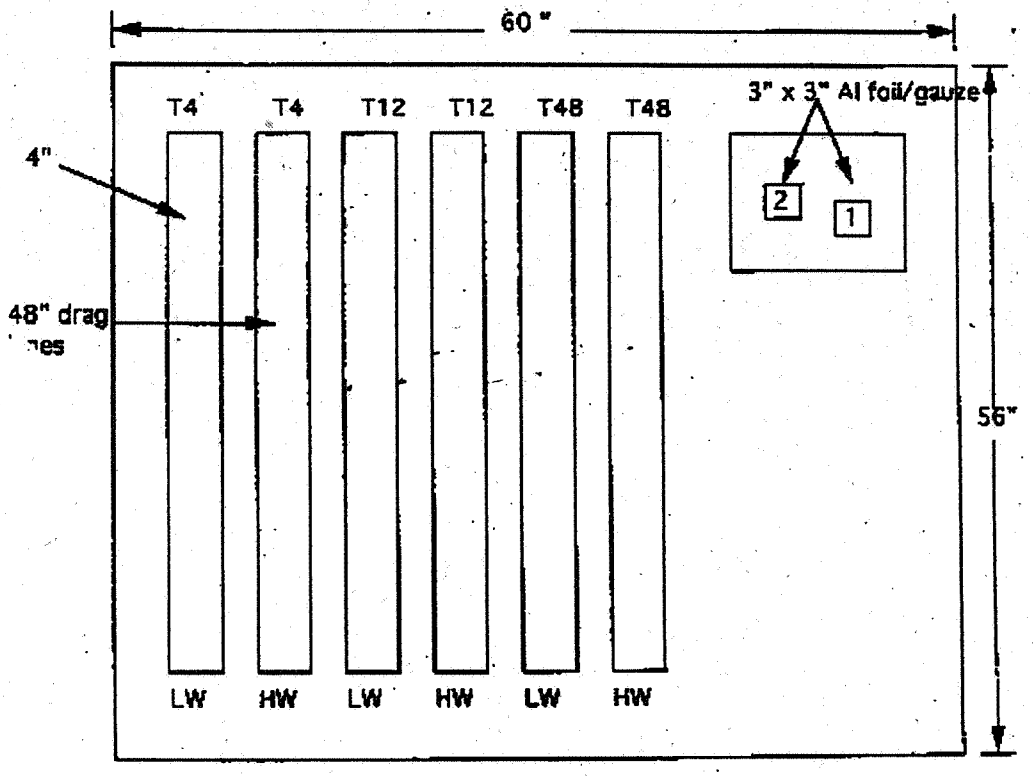


FIGURE 1

DIAGRAM 2

DIAGRAM OF MINI-AREA



LW; LOW WEIGHT

HW; HIGH WEIGHT

FIGURE 2

on aluminum foil coupons. Twenty one such coupons, with a target mass of 2910 μg/coupon, were prepared. Three of these were removed for analysis immediately after application and at intervals of 1, 2, 4, 8, 12, and 48 hours after treatment.

3.3 Human Activity Monitoring

Human activity monitoring was conducted on the second 20,000 ft^2 subplot. Five different activities were selected to represent the behavior of individuals on the treated turf and began at the time the turf dried, 4 hours after application. Activity started with a picnic lunch, eaten under an awning. This was followed by 30 minutes of frisbee. The participants then crawled on the turf for 30 minutes, imitating weeding activity or a child crawling. This was followed by a half hour of touch football. The activity period concluded with sunbathing for 30 minutes followed by a second 30 minutes of touch football. The touch football was intended to mimic a child walking/running; the sunbathing, a child sleeping; frisbee, a child walking; weeding, a child crawling; and picnicking, a child sitting on the turf. Sunbathing was conducted on a blanket, a typical behavior pattern, and was conducted under an awning to decrease exposure of the volunteers to sunlight. The activities and the representative respiratory volumes, used for estimation of the contribution of the inhalation route, are presented in Table 2. During the activity period, each participant wore only a T-shirt and shorts. Running shoes were added during touch football to prevent injury. Each volunteer was instructed to wait at least 4 hours following the activity period before showering to allow absorption of any chlorpyrifos from the skin.

Table 2. Activities and Respiratory Volumes Used to Calculate Exposures of Volunteers to Chlorpyrifos After Treatment of Turf with a 0.29 Percent Spray of Dursban Turf Insecticide.

Activity	Time (min)	Activity Category	Resp Rate(l/min)[1]			Height of Sampler[3]
			Adult Male	Adult Female	Child[2]	
Touch Football	60	Heavy	40.9	26.5	4.2	60 in.
Sunbathing	30	Rest	12.2	5.7	1.5	15 in.
Frisbee	60	Heavy	40.9	26.5	4.2	60 in.
Weeding	30	Light	13.8	8.1	4.2	15 in.
Picnicking	60	Rest	12.2	5.7	1.5	15 in.
Total	**240**	**TWA =**	**27**	**16**	**3.2**	

[1] Values obtained from Exposure Factors Handbook (4)
[2] Values for children not available from the Exposure Factors Handbook, those provided by the registrant were used for calculations. No data available for heavy work, light task values used.
[3] Sampler Height of 15 inches used for all calculations for children.

3.4 Hand Rinse

At the end of the activity period the hands of each subject were rinsed with a dilute of the surfactant, dioctyl sodium sulfosuccinate (DSS). The persons hands were held over a bowl and doused with 250 ml of the solution. This wash was followed by a rinse with 250 ml of deionized water. Sodium chloride (15 g) was added to facilitate phase separation. The rinsate was then partitioned with ethyl acetate (200 ml) which was also used to rinse the bowl. The ethyl acetate phase was analyzed for chlorpyrifos. All liquids were stored on ice prior to analysis.

Urine Collection

All urine voided was collected on the day prior to the start of the study and for the next five days. Each daily sample was collected as two specimens, each representing the total urine voided during a 12 hour period. The first collection period started after the first voiding in the morning and ended at approximately 7 PM. The second began with the first voiding after this time and ended with the first voiding the next morning. Urine voided at the start of the first pre-study collection period was discarded. Urine voided at the start of each succeeding period was added to the previous intervals total. Specimens were collected at ambient temperatures in 4-liter amber Polypac containers.

The specimens were weighed upon receipt and the volume calculated by weight, assuming a specific gravity of 1.00. Aliquots were removed, transferred to glass containers, and stored frozen until analysis for creatinine and 3,5,6 -trichloro-2-pyridinol (3,5,6-TCP), a metabolite of chlorpyrifos. Urinary 3,5,6-TCP was isolated from the urine samples after acid hydrolysis and extraction with ether. The extracts were derivatized and quantified by GC/MS. To document that 3,5,6-TCP was not lost during storage or analysis pre-study urine samples were fortified and analyzed with the study specimens.

3.4 Analytical Methods

Chlorpyrifos residues were quantified by capillary gas chromatography using a flame ionization detector. Standards of chlorpyrifos in an appropriate solvent were analyzed with the study samples to determine a mean response factor or to determine a regression equation. The average recovery for spikes with each type of sampling medium were comparable with the method recoveries. Average recovery for the spikes was 99.4 $\pm$ 12.2 percent.

The 3,5,6-TCP concentrations were determined using negative-ion chemical-ionization gas chromatography-mass spectrometry (NCI-GC/MS). Five ml aliquots of urine were fortified with 3,4,5-TCP and acidified to pH 1 with 0.5 ml of concentrated HCL. The samples were then hydrolyzed at 80 °C for 2 hours. After cooling the samples were extracted with 5 ml of diethyl ether. The ether extracts were then evaporated tom dryness under nitrogen and taken up in 1 ml of o-xylene. This was followed by derivatization with 0.1 ml N-(t-butyldimethylsilyl)-N-methyltrifluoroacetamide to form dimethylsilyl derivatives of TCP and 3,4,5-TCP. This was then followed by quantification by NCI-GC/MS. Urinary concentrations of TCP were corrected for daily recovery obtained from fortified control urine samples.

The assessment of the completeness of urine sampling was determined by analysis of the creatinine content of the urine samples. The creatinine concentration and urine volumes were used to determine total creatinine output. This was then normalized by the subjects body weight. The resulting values were compared to standard literature values of 14 to 26 mg/kg/day (5). The results were also compared to other samples from the same individual for consistency. Urine collection was considered complete if the creatinine excretion was within or exceeded the normal range and/or if the excretion rate was consistent within that individual.

4.0 Results and Calculation of Exposures

4.1 Biological Monitoring (Direct Methods)

4.1.1 Blood

Two blood samples were collected on separate days from each participant during the week prior to the conduct of the study. Additional 5 ml samples were collected approximately 24 and 48 hours after the exposure period. These samples were analyzed for plasma cholinesterase activity. Collections and assays were performed by the Medical Department of the registrant. The measured plasma cholinesterase levels are presented in Table 3.

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Table 3. Measurements of Plasma Cholinesterase in Volunteers Exposed to Chlorpyrifos Applied to Turf.

Volunteer	Pre-Study Baseline	24 Hour	% of Baseline	48 Hour	% of Baseline
1	2490	2304	93	2374	95
2	4608	4449	97	No Sample	No Sample
3	2002	2130	106	2072	103
4	4027	3597	89	3783	94
5	5003	5158	103	4399	88
6	3876	3566	92	3690	95
7	3980	3566	90	3787	95
8	2691	2335	87	2660	99
MEAN	**3585**	**3388**	**95**	**3252**	**.96**

4.1.3 Estimation of Exposure from Urinary 3,5,6-trichloro-2-pyridinol (3,5,6-TCP) Measurements

The registrant calculated exposures from urinary metabolites using two separate methods. One method estimated the absorbed dose by dividing the cumulative amount of the metabolite 3,5,6-TCP excreted by the fraction of absorbed dose expected to be excreted during the collection period. The collection period lasted approximately 6 days (138 hours) during which approximately 89 percent of the absorbed chlorpyrifos would be predicted to be excreted. The registrant used an interval of 144 hours (91 percent excretion), resulting in a negligible difference in exposure values. OREB used the registrant's value during calculations. The cumulative amount of 3,5,6-TCP excreted was divided by the expected portion of total excretion (0.91) and also by 0.72. The latter factor results from the finding that only 72 percent of an oral dose is excreted in the urine. Additional correction was necessary for the ratio of the molecular weights of 3,5,6-TCP (198) and chlorpyrifos (350.6) The pharmacokinetic model used to determine the portion expected to be excreted is presented in Appendix B. The registrant used a computer program to estimate the cumulative percent of excretion at differing time intervals. OREB has previously duplicated these predictions, within rounding error, using a personal computer spreadsheet program (2).

The second method was derived from a one compartment model designed to describe the time course of 3,5,6-TCP excretion in volunteers after administration of chlorpyrifos to their forearms. A previous study by the registrant indicated that 71 percent of the administered chlorpyrifos was excreted in the urine. The absorption and elimination constants from this study were 0.0308/hr and 0.0258/hr, respectively. This study has been reviewed by Toxicology Branch (6). However, that document did not mention the kinetic constants presented by the registrant. Exposures derived from both the pharmacokinetic model and that based on the literature study were in excellent agreement. OREB calculated exposures

based on the equation presented in Appendix B only, with the assumption that the parameters of that model are correct but notes that the first order rate constants used in the calculations were obtained from that literature study. The suitability of these constants and the model should be verified by Toxicology Branch. Estimates of total chlorpyrifos absorbed were obtained by inserting the interval during which urine was collected into the model presented in Appendix B. Approximately 91 percent of the total excretion would be expected to occur within 6 days of dosing. The estimated dose then becomes:

$$\text{Estimated dose } (\mu g) = \frac{\mu g \text{ TCP excreted}}{0.91 \times 0.72} \times \frac{350.6 \ \mu g \text{ Chlorpyrifos}}{198 \ \mu g \text{ TCP}}$$

$$= \mu g \text{ TCP excreted} \times 2.7 \text{ or } \mu g \text{ TCP excreted} \div 0.37$$

A correction was also made for the presence of 3,4,5-TCP in pre-study urine samples. Although the participants were instructed to avoid exposure to chlorpyrifos for at least a week prior to the study, measurable quantities of 3,5,6-TCP were found in pre-study urine specimens. These pre-study 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 six days after study exposure. The excretion data was therefore corrected to determine the exposure to chlorpyrifos associated with the study exposure. If the background exposure is constant, the amount excreted in the urine per day can be used to estimate the daily exposure by dividing by the proportion excreted in urine (0.72) and the ratio of molecular weights as described above. For example subject 1 (weighing 59.0 kg) excreted 7.88 μg of 3,5,6-TCP on the day prior to the study. The background exposure would be:

7.88 μg 3,5,6-TCP/day x (350.6 μg chlorpyrifos/198 μg 3,5,6-TCP) ÷ 0.72

= 19.4 μg chlorpyrifos/day or 0.33 μg/kg/day

The registrant then corrected the total excretion of 3,5,6-TCP to account for this background level. It was assumed that the background excretion remained constant throughout the sampling period of approximately 6 days. The total amount of 3,5,6-TCP excreted was adjusted to account for this phenomenon. The formula for this correction was:

Corrected Excretion = [Cumulative excretion - (6 days x pre-study excretion)]/0.37

where:

Cumulative excretion = μg 3,5,6-TCP excreted during the post-exposure sampling interval (138 hours or approximately 6 days)

Pre-Study excretion = μg 3,5,6-TCP excreted on the day before the study

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The registrant determined that seven of the urine samples were either incomplete or erroneously place in the wrong sampling container based on the creatinine output rate. Correction of these seven samples was achieved by multiplying the amount of 3,5,6-TCP in the specimens by the ratio of the mean creatinine excretion rate for that individual to the amount in that particular specimen. Application of this correction factor resulted in only minor changes in the total 3,5,6-TCP excretion and the correction was not used by OREB in the calculation of total absorption. The estimates of total chlorpyrifos absorption based on urinary excretion data are presented in Table 4. The registrant corrected the values for only three of the eight volunteers to account for background. OREB corrected the results for all of the participants, resulting in slightly lower exposure values than those ealculated by the registrant in some cases.

4.2 Indirect Measurements

4.2.1 Total Deposition

The results of sampling of the aluminum foil coupons, removed immediately after application to determine deposition ($\mu g/ft^2$) are presented in Table 5. The maximum label rate for Dursban Turf Insecticide (4 lbs ai per gallon) is 3 fluid ounces of concentrate per 1000 ft^2. Most applications occur at approximately 1/4 of this concentration. Three fluid ounces of concentrate would contain:

lbs ai/1000 ft^2 = 3 fl oz x 1 gal/128 fl oz x 4 lbs ai/gal

= 0.094 lb ai/1000 ft^2 = 0.000094 lb/ft^2

= 0.0426 g/ft^2 = 4.26 x 10^4 $\mu g/ft^2$ = 46 $\mu g/cm^2$

Analysis of deposition coupons averaged 34 $\mu g/cm^2$ (Range 9-70 $\mu g/cm^2$), well within the range to be expected when a chemical is applied to a lawn using conventional lawn care equipment. The material appears to have been applied at the proper rate.

Table 4. Estimated Absorption of Chlorpyrifos Following Treatment of Turf with a 0.29 Percent Spray. Estimates are derived from 3,5,6-TCP excreted in the urine over a six day period after performing activities on the turf.

Subject	BW (kg)	Cumulative 3,5,6-TCP µg Excreted	Pre-Study 3,5,6-TCP µg Excreted	Pre-Study Chlorpyrifos µg Excreted	Pre-Study 3,5,6-TCP (µg/kg/day)	Pre-Study Dose (µg/kg/day) Chlorpyrifos	Cumulative 3,5,6-TCP µg Excreted[1]	Chlorpyrifos (µg) Uncorrected	Chlorpyrifos (µg) Corrected	Absorption (µg/kg) Uncorrected	Absorption (µg/kg) Corrected
1	59	109.4	7.88	14	0.19	0.34	102	276	148	4.7	2.5
2	88.5	293.7	9.81	17.4	0.15	0.27	284	768	608	8.7	6.9
3	49.9	191.9	1.93	3.4	0.05	0.09	190	514	482	10.3	9.7
4	77.2	191.2	5.64	10	0.1	0.18	186	503	411	6.5	5.3
5	74.5	230.2	15.7	27.8	0.29	0.51	215	581	326	7.8	4.4
6	78.1	126.5	5.52	9.8	0.1	0.18	121	327	238	4.2	3
7	80.4	396	19.63	34.8	0.34	0.6	376	1016	698	12.6	8.7
8	49.9	120.9	5.06	9	0.14	0.25	116	314	231	6.3	4.6
MEAN	69.7	207.5	8.9	15.8	0.2	0.3	199	537	394	8	5.6
STD. DEV.	14.7	98.3	6	10.6	0.1	0.2	94	253	156	2.8	2.6

[1] Corrected for pre-study excretion.

Pre-Study 3,5,6-TCP (µg/kg/day) = Pre-Study 3,5,6-TCP excreted/0.72/BW
Pre-Study Chlorpyrifos (µg/kg/day) = Pre-Study 3,5,6-TCP * 350.6/198
Chlorpyrifos (Uncorrected) = Cumulative 3,5,6-TCP/0.37
µg Chlorpyrifos (Corrected) = µg Chlorpyrifos (Uncorrected) - (6 * µg Pre-Study Chlorpyrifos)/0.37
Absorption, ug/kg (Uncorrected) = Chlorpyrifos (Uncorrected)/BW
Absorption, µg/kg (Corrected) = Chlorpyrifos (Corrected)/BW

Table 5. Deposition of Chlorpyrifos on Aluminum Foil Coupons Following Treatment of Turf with a 0.29 Percent Spray. The area of each coupon was 58 cm^2.

Mini-area	Deposition (Average of Two Replicates per Mini-area)		
	µg/coupon	µg/sq cm	µg/ft^2
1	1225	21	339
2	1585	27.5	25000
3	2090	36	32728
4	1522	26	23636
5	2785	48	43636
6	2425	42	38182
7	3010	51.5	46818
8	2335	40.5	36818
9	1940	33.5	30455
10	850	14.5	13182
Mean	1977	34	29079

4.2.2 Dislodgeable Residues

Dislodgeable residues were determined by dragging a weighted block over one square foot of turf (36 in x 4 in) using a sampler described in Appendix A. Two different pressures were used, one to imitate the force of a child and the other to mimic the force of an adult female. The results of this drag sampling are presented in Table 6. There was no significant difference between high and low pressure sampling up to the 48 hour interval (Wilcoxon Rank Sum, $p<0.05$). After 48 hours the high pressure sampling dislodged about twice the amount of the low pressure (mean = 20.3 µg/ft2 for high pressure, 10.3 µg/ft2 for low pressure). Table 6. The data are presented graphically in Figure 2. The two pressures used tended to yield separate results after 48 hours, perhaps indicating a stronger binding of the chlorpyrifos to the turf over time. However, lack of a clear difference between the time periods, as illustrated in Figure 3, precludes development of a regression equation to define changes in dislodgeable residues over time. It may be possible that continued sampling after 48 hours would have shown the presence of a trend but these data are not available. OREB has assumed that, for each pressure, the dislodgeability of chlorpyrifos from grass is constant over time. The data for each pressure was pooled to yield an overall mean. These means are also presented in Table 6.

4.2.3 Air Monitoring

The results of air sampling are presented in Table 7. Two different types of samples were collected during the study; a series of one hour samples to determine dissipation of airborne chlorpyrifos; and a four hour sample taken during the activity period to determine the time weighted average (TWA). The TWA sample was used to estimate the respiratory component of exposure as described below.

4.2.4 Hand Rinse

Hand rinse samples were collected at the end of the activity period using the surfactant, dioctyl sodium sulfosuccinate (DSS). These samples were used to estimate the potential oral exposure that might occur from hand to mouth activity of a child. The data are presented in Table 8. The calculations to determine total exposure are presented in Section 4.3.

4.3 Estimation of Total Exposure, the Contribution from Different Routes, and Surface Area Contacted Using Indirect and Biological Monitoring

4.3.1 Total Exposure and Contribution from Different Routes

The registrant estimated the contribution of the inhalation, dermal, and hand/oral routes to the total exposure using biomonitoring (urine) data, dislodgeable residues, air monitoring and hand rinse data. Biological monitoring does not differentiate between the different routes but rather is an indicator of the total internal dose. The contribution of the dermal route was estimated by subtracting the respiratory exposure in Table 7 from the biomonitoring total exposure values obtained from urinary data in Table 4. In order to estimate hand/oral exposure it was assumed that all of the material measured by hand rinse was available for subsequent ingestion. Table 9 combines the results of direct and indirect monitoring and provides an estimate of the contribution of the various exposure routes.

4.3.2 Estimation of Surface Area Contacted

The registrant derived an estimate of the amount of surface area contacted from the estimated dermal dose and the dislodgeable residues. Dermal dose would be:

$$\text{Dermal dose } (\mu g/kg) = \frac{\text{Dislodgeable Residues } (\mu g/ft^2) \times \text{Surface Contacted } (ft^2) \times \text{pct absorbed}}{\text{BW (kg)} \times (0.01)}$$

Rearranging to solve for surface area:

$$ft^2 \text{ Contacted} = \frac{\text{Dermal Dose x kg BW}}{0.01 \times \mu g/ft^2 \text{ dislodged}}$$

The registrant used a dermal absorption of 3 percent, OREB used 1 percent in the calculations in accordance with a memorandum from Toxicology Branch (5). The estimates of surface area contacted are presented in Table 10.

4.3.3 Extrapolation of Exposure from Adults to Children

The registrant extrapolated from the estimated respiratory, dermal and handwash data for adults to derive an estimate of the potential exposure of a one year old child. A number of assumptions were necessary for this extrapolation. OREB used a dermal absorption value of 1 percent rather than the 3 percent used by the registrant:

1. A one year old child weighs 10.2 kg and has respiratory volumes of 1.5 L/min and 4.2 L/min while at rest and while active, respectively. The time weighted average respiratory volume over a 4 hour period is 3.2 L/min (Table 1).

2. The area contacted by a child is 20 percent of the area contacted by an adult performing the same activities.

3. The dislodgeable residues obtained from the low pressure drag sled were used for the calculations. The average of the 4 and 8 hour sampling was 19.3 $\mu g/ft^2$.

4. A child's hand has a surface area approximately one quarter that of an adult.

The calculations for determination of a child's exposure are the similar to those for adults. The results are presented in Table 11.

4.2.3 Air Monitoring

Air was monitored at heights of 15 inches and 60 inches from a single sampling station located at the center of the field. The results of this sampling are presented in Table 7. Samples collected at the lower level tended to be higher than the 60-inch height at all sampling intervals.

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Table 6. **Dislodgeable Residues of Chlorpyrifos from Lawns Treated with a 0.29 Percent Spray. The DOW drag sled was used for sampling (see Appendix A).**

	Replicate	4 Hrs	8 Hrs	12 Hrs	24 Hrs	48 Hrs
Low Pressure:	Low-1	10.6	13.5	21.6	19.3	12.3
	Low-2	29.4	17.7	23.8	37	12.4
	Low-3	7.6	12.6	11.7	26.6	7.2
	Low-4	39	11.1	24.6	24.4	7.6
	Low-5	31.4	20.4	29.5	22.5	11.9
	Mean	**23.6**	**15.06**	**22.24**	**25.96**	**10.3**
	Std. Dev.	**13.8**	**3.9**	**6.6**	**6.7**	**2.6**
High Pressure:	High-1	24.2	21.1	27.4	29.8	18.4
	High-2	40.4	13.6	28.5	23.5	21.2
	High-3	10.5	16.2	17.9	27.7	18.1
	High-4	29.7	16.2	27	23.3	25.2
	High-5	34	14.6	39.4	28.7	18.8
	Mean	**27.76**	**16.34**	**28.04**	**26.6**	**20.3**
	Std. Dev.	**11.3**	**2.9**	**7.6**	**3**	**3**

4.2.4 Positive Control (Dissipation) Samples

The dissipation of chlorpyrifos was measured on a non-porous surface, aluminum foil. This would be expected to yield a relatively rapid dissipation of the material and would not necessarily represent environmental surfaces contacted by individuals. They do, however, provide a uniform surface to assess the loss of material in the environment. Three positive control coupons, each spiked with a target mass of 2910 μg, were collected immediately after treatment and at intervals of 1, 2, 4, 8, 12, and 48 hours after application. The results of these samples are presented in Figure 4. The percent loss of material is presented in Figure 5. The average percent loss after 48 hours was 22.5 percent (range 17.4-30.3). There were no data documenting the kinetics of any further dissipation provided in the submission. While Figure 4 indicates that the material does tend to dissipate with time, the material appears to maintain a relatively constant level for the first 12 hours, followed by a decrease over the next 24 hours.

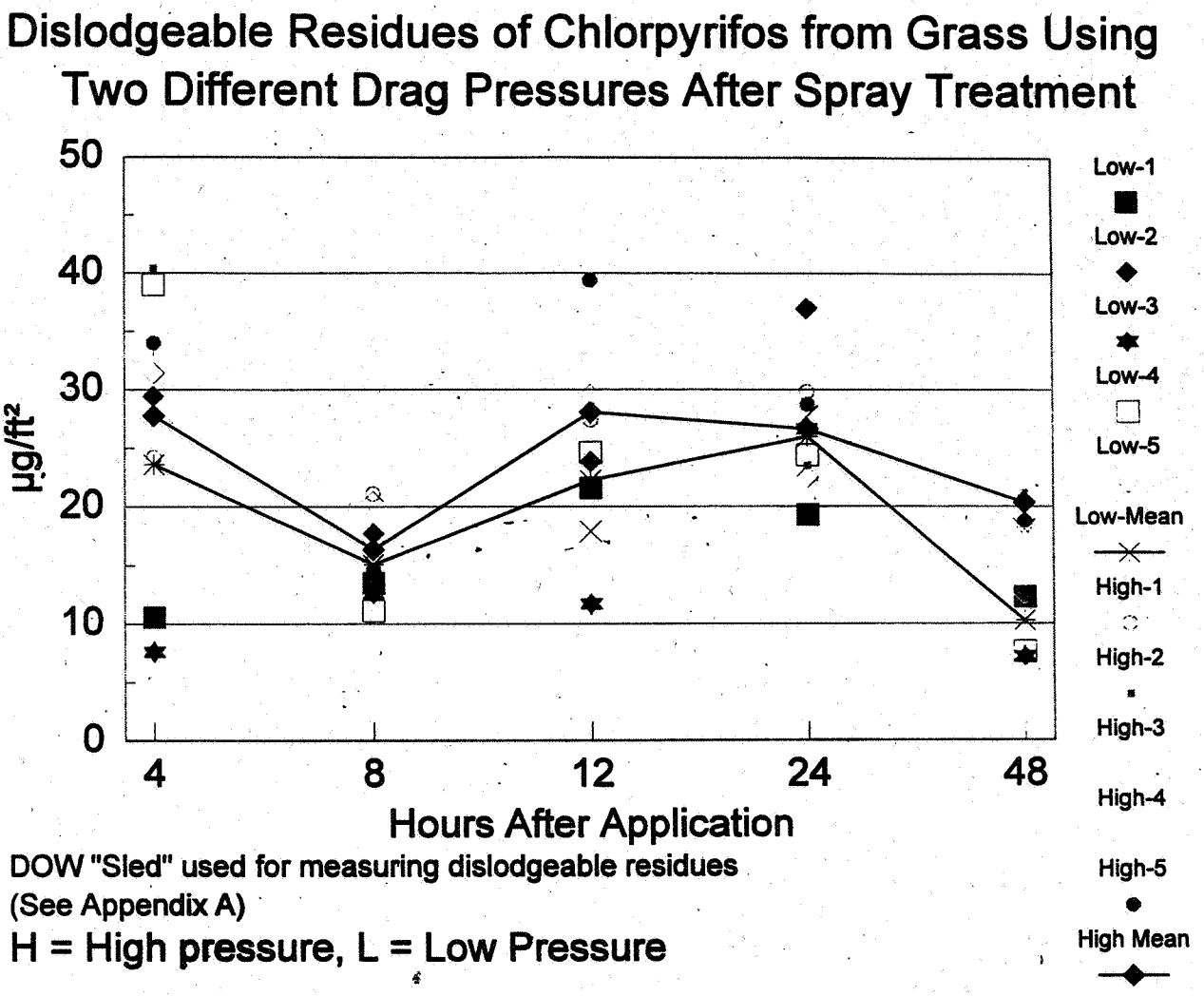

Dislodgeable Residues of Chlorpyrifos from Grass Using Two Different Drag Pressures After Spray Treatment
50
40
30
20
10
0
µg/ft²
4
8
12
24
48
Hours After Application
Low-1
Low-2
Low-3
Low-4
Low-5
Low-Mean
High-1
High-2
High-3
High-4
High-5
High Mean
DOW "Sled" used for measuring dislodgeable residues
(See Appendix A)
H = High pressure, L = Low Pressure

FIGURE 3

Table 7. Air Concentrations of Chlorpyrifos Following Spray Application of a 0.29 Percent Solution to Turf. Low height was 15 inches and high height was 60 inches.

Height	Interval (Hrs)	0	1	2	4	8	12	24	48
LOW:	Time (min)	74	61	58	59	60	35	60	61
LOW:	Flow (LPM)	0.98	0.98	1.02	1.03	1.02	0.98	1	0.99
LOW:	μg Detected	0.71	1	1.21	1.06	0.58	0.03	0.52	0.22
LOW:	Conc. (μg/cu m)	9.79	16.73	20.45	17.44	9.48	0.87	8.67	3.64
HIGH:	Time (min)	73	62	58	59	60	35	60	61
HIGH:	Flow (LPM)	1.02	1	1.03	1.03	1.02	1.02	1.03	1.02
HIGH:	μg Detected	0.25	0.4	0.44	0.38	0.22	ND	ND	0.12
HIGH:	Conc. (μg/cu m)	3.36	6.45	7.37	6.25	3.59	0.09	0.09	1.93

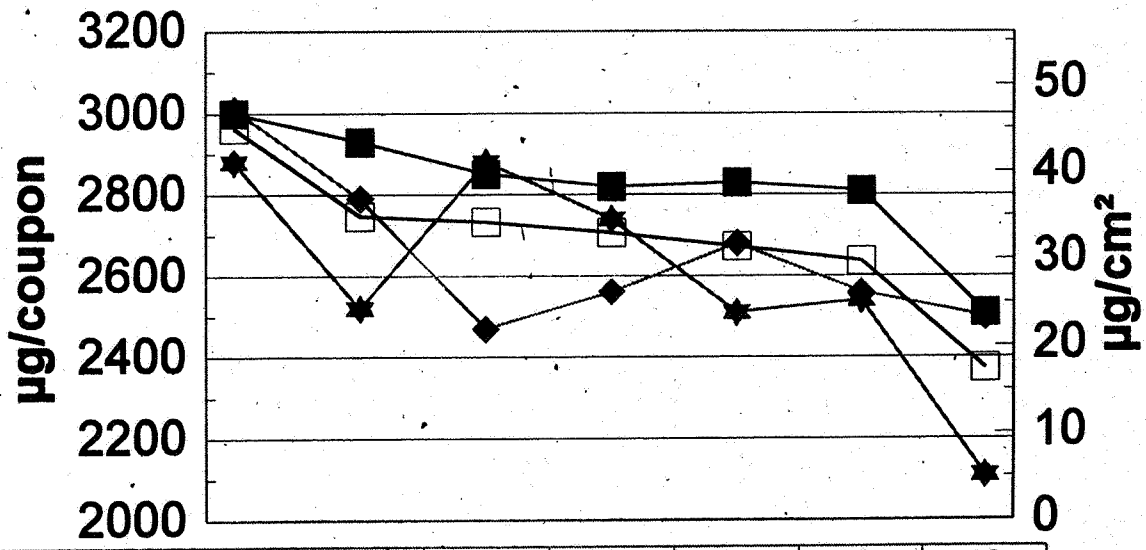
Level of Detection =0.17 $\mu g/m^3$

TIME WEIGHTED AVERAGES (During Activity Period)[1]:

	High	Low
Sample Time (min)	233	233
Flow Rate (LPM)	0.98	1
μg Chlorpyrifos Detected	1.16	3.53
Concentration ($\mu g/m^3$)	4.98	15.15

[1] Note: A separate sampler was used during the activity period.

Dissipation of Chlorpyrifos from Aluminum Foil Coupons Used as Positive Controls for Turf Reentry Study



Hours After Application	0	1	2	4	8	12	48
Replicate 1	3,000	2,930	2,850	2,820	2,830	2,810	2,510
Replicate 2	3,010	2,790	2,470	2,560	2,680	2,560	2,500
Replicate 3	2,880	2,520	2,880	2,740	2,510	2,540	2,110
Mean	2,963	2,747	2,733	2,707	2,673	2,637	2,373

Each Coupon has a surface area of 50 cm²

FIGURE 4

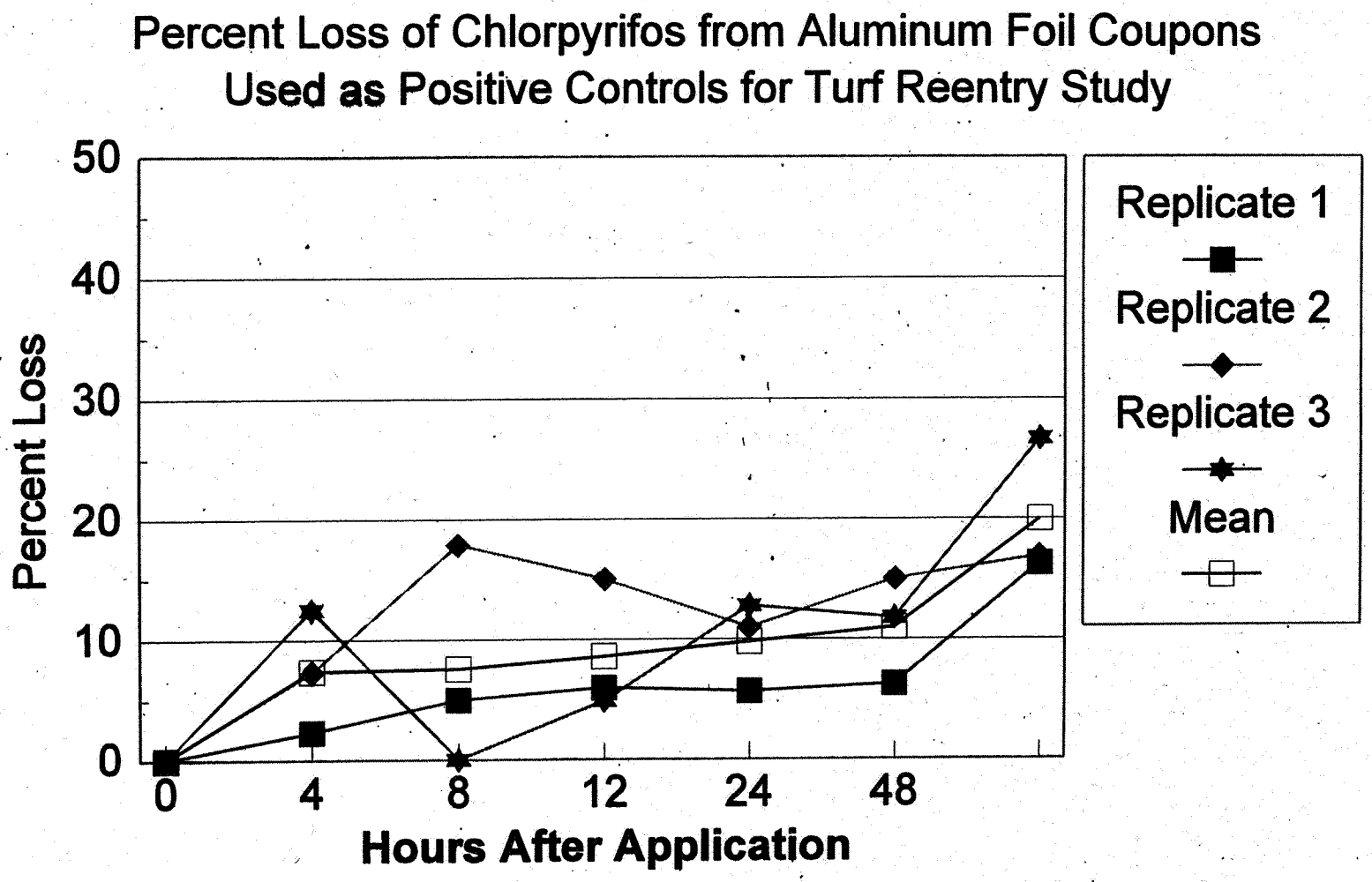

Percent Loss of Chlorpyrifos from Aluminum Foil Coupons
Used as Positive Controls for Turf Reentry Study
Percent Loss
50
40
30
20
10
0
0
4
8
12
24
48
Hours After Application
Replicate 1
Replicate 2
Replicate 3
Mean

FIGURE 5

Table 8. **Results of Hand Rinse Sampling of Volunteers After Performance of Activities on Turf Treated with Chlorpyrifos.**

Volunteer	Sex	BW (Kg)	µg Found	µg/kg
1	F	59	72	1.22
2	M	88.5	122	1.38
3	F	49.9	18.4	0.37
4	M	77.2	40.2	0.52
5	M	74.5	54.2	0.73
6	M	78.1	37.6	0.48
7	M	80.4	14.5	0.18
8	F	49.9	17.6	0.35
Mean (Females)			**36**	**0.64**
Mean (Males)			**53.7**	**0.66**
Mean (All)			**47.1**	**0.65**
Overall Std. Dev.			**36.2**	**0.43**

Table 9. Estimates of Total Exposure of Subjects to Chlorpyrifos and Contribution of Different Routes After Performing Activities on Turf Treated with Dursban Turf Insecticide.

		Exposure (μg/kg)					
	BW (kg)	Biomonitoring	Respiratory	Dermal	Oral/Hand	Total	Pct from Hands
Male:	**77.2**	5.3	0.61	4.7	0.52	5.8	9.0
	74.5	4.4	0.63	3.8	0.73	5.1	1.2
	78.1	3.0	0.60	2.4	0.48	3.5	14.0
	80.4	8.7	0.59	8.1	0.18	8.9	14.0
	88.5	6.9	0.53	6.4	1.4	8.3	2.0
Mean		**5.7**	**0.59**	**5.1**	**0.66**	**6.3**	**11.0**
Maximum		**8.7**	**0.63**	**8.1**	**1.4**	**8.9**	**14.0**
Minimum		**3.0**	**0.53**	**2.4**	**0.18**	**3.5**	**2.0**
N		**5**	**5**	**5**	**5**	**5**	**5**
Female:	**59.0**	2.5	0.46	2.0	1.2	3.7	32.0
	49.9	4.6	0.55	4.1	0.37	4.9	7.6
	49.9	9.7	0.55	9.2	0.35	10.1	3.5
Mean		**5.6**	**0.52**	**5.1**	**0.64**	**6.2**	**14.0**
Maximum		**9.7**	**0.55**	**9.2**	**1.2**	**10.1**	**32.0**
Minimum		**2.5**	**0.46**	**2.0**	**0.35**	**3.7**	**3.5**
N		**3**	**3**	**3**	**3**	**3**	**3**
Combined:							
Mean		**5.6**	**0.57**	**5.1**	**47.1**	**52.7**	**12.0**
Std. Dev.		**2.4**					**9.5**
Maximum		**9.7**	**0.63**	**9.2**	**122.0**	**128.9**	**14.0**
Minimum		**2.5**	**0.46**	**2.0**	**14.5**	**23.0**	**2.0**
N		**8**	**8**	**8**	**8**	**8**	**8**

Table 10. Estimates of the Surface Area Contacted While Performing Activities on Turf Treated with Chlorpyrifos. A 1 percent dermal absorption is assumed and the average between 4 hour and 8 hour dislodgeable residues were used in the calculations.

Subject	BW (kg)	Dermal	Sq ft Contacted
4	77.2	4.7	1649
5	74.5	3.8	1287
6	78.1	2.4	852
7	80.4	8.1	2960
2	88.5	4.1	1649
1	59	2	536
3	49.9	4.1	930
8	49.9	9.2	2087
MEAN			1494

Table 11. Calculation of the Area Contacted and Estimated Exposure of Children Performing Activities on Turf Treated with 0.29 Percent Chlorpyrifos.

Subject	Sq ft Contacted By Adult	Sq ft Contacted By Child	Handrinse (μg)	Exposure (μg/kg) of Child			
				Dermal	Respiratory	Hand/Oral	Total
1	536	107	72.0	2.02	1.14	1.76	4.9
2	1649	330	122.0	6.24	1.14	2.99	10.4
3	930	186	18.4	3.52	1.14	0.45	5.1
4	1649	330	40.2	6.24	1.14	0.99	8.4
5	1287	257	54.2	4.86	1.14	1.33	7.3
6	852	170	37.6	3.22	1.14	0.92	5.3
7	2960	592	14.5	11.2	1.14	0.36	12.7
8	2087	417	17.6	7.89	1.14	0.43	9.5
MEAN	**1494**	**299**	**47.1**	**5.65**	**1.14**	**1.15**	**8.0**

Dislodgeable residue = 19.3 μg/sq ft.
Dermal Absorption = 1 percent
Body Weight = 10.2 kg
Child Hand Factor = 0.25
Air Concentration = 15.2 μg/cu m
TWA Respiratory Volume = 3.2 L/min

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REFERENCES

1. Memorandum from P. Perreault (OREB) to J. Edwards (RD) titled "Review of Protocols for Occupational and Residential Exposure Monitoring Studies Submitted in Response to the 9/18/91 Reregistration DCI for Chlorpyrifos", dated October 7, 1992.

2. Hurro, K.A. and M.G. Prinster (1993) Dissipation of Turfgrass Foliar Dislodgeable Residues of Chlorpyrifos, DCPA, Diazinon, and Pendamethalin. IN Pesticides in Urban Environments. American Chemical Society Symposium Volume 522, K.D. Racke and A.R. Leslie Eds. American Chemical Society , Washington, D.C.

3. Memorandum from D. Jaquith (OREB) to D. Edwards (RD) titled "Review of Study Measuring Indoor Levels of and Exposure to Chlorpyrifos Following Carpet Treatment", dated August 18, 1995.

4. EPA (1990) Exposure Factors Handbook. EPA/600/8-89/043.

5. Tietz, N.E. (1976) Fundamentals of Clinical Chemistry. W.B. Saunders Company, Philadelphia, pg. 998.

6. Memorandum from A. Levy (TB-I) to L. Propst (SRRD) titled "CHLORPYRIFOS - Human Oral and Dermal Absorption", dated March 6, 1995.

cc: Chlorpyrifos file
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APPENDIX A. **Comparison of the pressure exerted on the Dow "Sled" and that from a One Year Old Child. (Note: This Appendix was extracted verbatim from the registrant's submission, MRID No. 420084-00)**

"To provide uniform pressure, a drag system was used to obtain wipe test results. A 3" x 3" x 3/4" piece of plywood was used as the base of the drag system. On the top of the plywood, a cradle to hold an 8.5 pound lead sphere, commonly used as a downrigger in fishing, was constructed. The rationale for using this weight was that it approximated the pressure exerted by a child standing (on two feet) and/or crawling with hands and knees touching the floor. The pressure applied by the 8 1/2 pound sphere, on the block, was 8.5 x 454 g/lb divided by 9 in^2, which is equal to 492 g/in^2 or 0.944 lbs/in^2. A one year old child has an approximate weight of 20-25 pounds (average 22.5 pounds). The approximate area of a one year old's hand is 2" x 4" or 8 in^2; two hands equal 16 in^2. The contact area of a one year old's knee is approximately 2" x 2" or 4 in^2; two knees equal 8 in^2. Therefore, the approximate area of two hands and two knees is 16 in^2 + 8 in^2 = 24 in^2. The weight of the child when crawling id supported by two hands and two knees. Minimum balance support is given by the top of the feet. Using 22.5 pounds x 454 g/lb, divided by 24 in^2 is equal to 426 g/in^2 or 0.938 pounds per in^2. A 22.5 pound child standing supports his/her weight on two feet approximately 5" x 2.5" or 12.5 in^2; two feet have 25 in^2 of surface. The pressure applied by a 22.5 pound child is 22.5 lb x 454 g/lb divided by 25 in^2 equals 408.6 g/in^2 or 0.9 lbs/in^2. The pressure applied by the proposed drag system approximates the pressure applied by a one year old child weighing 22.5 pounds. The 8 1/2 pound lead sphere was placed in the cradle to distribute uniform pressure on the 9 in^2 piece of plywood. To the underside of the 9 in^2 plywood block, a 4" x 4" denim pad was fastened to the front eye hook. The pad was folded up the front of the plywood block such that the entire bottom surface was covered by the denim."

Appendix B. Pharmacokinetic Model Used by DowElanco to Estimate the Amount of Chlorpyrifos Absorbed After Exposure.

The Model is of the form:

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

Where:

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

Day	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	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	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	38.2	0.2820	0.0879
	60	0.0222	32.47	42.53	26.4	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	12.6	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
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
	252	0.0222	32.47	0.30	0.07	0.7157	0.0017