State of California
Memorandum

HSM-95002
(Numbered after original issuance)

To: Ralph Shields, Registration Specialist
Pesticide Registration Branch

Date: February 14 , 1995

Place: Sacramento

Phone : 445-4244

From: Tareq A. Formoli, Associate Environmental Research Scientist
Department of Pesticide Regulation:
Worker Health and Safety Branch

PRODUCT NAME: Rx For Fleas Plus®
ACTIVE INGREDIENT: Orthoboric acid
COMPANY NAME: Rx for Fleas, Inc.
I.D. NUMBER: 50366-100
DOCUMENT NUMBER: 149898-E
EPA REGISTRATION NUMBER: 59111-1

Subject: **TITLE:** Dosimetry Study for Rx For Fleas Plus®: Toxicology Review, Exposure Assessment, Risk Characterization

BACKGROUND:
This data volume consists of three parts. Part 1 is the toxicology review of boric acid and its salts. Part 2 is a roller press study to estimate transfer of Rx For Fleas Plus® (dislodgeable residues) from treated carpets to dosimeter patches in contact with the treated carpets in an indoor residential setting. Part 3 is the dose estimation and risk characterization for residential occupants exposed to carpets treated with Rx For Fleas Plus®. Rx For Fleas Plus® (64% boric acid and 36% sodium sulfate by weight) is a powder that can be used in various indoor sites including homes for fleas and other insect control. In homes, it can be applied as spot treatment or directly on carpets and worked deep into the fibers. Any powder visible after application is brushed into the carpet fibers or vacuumed.

REVIEW OF PART 2:
The purpose of the roller press study (Part 2) was to estimate the transfer of boric acid on carpet to humans by using the method suggested in Ross *et al*. 1991. Sampling patches were pressed against the treated carpet by a roller that approximated the mass per unit area of a crawling child. Several variables were included in the study to imitate the potential residential conditions and application techniques. The roller press study was conducted in a clean one-room cottage approximately 15 ft x 13 ft. The carpets were treated with protective treatments (StainMaster® or Scotchguard®) by the manufacturers before the installation. The locations of carpet swaths were randomly selected. The roller press study was divided into two stages. In stage I, carpets were treated with Rx For Fleas Plus® at an application rate of 3.8 g/ft^2. Four variables (application method, carpet pile type, sampling technique, and vacuuming) were included in the first stage. Rx For Fleas Plus® was applied to textured, plush, or level loop carpet piles. The carpet piles received either misting or no misting following application but before grooming. Dry or moistened sampling patches were used. Samples were taken before and after the treated carpets were vacuumed six times. It was determined in stage I that textured pile carpets, misting following application, using moistened sampling dosimeters, samples taken prior to vacuuming combination was the extreme case.

In stage II, Rx For Fleas Plus® was applied to carpets at an application rate of 9.1 g/ft^2, using the extreme case combinations. Two variables (carpet material and pile height) were included in this stage. Rx For Fleas Plus® was applied to synthetic (nylon) with a pile height of 3/8 or 5/8 inches or wool carpets.
A total of 120 samples and six blanks were collected in stage I and 40 samples and four blanks were collected in stage II. In addition, 20 deposition samples and 10 spikes were also collected during the study.

The deposition samples were taken by placing dosimeter patches over the carpet swaths at random locations just before the application. The product was sprinkled over each carpet swath using a plastic container with several small holes in the cap. The deposition sampling patches were collected following the product application.

In stage I, a hand-held water mister was used to spray tap water over the carpet swaths that were randomly selected to receive the misting. The other carpet swaths (non-misted) were covered with polyethylene sheeting during misting. The misted carpet swaths were groomed with a carpet grooming machine after the misting operation. The polyethylene sheets were removed from the non-misted carpet swaths. The non-misted carpet swaths were also groomed. In stage II, once the deposition samples were collected, each carpet swath was misted and then groomed.

The dislodgeable residue sampling media were made of 17 x 17 inch patches of white percale bed sheet (50% polyester/ 50% cotton). The dislodgeable residue sampling patches were placed over the carpet sampling areas. The sampling patch was covered with a 20x20 in. piece of thin polyethylene. A 24x24 in. piece of cotton towel was placed over the polyethylene sheet. The near and far edges of polyethylene and towel were pinned into place using wood strips with projecting nails. A swivel handled roller weighing 25 lb was rolled 10 cycles, back and forth, over the towel. The towel and the polyethylene sheet were removed and the dislodgeable residue sampling patch was placed into a plastic bag. For the first 15 samples in stage I (non-misted), some bunching and/or folding of the sampling patches occurred. This was prevented or minimized for the remainder of samples by securing the far-side wooden strips into place with an iron bar loaded with a steel box.

After the first round of dislodgeable residue sample collection in each stage, all carpet swaths were vacuumed six times. A second round of sample collection was conducted approximately three hours after the vacuuming. All collected samples were stored at room temperature two to ten days until submitted to the analytical laboratory. Samples were analyzed for boron, using U.S. EPA Method 6010. The average recovery for spiked samples was 90.4 percent. Because the sampling medium was 50% polyester, much of the material did not digest in the sample preparation acid. To determine the amount of boron remaining in the sampling medium, three random-selected samples from the first 20 samples were turned to ash in a crucible. The ashes were analyzed for boron. The analytical method reporting limit was 25 ug boron/sample. Samples below the reporting limit were assumed at the reporting limit.

Based on the data in stage I, the following variable categories produced significantly ($P < 0.005$) higher transfer of boron to sample patches and they were considered extreme case conditions: textured pile type carpet, unvacuumed, misted application, and moistened sampling patches. In stage II, nylon, unvacuumed, low pile carpets were considered extreme case conditions. The results were reported both as boron and boric acid, using the 1:5.72 factor for stoichiometric conversion of boron to boric acid.

No significant difference was observed between the stage I and stage II extreme case mean values despite the increased application rate in stage II ($P=0.26$). The application rate in the proposed label (included in the volume as an Exhibit and recently received by the Department following federal approval) is one pound/300 ft^2 (1.5 g/ ft^2), which is much lower than those used in the study. The misting during application increased the transfer rate, as indicated in the discussion section of the study. Since misting during application is not reflected in the label, it only helped in building a more conservative estimate of dislodgeable residue.

Table 1
Results of Deposition and Dislodgeable residue Samples

Stage	Application rate	Deposition*		Dislodgeable Residues* (a.i.)		Percent Transfer to Roller	
	Product g/ft^2	Product (g/sample)	a.i. (g/sample)	Standard (mg/sample)	Extreme (mg/sample)	Standard	Extreme
I	3.8	7.78 ± 0.84	4.67 ± 0.50	5.4 ± 0.92	45.2 ± 6.3	0.12	0.97
II	9.1	16.16 ± 2.19	9.70 ± 1.31	10.1 ± 1.89	36.6 ± 2.9	0.10	0.38

* - Mean ± standard error
Standard - All samples
Extreme - Extreme case conditions
Sample size = 2.0 ft^2 (1,860 cm^2)

REVIEW OF PART 3:
The third section (dose estimation and risk characterization) is the estimate of human exposure and absorbed dose based on the equilibrium model. It was assumed that boric acid transfer from the treated carpet to the human body was identical to that of sampling patches pressed against the treated carpets. Two scenarios were discussed: 1) total human body surface area will come in contact with the treated carpet, and 2) only the body surface area in contact with the floor during crawling motion (hands, forearms, feet, and lower legs) will come in contact with the treated carpet. Both of these scenarios are variants of what we have termed the "equilibrium model" of exposure assessment. This assumes that during the period of contact of the body with the treated surface that the concentration on the body will come into equilibrium with the dislodgeable concentration on the surface. The exposure to the skin surface area in contact with the treated carpet will be equivalent to the residues found in sampling patches pressed against the treated carpet (dislodgeable residues). Dermal dose estimates for the standard case were made based on dislodgeable residue rate of 5.4 mg/sample for the standard case in stage I. Dermal dose estimates for the maximum case were made based on the upper 95% confidence limit of the extreme case dislodgeable residues of 57.8 mg/sample in stage I (the highest observed dislodgeable residue value). The results are shown in Table 2. No estimates of orally absorbed dose from potential ingestion were made.

Table 2
Estimates of Dermally Absorbed Dose Made in Risk Characterization Section

Cases	Exposure Scenario	Estimate of Dermally Absorbed Dose[a] of Boric Acid (mg)		
		Male	Female	Child (3-6 years)
Standard	Total body	0.51	0.50	0.21
Standard	Crawling	0.15	0.12	0.07
Maximum	Total body	5.4	5.1	2.2
Maximum	Crawling	1.6	1.3	0.8

a. Dermal absorption of 1% and body surface area of 1.8, 1.7, and 0.7 m^2 for adult male, adult female, and child, respectively.

DISCUSSION:
Since there is no instruction for vacuuming in the proposed product label, the data (average) from all samples taken prior to vacuuming is more representative for estimating exposure. Because of the lack of label instruction for vacuuming following application, the dislodgeable residue rate that was obtained

from all samples (including after vacuuming) may not represent a realistic common scenario. Table 3 shows the dislodgeable residue and percent transfer rates that were calculated based on all samples taken prior to vacuuming.

Table 3
Results of Dislodgeable Residue Samples Prior to Vacuuming

Stage (# of samples)	Deposition (g a.i./sample[b])	Dislodgeable Residue[a] (mg a.i. /sample[b])	Percent Transfer
I (60)	4.67	9.65 ± 12.63	0.21
II (20)	9.70	17.81 ± 12.34	0.18
Weighted Average (80)	5.93	11.69 ± 13.05	0.20

a . Mean ± standard Deviation
b. Sample size = 2.0 ft^2 (1,860 cm^2)

Using the equilibrium model, Table 4 shows the estimates of dermally absorbed dosage for total body exposure based on the weighted average dislodgeable residue rate calculated in Table 3 for the standard scenario (11.69 mg/sample) and the upper 95% confidence limit of the extreme dislodgeable residues rate in Table 1 for the extreme scenario (57.8 mg/sample). Table 4 also shows the estimates of potential oral exposure from mouthing of contaminated hands. Indoor exposure studies have estimated that hand exposure accounted for approximately 14% of total dermal exposure (Ross *et al*., 1992, Formoli, 1994). The Oral dose in Table 4 was estimated assuming that 50% and 5% of total hand exposure of children and adults, respectively, will eventually be taken orally (Ross *et al*., 1992).

Table 4
Estimates of Dermally and Orally Absorbed Doses of Boric Acid
for Standard and Extreme Case Scenarios

		Dermal Dose[c]		Oral Dose[d]		Dermal + Oral Dose	
	Body surface area (cm^2)	Standard mg/person	Extreme mg/person	Standard mg/person	Extreme mg/person	Standard mg/person	Extreme mg/person
Male	19,400[a]	1.22	6.03	0.86	4.22	2.08	10.25
Female	16,900[a]	1.06	5.25	0.75	3.68	1.81	8.93
Child (1 year)	3,925[b]	0.25	1.22	1.73	8.54	1.98	9.76

Dislodgeable residue sample size = 1,860 cm^2
Standard case dislodgeable residues (DR) = 11.69 mg/1,860 cm^2 = 0.0063 mg/cm^2
Extreme case dislodgeable residues (DR) = 57.8 mg/1,860 cm^2 = 0.0311 mg/cm^2
a. Thongsinthusak et al., 1993
b. Snider et al., 1974
c. Dermal dose (mg/person) = Body surface area (cm^2) x Standard or extreme DR (mg/cm^2) x 0.01(Dermal absorption of 1%)
d. Oral dose (mg/person) = Body surface area (cm^2) x Standard or extreme DR (mg/cm^2) x 0.14 (hand exposure of 14%) x 0.5 or 0.05 (hand residue ingestion of 5% or 50% by children or adults).

Another method for estimating dermal exposure from dislodgeable residues is the transfer factor model. A transfer factor is calculated from the actual human dermal exposure values (ug/hour) observed over the

dislodgeable residues (ug/cm^2) observed. Using a dermal transfer factor of 43,800 cm^2/hour for an adult human that was obtained in evaluation of an indoor occupant exposure study (Formoli, 1994) and an average 0.2% dislodgeable residues obtained from this study (Table 3), absorbed doses are estimated for different rates of application in Table 5. We assume that one hour would be a reasonable upper bound estimate of aerobic contact of the full body with a carpet surface.

Table 5

Rate of application (g/ft^2)	Rate of Application (mg/cm^2)*	Dislodgeable Residues (DR) (mg/cm^2)	Transfer Factor (TF) (cm^2/hr)	Dermal Dose[a] (mg/person)	Oral Dose[b] (mg/person)	Dermal + Oral Dose (mg/person)
9.1	**9.8**	0.020	43,800	8.58	2.72	11.30
3.8	**4.1**	0.008	43,800	3.59	1.09	4.68
1.5	**1.6**	0.003	43,800	1.40	0.41	1.81

a. Dermal Dose (mg/person/hour) = DR (mg/cm^2) x TF (cm^2/hour) x 0.01(dermal absorption)
b. Oral dose (mg/person) = Body surface area (cm^2) x DR (mg/cm^2) x 0.14 (hand exposure of 14%) x 0.05 (hand residue ingestion of 5% by adults).

*- this should be reduced to 64% since the product is 64% a.i. resulting proportional decrease in dermal dose. This observation was made later in December 14, 1995. T. Formoli

The dislodgeable residue samples taken before vacuuming were significantly higher than those taken after vacuuming. While the samples before vacuuming were used as a more likely scenario to estimate exposure, the reduction in dislodgeable residues following vacuuming is an indicator of reduction in subsequent exposures. The permissible exposure level (PEL) for borates and boron oxide dust is 10 mg/m^3 for occupational exposure. However, no significant exposure via inhalation is anticipated due to lack of vaporization of boric acid and relatively large particle size and concomitant setting rate of the dust. The estimates of dermal exposure in Tables 2, 4, and 5 are made for residential occupants wearing no clothing. The estimates of the absorbed doses are based on 1% dermal absorption. These are conservative assumptions that result in conservative estimates of dermally absorbed doses. Clothing will provide significant dermal protection to the covered areas of the body and reduce dermal exposure. Dermal absorption of boric acid may be much less than 1%. Studies have shown no or insignificant absorption of boric acid from intact skin (Draize and Kelley, 1958; Stuttgen, *et al*., 1982; Pfeiffer, *et al*., 1945). However, boric acid is readily absorbed from broken or abraded skin (Stuttgen, *et al*., 1982; Pfeiffer, *et al*., 1945).

CONCLUSION:
Boron is present in food, water, laundry and hand soaps, cosmetics, and pharmaceuticals. The daily intake of boron from water and food has been estimated to range between 0.5 to 20 mg/day for an adult human, with an average of 3 mg/day (Hunt, et al., 1991; Seiler and Sigel, 1988; WHO, 1973; Nielsen, 1991). The range is equivalent to boric acid intake of 3 to 114 mg/day and the average is equivalent to 17.2 mg/day. A typical school lunch provides approximately 0.5 mg of boron (WHO, 1993), equivalent to 2.9 mg boric acid. **The estimates of absorbed doses of boric acid for adults and children in Table 2, 4, and 5 are below the average daily intake from the environment, except possibly for the extreme case scenario for children in Table 4. However, the extreme case scenarios in Table 4 are based on the highest dislodgeable residues for 3.8 and 9.1 g/ft^2 application rates. These application rates are 2.5 to 6 fold higher than the current product label rate. All estimates of exposure to boric acid from Rx For Fleas Plus® are within the referenced range.**

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