UNITED STATES ARMY ENVIRONMENTAL HYGIENE AGENCY

ABERDEEN PROVING GROUND, MD 21010

DERMAL PENETRATION AND DISTRIBUTION OF ^{14}C-LABELED PERMETHRIN ISOMERS
STUDY NO. 75-51-0351-83
FEBRUARY 1980 - DECEMBER 1982

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The insecticide permethrin was assessed for skin absorption potential in rabbits and dogs following a single application. Radiolabeled cis and trans isomers of permethrin were used. Radiocarbon appearing in excreta for one or two weeks following treatment was the measure of absorption. Rabbits absorbed about 30 percent of the topical dose, generally appearing in urine within 24 hours. Dogs demonstrated similar kinetics though only 10 percent absorption occurred. Enteric elimination was significant in dogs. Absorption of permethrin in man should be less than 8 percent of the applied dose.

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REPLY TO ATTENTION OF

HSHB-OT-P/WP

15 JUL 1983

SUBJECT: Dermal Penetration and Distribution of ^{14}C-Labeled Permethrin Isomers, Study No. 75-51-0351-83, February 1980 - December 1982.

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20307

EXECUTIVE SUMMARY

The purpose, essential findings/conclusions and recommendations of the inclosed report follow.

a. Purpose. The insecticide permethrin has been proposed as an impregnant in military fatigue uniforms. Formulations contain varying cis-trans isomer mixtures of the chemical. The potential for skin penetration and bodily distribution of individual isomers and a 50/50 mixture was assessed in dogs and rabbits using the radiolabeled chemicals.

b. Essential Findings/Conclusions. Absorption of topically applied permethrin isomers as measured in excreta through 7 or 14 days registered 30 percent in rabbits and 10 percent in dogs. Urinary excretion was the primary elimination pathway accounting for nearly 75 percent of radioactivity appearing in excreta, usually within the first 24 hours. Radiocarbon recovered in feces was consistently higher (2.5 X) following cis permethrin application than for trans. Absorption/elimination kinetics for the cis-trans mixture generally fell between values observed for the individual isomers. No affinity for tissue binding of permethrin moieties was observed in either animal model. Based on the current and earlier tests, absorption of permethrin in man should be less than 8 percent of the applied dose. The projected bioavailability to man from permethrin impregnated fabric (0.125 mg/cm^2) should be less than 0.026 mg/kg/day.

c. Recommendations. It is recommended that permethrin be approved for further testing as a clothing or fabric impregnant at concentrations to 0.125 mg/cm^2 and that the trans isomer significantly predominate in commercial formulations.

FOR THE COMMANDER:

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REPLY TO ATTENTION OF
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DERMAL PENETRATION AND DISTRIBUTION OF ^{14}C-LABELED PERMETHRIN ISOMERS
STUDY NO. 75-51-0351-83
FEBRUARY 1980 - DECEMBER 1982

1. AUTHORITY.

a. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the Department of Agriculture, Agricultural Research, Science and Education Administrations; titled Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

b. Letter, AFPCB, Armed Forces Pest Control Board, 21 October 1975, subject: Request for Toxicological Evaluation.

c. Letter, AFPCB, Armed Forces Pest Control Board, 5 April 1977, subject: Request for Toxicological Evaluation.

2. REFERENCE. Toxicology Division, this Agency, Standing Operating Procedure, Radioisotope Studies, April 1981.

3. BIBLIOGRAPHY. See Appendix A for selected bibliography.

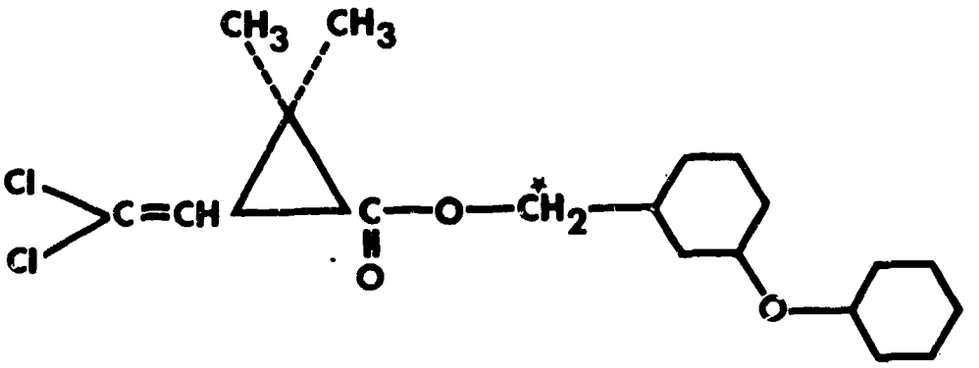
4. PURPOSE. The purpose of this study was to determine the dermal penetration and distribution of ^{14}C-labeled permethrin in dogs and rabbits. The rate and amount of absorption was assessed by monitoring radioactivity in urine and feces daily for 7 or 14 days and selected tissues at necropsy. Each isomer of permethrin, cis or trans, was tested independently in rabbits and dogs. Treatment in dogs also included an equal cis-trans mixture. The methodology was earlier developed and reported in this laboratory (paragraph 2, this report).

5. BACKGROUND. The insecticide permethrin has been proposed by the Armed Forces Pest Management Board (AFPMB) as a cloth impregnant for the protection of military personnel against the bites of medically important arthropods. Benefits of this uniform treatment are well documented.[1] Although extensive toxicological evaluations have been reported by this laboratory[2], information regarding absorption kinetics and bioelimination following topical application is lacking. It was determined that additional evaluations be performed in animals to define absorption, metabolic elimination, and tissue distribution of topically applied permethrin isomers.

Use of trademarked names does not imply endorsement by the US Army, but is intended only to assist in identification of a specific product.

6. MATERIALS.

a. The chemical name of permethrin is 3-(phenoxyphenol) methyl (±)-cis, trans-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropane carboxylate. Permethrin formulations contain various cis-trans isomer mixtures. The structural formula is:



b. Cis and trans isomers of permethrin, ^{14}C-labeled in the alcohol moiety, were provided by Dr. James Hubbell, the Wellcome Research Laboratories, Burroughs Wellcome Company, Research Triangle Park, North Carolina. Reported radiochemical purity was greater than 98 percent for both isomers. Specific activity of the cis isomer, designated NRDC 148, was 59.7 millicuries per millimole (mCi/mM). The trans isomer, designated NRDC 146, had the same specific activity.

c. Each isomer was received in 1.0 mL of toluene. Dilutions for animal testing were made in absolute ethyl alcohol.

d. Additional cis permethrin was purchased from New England Nuclear, Boston, Massachusetts, to complete the study in dogs after the original radiochemicals had been depleted. The site of ^{14}C-labeling was the same as for the original isomers. Specific activity was 51.2 mCi/mM. The labeled chemical was received in 0.86 mL of methylene chloride and was diluted in absolute ethyl alcohol for animal administration.

7. ANIMALS.

a. Twelve male albino rabbits, weighting between 1.8 and 2.8 kg, were purchased commercially from Dutchland Laboratories, Denver, Pennsylvania. Each animal was individually housed in a Wahmann stainless steel metabolism cage and identified by ear number and cage label. A commercial laboratory diet, Purina® Rabbit Chow Checkers G, and water were available ad libitum.

® Purina is a registered tradename of Ralston Purina Company, St Louis, Missouri.

b. Nineteen male Purebred beagle dogs, 8 to 14 months old, were selected from USAEHA kennel stock. The animals had been purchased earlier from Laboratory Research Enterprises, Inc., Kalamazoo, Michigan. Dogs were identified by ear tattoo and housed in individual stainless steel metabolism cages for excreta collection. A commercial laboratory diet, Agway Certified Canine Diet, Pro-Pet, Inc., Syracuse, New York, and water were available ad libitum.

8. METHODS.

a. Specific methodologies for compound administration, collection of excreta, treatment of tissue specimens and calculations have been earlier reported (paragraph 2, this report). Briefly, for intravenous administration, the radiochemical was injected into the animals in a 2 to 3 mL saline infusion. For topical application, the labeled chemical was delivered to the clipped, mid-lumber area of the animals' back. The measured application area was demarcated with petrolatum to contain the chemical at the site and assure the correct application rate. The entire area was then covered with a nonocclusive patch (breathable) and secured with adhesive tape. This appliance was changed after 24 hours and whenever evidence of disturbance by the animal was observed. At 7 days the patches were removed and the application area swabbed with ethanol soaked cotton to remove residual radioactivity (only in dogs tested for 14 days).

b. Three rabbits each received an intravenous injection of either cis or trans permethrin. The radioactive dose was 5 μCi with a chemical mass of 32.75 μg to each animal. An additional three rabbits per group received either cis or trans permethrin topically. The dosage was identical to the intravenous animals and applied to a 8.2 cm^2 area or an application rate of 4 $\mu g/cm^2$.

c. Twelve dogs were similarly treated in groups of three. Half of the animals received either cis or trans permethrin intravenously. The total radioactive dose was 10 μCi per animal and chemical mass was 65.5 μg. The same dose of either isomer was applied topically to the remaining six animals (three per isomer) to a 16.4 cm^2 area. Application rate was 4 $\mu g/cm^2$. An additional six dogs were treated intravenously or topically with a 50/50 mixture of the cis-trans permethrin isomers in a single dose. Total radioactivity in each dose was 20 μCi and contained 131 μg of the radiochemical. Topical application was made to a 16.4 cm^2 area of the animals' back to assure a rate of 8 $\mu g/cm^2$.

d. One additional dog was treated intravenously with the cis-trans mixture to assess respiratory elimination as $^{14}CO_2$. The animal, under pentobarbital anesthesia, was connected via an endotracheal tube to a two-way valve such that inspiration was drawn from a 120 L spirometer. Following injection of 20 μCi of the isomer mixture, expired air was collected in 20 L plastic bags attached to the two-way valve. Collection was for 5 hours. As the bags were filled with expired air they were immediately evacuated through a series of glass scrubbers, each containing 15 mL of Oxifluor®-CO_2, a CO_2 absorber and scintillant. After evacuation, the bags were cut in small pieces and placed in methanol for extraction of radioactive residue. Timed urine and blood collections were made via in-dwelling catheters.

® Oxifluor is a registered tradename of New England Nuclear, Boston, Massachusetts.

e. Urine and fecal collections were measured daily for 7 days in rabbits and 14 days in dogs. Aliquots (0.2 mL) of urine were combined with 15 mL of PCS● II and radioactivity measured on a model LS9000 Beckman liquid scintillation counter. Feces was collected and weighed daily, homogenized in toto in an equal volume of water and 0.25 to 0.50 mL of the aqueous supernate oxidized to $^{14}CO_2$ and counted. Oxidation was performed using a Hewlett Packard Biological Materials Oxidizer.

f. Dogs receiving intravenous permethrin isomers or the mixture were monitored at timed intervals following injection to assess radiocarbon disappearance rates (t 1/2) from circulating blood. Blood specimens were collected and 0.2 mL aliquots oxidized to $^{14}CO_2$ and radioactivity measured. A semilog plot of radiocarbon levels versus time was constructed using the "stripping" method.[3] The t 1/2 was determined for the rapid disappearance phase (alpha) and the delayed elimination phase (beta).

g. At the end of the study period, animals were euthanized and representative tissue and fluid specimens collected and measured for radioactivity. Specimens included heart, lung, liver, spleen, kidney, testes, brain, adrenal glands and thyroid glands. Also collected were urinary bladder, gall bladder, bone (without marrow), omental fat, muscle, skin (normal), bile and blood. The skin from the site of topical application was removed in toto, radioactivity extracted in ethanol and measured. Levels of activity from alcohol swabs of the test site were later added to this value. Nonocclusive patches were cut into small pieces and extracted for unabsorbed radiocarbon. Tissues (0.25 to 0.50 g) and body fluids (0.2 mL) were oxidized to $^{14}CO_2$ and evolved radioactivity measured. Aliquots (0.2 mL) of ethanol extracts were combined with PCS II and counted. Appropriate standards and backgrounds were included to determine efficiencies of the operations and quench correction.

h. Urinary and fecal excretion of radiocarbon was quantitated over a 7-or 14-day study period. Excretion rates for each day's collection were calculated as the percent of the initial injected or applied dose. Calculations for tissue specimens collected at necropsy were based on dpm/gram of wet tissue and later converted to ppm permethrin equivalents/gram.

9. RESULTS.

a. Rabbit Study.

(1) The metabolic elimination of cis or trans permethrin from rabbits following a single intravenous injection was rapid. Urinary excretion accounted for about 70 percent of the eliminated radiocarbon during the first 24-hour collection period (See Table B-1, Appendix B). Bioelimination was essentially complete after the fourth day with less than 1 percent per day of injected cis or trans permethrin appearing in excreta between days 5 and 7. Enteric elimination of the cis isomer, as measured by radioactivity appearing in feces, accounted for nearly 25 percent of the excreted chemical while trans permethrin measured 13 percent.

● PCS is a registered tradename of Amersham Corporation, Arlington Heights, IL.

(2) Absorption of topically applied isomers to rabbits measured 30 percent of the applied dose through the 7-day study period (see Table B-2, Appendix B). About half of all radiochemical absorption occurred during the first 24 hours and was recovered primarily in the urine. Feces contributed 5 percent of the applied cis dose and 2 percent of the trans. Less than 2 percent absorption occurred between days 5 and 7.

(3) Unabsorbed radiochemical from rabbits treated dermally appeared in the nonocclusive patches or at the application site (Table B-2, Appendix B). As the patches did not contact the application area, the radioactivity probably was contributed by evaporating chemical or from exfoliated skin contained by the appliance. Adding the unabsorbed and absorbed fractions, total permethrin accountability was 83 and 67 percent for the cis and trans isomers, respectively.

(4) Tissue specimens collected at necropsy from rabbits 7 days after intravenous injection of permethrin isomers failed to indicate any marked accumulation of radioactivity (Table B-3, Appendix B). Generally, only highly perfused tissue retained any measurable radiocarbon which was always less than 5 ppb. No differences in distribution were observed between the two isomers. After topical application of permethrin, no retention of radiocarbon was noted in any tissues.

b. Dog Study.

(1) The elimination kinetics of injected permethrin to dogs, individual or combined isomers, is shown in Table B-1, Appendix B. About 73 percent of the eliminated radioactivity appeared in excreta during the first day and fell to less than 1 percent after the third day. This pattern was typical for each isomer and the 50/50 mixture of the two. Radiocarbon measured in feces indicated significant enteric elimination following injection of the cis-isomer and cis-trans mixture accounting for nearly 40 percent of all recovered radioactivity. For the trans isomer, the feces contribution was 28 percent through 14 days.

(2) The disappearance of injected permethrin from circulating blood in dogs generally followed first order kinetics through the first 4 hours. The observed half-life for permethrin isomers during the alpha phase was 86 minutes for the cis isomer, 60 minutes for trans and 80 minutes for the 50/50 mixture. At 4 hours postinjection, the rates of disappearance markedly decreased and assumed linear, beta phase kinetics. The observed half-lives for beta phase disappearance were 23 hours for the cis and cis-trans mixture and 25 hours for the trans isomer.

(3) One dog treated intravenously with the cis-trans permethrin mixture failed to demonstrate any significant respiratory elimination of radiocarbon ($^{14}CO_2$) during a 5-hour period. Carbon-14 levels in expired air were briefly detectable 10 to 15 minutes after injection, then returned to background levels. Concurrent urine samples monitored hourly showed a marked increase in radioactivity 4 hours after injection and were rapidly increasing at 5 hours, the last collection period. By 24 hours, radioactivity in urine was approaching background.

(4) Tissue specimens from dogs treated intravenously with permethrin isomers or a combination did not show an affinity of the material for any separate organ. No tissue contained more than 7 ppb of permethrin nor were any deposition patterns distinguishable (Table B-3, Appendix B).

(5) The absorption potential of permethrin isomers, individually or in combination, following topical application to dogs is shown in Table B-4, Appendix B as radioactivity appearing in excreta. Less than 12 percent absolute absorption occurred over the 7- or 14-day test, independent of isomer or combination. Maximum radiocarbon output appeared in excreta 2 to 3 days after application. Beyond 4 days, levels of radioactivity in urine and feces diminished to less than 1 percent/day of the applied dose. Fecal elimination contributed 35 percent of excreted activity in cis-treated animals, 16 percent for trans and 24 percent in those receiving the cis-trans mixture. Differences in absorption potential between permethrin isomers were not remarkable.

(6) Unabsorbed radiochemical from topically treated dogs was recovered in extracts of the nonocclusive patches, from alchohol swabs or the excised skin from the application sites (Table B-4, Appendix B). About 65 percent of the applied radioactivity was recovered by these methods.

(7) No radioactivity was distinguishable in any tissue specimen (except one naive skin section) from dogs 14 days after topical application of permethrin isomers (See Table B-3, Appendix B).

10. DISCUSSION.

a. The insecticide permethrin offers several advantages as a uniform impregnant. It poses no serious hazard from the dermal route of administration.[2] One reported occupational exposure in man to a permethrin formulation resulted in no detectable abnormalities nor complaints by a sprayman. The absorbed dose of 1 to 2 mg of permethrin for each 12-hour work period was estimated from measurements of urinary metabolities.[4] Permethrin is essentially odorless and retains its high insecticidal activity, particularly against mosquitoes and ticks, even after several washings of the impregnated fabric.[5] Despite its lipophilic nature and chlorine content,[6] permethrin presents little environmental persistence and is readily biodegraded in soil.[7]

b. Earlier investigations have characterized the metabolic degradation of both cis and trans isomers of permethrin following oral administration to animals.[6,8] Generally, the isomers are rapidly metabolized by ester cleavage, by hydroxylation of the geminal dimethyl group in the acid moiety or the phenoxy group of the alcohol, and by conjugation of the resulting carboxylic acids and phenols. The dichlorovinyl side chain is not metabolically altered. The metabolites are excreted quickly, primarily in the urine and do not persist significantly in tissues. Deposition data from the current study following parenteral or dermal administration of permethrin is consistent with this observation.

c. It is generally felt that trans permethrin is more chemically labile in the body than the cis isomer.[9] Excretion kinetics in rabbits and dogs support this observation. Comparative residence of the radioisomers in dog blood following intravenous injection showed a faster disappearance of the trans isomer versus the cis by more than 20 minutes. Further, the proportion of enteric involvement in the elimination process was always greater in cis treated animals. It appears from a inspection of the data in dogs that the 50/50 cis-trans mixture favors cis bioelimination kinetics.

d. The dermal absorption and subsequent bioavailability of a substance is limited by the effectiveness of the dermal barrier. As such, rabbits usually demonstrate maximum porosity while dogs are more representative of human absorption potential.[10,11] Since man's defense against insult from topical chemicals is comparatively greater than that reported for animals,[10,12] penetration of permethrin should be well below that observed in the animal tests.

e. Studies in this laboratory have shown that about 4.5 percent of permethrin (43.4/56.6 cis-trans ratio) from impregnated military fabric migrates to the skin surface through 7 days.[13] Assuming an effective insecticidal level of impregnation (0.125 mg/cm^2), 2.5 g of permethrin would be contained in a complete fatigue uniform (2 m^2 fabric). Based on the observed fallout potential, about 113 mg of the insecticide could be expected to reach the skin surface of a man during 1 week of continuous wear. If 10 percent absorption occurred, the bioavailabilty of permethrin to a 70 kg man would be expected to be 0.023 mg/kg/day. Comparatively, the NOEL (no-observed-effect level) in rabbits is reported to be 43,000 times higher.[2]

11. CONCLUSIONS. Based on the above findings, the insecticide permethrin should not present a dermatotoxic hazard to man within the intended use as a fabric impregnant at concentrations of 0.125 mg/cm^2. Absorption of the insecticide, either cis or trans isomers or an equal combination, should be less than 8 percent of that reaching the skin surface of man. Metabolic degradation of the absorbed chemical should be rapid with bioelimination occurring primarily in urine by 3 to 4 days. Significant enteric elimination may occur, particularly from the cis isomer. No predisposition for tissue binding of permethrin metabolites has been observed in the animal model. The projected bioavailability to man from permethrin impregnated fabric is 0.023 mg/kg/day.

12. RECOMMENDATIONS. It is recommended that (a) permethrin, be approved for further testing as a clothing or fabric impregnant at concentrations to 0.125 mg/cm^2 and (b) that the trans isomer significantly predominate in commercial formulations.

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APPENDIX A

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Study No. 75-51-0351-83, Feb 80 - Dec 82

APPENDIX B

TABULAR RESULTS

FATE OF ^{14}C-LABELED PERMETHRIN IN ANIMALS

TABLE B-1. EXCRETION OF ^{14}C-LABELED PERMETHRIN ISOMERS FOLLOWING INTRAVENOUS ADMINISTRATION TO RABBITS AND DOGS.

		PERCENT OF INJECTED DOSE						
		DAY 1	2	3	4	5-7	8-14	TOTAL
Rabbit, Cis	Urine	35.10 ± 2.33	8.57 ± 3.12	2.07 ± 0.17	1.20 ± 0.59	2.01 ± 0.69	-------	50.15 ± 3.37
	Feces	7.56 ± 5.92	5.97 ± 3.92	1.93 ± 1.99	0.72 ± 0.58	0.95 ± 0.38	-------	17.13 ± 8.70
								67.28 ± 11.90
Rabbit, Trans	Urine	46.06 ± 9.97	6.53 ± 3.34	1.92 ± 0.28	1.37 ± 0.62	1.89 ± 0.53	-------	57.77 ± 7.75
	Feces	1.62 ± 0.84	3.20 ± 2.37	1.79 ± 0.04	1.11 ± 0.32	1.08 ± 0.30	-------	8.80 ± 2.71
								66.57 ± 9.26
Dog, Cis	Urine	18.66 ± 0.89	3.42 ± 1.50	1.52 ± 0.47	0.53 ± 0.07	0.98 ± 0.18	-------	25.11 ± 1.94
	Feces	11.37 ± 1.74	5.27 ± 3.02	1.28 ± 0.66	0.64 ± 0.33	0.87 ± 0.28	-------	19.43 ± 4.45
								44.54 ± 6.38
Dog, Trans	Urine	37.78 ± 0.87	7.19 ± 0.94	2.14 ± 0.65	0.88 ± 0.08	0.76 ± 0.02	0.74 ± 0.23	49.49 ± 0.51
	Feces	10.03 ± 4.75	2.62 ± 1.19	0.46 ± 0.17	0.18 ± 0.09	0.27 ± 0.09	0.22 ± 0.06	13.78 ± 3.60
								63.27 ± 4.11
Dog, Cis/Trans	Urine	25.87 ± 3.50	2.85 ± 0.85	3.86 ± 3.25	0.58 ± 0.22	0.99 ± 0.49	0.77 ± 0.35	34.92 ± 8.14
	Feces	16.77 ± 0.54	2.06 ± 0.93	0.78 ± 0.39	0.39 ± 0.17	0.41 ± 0.09	0.40 ± 0.06	20.81 ± 1.19
								55.10 ± 7.74

TABLE B-2. EXCRETION OF ^{14}C-LABELED PERMETHRIN ISOMERS FOLLOWING TOPICAL APPLICATION TO RABBITS

		PERCENT OF APPLIED DOSE					
		DAY 1	2	3	4	5-7	TOTAL
Rabbit, Cis	Urine	10.59 ± 5.36	5.83 ± 0.46	3.04 ± 2.03	2.45 ± 1.88	1.04 ± 0.18	22.95 ± 2.99
	Feces	2.16 ± 1.22	1.02 ± 1.01	0.62 ± 0.27	0.51 ± 0.15	0.80 ± 0.42	5.11 ± 2.41
							28.06 ± 1.50
Rabbit, Trans	Urine	13.85 ± 1.41	5.30 ± 1.76	5.61 ± 2.41	2.42 ± 0.91	1.34 ± 0.15	28.52 ± 0.65
	Feces	0.85 ± 0.22	0.36 ± 0.12	0.24 ± 0.10	0.21 ± 0.08	0.52 ± 0.20	2.18 ± 0.63
							30.70 ± 0.43

	UNABSORBED			ABSORBED		
	Patches		Skin, Appl.			Total %
	24 Hour	7 Day	Site	Urine	Feces	Recovery
Rabbit, Cis	21.58 ± 17.37	26.73 ± 9.06	6.87 ± 6.57	22.95 ± 2.99	5.11 ± 2.41	83.24 ± 11.57
Rabbit, Trans	6.37 ± 3.02	18.99 ± 7.68	11.18 ± 10.07	28.52 ± 0.65	2.18 ± 0.63	67.24 ± 5.37

TABLE B-3. TISSUE DISTRIBUTION OF ^{14}C-LABELED PERMETHRIN ISOMERS FOLLOWING INTRAVENOUS OR (TOPICAL) ADMINISTRATION TO RABBITS AND DOGS

ppm permethrin equivalents

	Rabbit		Dog		
	Cis	Trans	Cis	Trans	Cis/Trans
Bladder, Urinary	-------	------	-------	-------	-------
Bone, Femur	-------	------	-------	-------	-------
Brain	-------	------	-------	-------	-------
Fat, Omental	0.002	0.001	-------	-------	-------
Gallbladder	-------	------	-------	-------	0.001
Gland, Adrenal	0.002	0.003	0.001	0.002	0.007
Gland, Thyroid	-------	------	-------	-------	-------
Heart	-------	------	-------	-------	-------
Kidney	-------	------	-------	-------	0.001
Liver	0.001	0.001	0.002	0.002	0.003
Lung	0.003	0.004	0.001	-------	0.001
Muscle	-------	------	-------	-------	-------
Skin	-------	------	-------	-------	(0.001)
Spleen	0.002	0.002	0.001	0.001	0.002
Testes	-------	------	-------	-------	-------
Bile	0.001 (0.002)	------	0.003 (0.001)	0.001 (0.001)	0.003 (0.002)
Blood	-------	------	-------	-------	-------

TABLE B-4. EXCRETION OF ^{14}C-LABELED PERMETHRIN ISOMERS FOLLOWING TOPICAL APPLICATION TO DOGS.

		PERCENT OF APPLIED DOSE						
		DAY 1	2	3	4	5-7	8-14	TOTAL
Dog, Cis	Urine	0.78 ± 0.17	1.49 ± 0.31	1.46 ± 0.31	0.86 ± 0.34	1.69 ± 0.27	-------	6.28 ± 1.01
	Feces	0.09 ± 0.05	0.90 ± 0.70	0.58 ± 0.03	0.69 ± 0.25	1.18 ± 0.39	------	3.44 ± 0.92
								9.72 ± 1.92
Dog, Trans	Urine	1.42 ± 0.41	2.08 ± 0.26	1.97 ± 0.38	1.42 ± 0.62	2.24 ± 0.97	0.75 ± 0.44	9.88 ± 2.78
	Feces	0.13 ± 0.12	0.60 ± 0.14	0.29 ± 0.01	0.23 ± 0.03	0.45 ± 0.18	0.18 ± 0.17	1.88 ± 0.40
								11.75 ± 2.95
Dog, Cis/Trans	Urine	0.62 ± 0.19	1.45 ± 0.53	1.02 ± 0.13	0.70 ± 0.36	1.89 ± 0.67	1.11 ± 0.27	6.79 ± 2.04
	Feces	0.06 ± 0.04	0.30 ± 0.17	0.53 ± 0.23	0.23 ± 0.18	0.53 ± 0.09	0.48 ± 0.11	2.13 ± 0.54
								8.92 ± 2.54

	UNABSORBED			ABSORBED		TOTAL % RECOVERY
	PATCHES		SKIN, APPL. SITE	URINE	FECES	
	24 HOUR	7 DAY				
Dog, Cis	17.85 ± 10.65	21.52 ± 3.00	27.26 ± 6.01	6.28 ± 1.01	3.44 ± 0.92	76.35 ± 1.33
Dog, Trans	23.02 ± 13.50	35.72 ± 7.97	6.58 ± 4.29	9.88 ± 2.78	1.88 ± 0.40	77.08 ± 6.40
Dog, Cis/Trans	16.89 ± 12.42	35.83 ± 14.96	11.42 ± 6.34	6.79 ± 2.04	2.13 ± 0.54	73.06 ± 3.17