

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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Company Name : Coulston International Corporation

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 Biological Analysis Branch/BEAD

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 X Toxicology Branch-Insecticide/Rodenticide Support

 Toxicology Branch-Herbicide/Fungicide/Antimicrobial Support

 Other ()

1.0. INTRODUCTION

1.1. CHEMICAL/FORMULATION

This submission concerns the use of PERMANONE on military clothing, fabric, and other inanimate objects. PERMANONE consisting of a 0.50% spray of the synthetic pyrethroid, permethrin. Permethrin is marketed for its insecticidal properties, specifically for the control of ticks, mosquitoes, and chiggers. PERMANONE contains a mixture of approximately 35% cis and 65% trans permethrin in the 0.50% active ingredient portion of the spray mixed with 99.50% inerts.

1.2. REGISTRANT

PERMANONE is a product of Coulston International Corporation.

1.3. STATUS OF STUDY: NEW OR RESUBMITTED

This submission represents a repetition of the many attempts that the Department of Defense, DOD, has made in the past to register the use of permethrin on clothing, fabric and other inanimate objects. Edwin Tinsworth, Director of RD has sent Anne Barton, Deputy Director of the Environmental Fate and Effects Division, an "expedite" request for review of these petitions for military/general uses of permethrin on 8/29/88.

It appears that the majority of the current DOD data may have been submitted previously. Unfortunately, it is difficult or impossible to make this determination with certainty.

John Dougherty of the Toxicology Branch (TB) concluded in his 5/5/87 review that permethrin use on clothing represented a chronic exposure. He used R. Moraski's 3/20/83 permethrin review for the estimation of exposure, the Acceptable Daily Intake (ADI) for permethrin and the assumption that all the permethrin was 100% absorbed dermally. Dougherty concluded that the potential daily exposure, roughly estimated using Richard Moraski's exposure estimate of 3/20/83 (0.28 and 0.33 mg/kg/day for a 70 kg male and female, respectively, was predicted to be 7X higher than the ADI. TB further concluded that this was an unacceptably high risk.

Unfortunately, the value reported by Moraski in his 3/20/83 review was only a very rough estimate, based on the surrogate chemical DEET. The rationale and calculations for these estimations were not given; NDEB does not feel they are adequate to estimate the exposure from the propose use(s) of permethrin on clothing and inanimate objects.

The conclusion made in Dougherty's 1/28/88 memo following was that the DOD could possibly lower the risk estimate to an acceptable level if they could (1) show less than 100% transfer of permethrin

from the fabric to the skin or (2) show less than 100% dermal absorption of permethrin through the skin.

1.4 PURPOSE AND ORIGINATOR OF REQUEST

DOD (the Army, Navy, and Air Forces) is requesting that EPA register two separate uses for PERMANONE. One is for the use of a permethrin spray on military clothing and the other is for the spray treatment of clothing, fabric or inanimate objects. (See Section 3.1 concerning the proposed label.)

2.0 RECOMMENDATIONS/CONCLUSIONS

- A. NDEB is unable to reach any final conclusion regarding the estimated dermal exposure to permethrin due to its proposed use as a spray on clothing and indoor inanimate objects without the submission of further data relating to the amount of permethrin sprayed and the frequency of use. This information is not included in the current submission or the proposed label. For example, if optimum treatment rate of clothing is 0.125 mg/cm² to 0.200 mg/cm², as DOD studies suggest, 8.5 to 13.5 6-oz. cans of 0.5% permethrin spray would be needed to treat a typical uniform. Use information should be routed through the Biological Analysis Branch of BEAD for their review.
- B. Data concerning the density of BDU fabrics and the rate of impregnation are necessary to evaluate the capacity of fabric to hold and retain permethrin. Also, data should be provided on the effect of retreatment or residue buildup and release from BDU fabrics.
- C. NDEB is also concerned with potential aerosol and mist inhalation exposure resulting from the proposed use of spray cans. It is not possible to evaluate this exposure without further rate and frequency data.
- D. Loss of permethrin in BDUs could be expected after wear and after laundering. Study III (see Detailed Considerations below) suggests that up to 30% of clothing impregnated up to 0.125 to 0.200 mg/cm² may be lost after 5 days of wear. Study II also shows that up to 70% of the permethrin may be lost after 4 washes. Study V concluded that the first wash leads to the greatest loss of permethrin on clothing, and that after 10 washes about 40% of radiolabelled permethrin on cotton was lost and 55% on nylon/cotton. Without data concerning the rate/frequency of intended use, we can not determine the quantitative effect on long-term exposure.
- E. NDEB defers to TB-IRS concerning Studies VI and VII of the transfer of permethrin through rabbit skin with respect to

pharmacokinetics and dermal penetration. We also defer to TB-IRS as to the significance of the change of formulation on those results, the suitability of testing conditions and protocol, etc. See Section III (Detailed Discussion) for additional comments.

- F. NDEB requests that the registrant submit future registration actions in an organized fashion, drawing scientifically defensible conclusions related to potential exposure based upon data from relevant studies. See Section III (Detailed Discussion) for additional comments.
- G. If methods of application other than the use of small spray cans is anticipated, DOD should ammend their submission to include such process(es) used for clothing impregnation. In their absence, only spray can use is considered for regulatory purposes in this review.
- H. The spray may also not be advisable if there is a danger that the can may explode at temperatures above 135F, as the label indicates. The Product Manager (PM) may wish to inform DOD of this possibility.

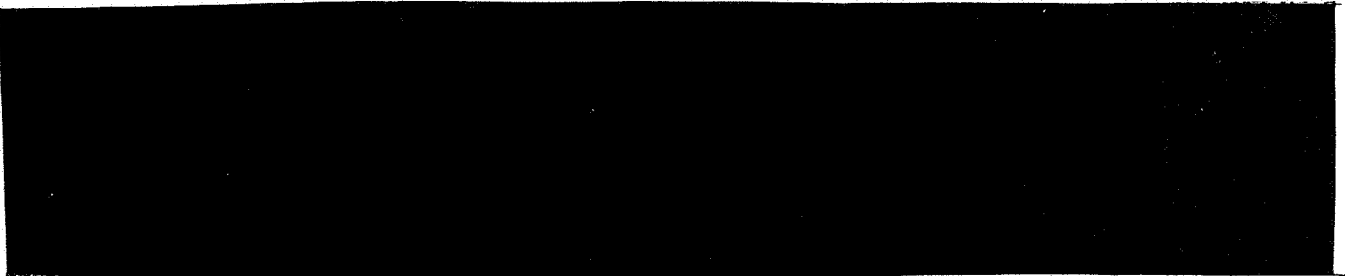
3.0 DETAILED CONSIDERATIONS

Detailed below is a summary of the data/information contained in each of the nine packages of reports submitted by the registrant. The information included in each package is summarized separately in Appendix II. References are identified in the remainder of this review by the Roman numeral assigned in Appendix I-List of Individual Studies.

Based on the limited amount of use information/data available in these studies, NDEB has attempted to calculate a gross estimate of potential dermal exposure. Without detailed use information regarding application rates, frequency of use, etc., refinement of this estimate will not be possible.

3.1 PROPOSED USE

The proposed general label for the major use contains the following directions:



The proposed draft label for the other intended use contains the following statements:

Permethrin Arthropod Repellent. For Distribution within the DOD and Use on Standard Issue Fabrics Only. Clothing and Other Inanimate Object treatment only. Do not apply to skin. Active Ingredient 0.50% of a minimum of 35% cis permethrin.

CAUTION--Avoid contact with face, eyes or skin. Avoid breathing vapors or spray mist. Do not allow contact with treated surfaces until spray has dried. Do not allow spray to contact food, feedstuffs, or water supplies. Thoroughly wash dishes and food handling utensils contaminated with this product. Shake well before using. To be used for treatment of clothing, fabric and other inanimate objects only.

For protection against ticks chiggers, and mosquitoes select an area protected from the wind, spray outer surfaces of clothing (while not being worn) and other items e.g. bednets, and headnets and field bedding with a slow sweeping motion to lightly moisten the surface of the fabric. Treat the clothing and allow to dry prior to being worn. Hold can at a distance of 6 to 8 " from the object being treated.

Treat the entire outside surface of clothing with special attention to socks, trouser cuffs, shirt cuffs, and caps. Pant cuffs should be worn inside the socks or footwear to ensure full protection against ticks and chiggers. This item must be used in conjunction with the standard issue repellent approved for application to exposed skin areas to achieve maximum protection from mosquitoes.

Exposure to temperatures above 130 Degrees F may cause bursting (of the pressurized container).

The EPA Reg. No. is 50404-, EPA Est. No. is 10900-OH-1. The spray is a product of Coulston Int'l Co.

3.2 CALCULATED EXPOSURE

For permethrin impregnated in NYCO fabrics only, NDEB concludes from Study I that the surface area coming into contact with the wearer is about 5.72 m² or 57200 cm². Using this number, and multiplying by the amount of permethrin impregnated into NYCO we could estimate the amount of permethrin available dermally from the BDU.

The concentration of permethrin in impregnated NYCO was given in Study II and V as 0.125 mg/cm². Assuming this was the rate of impregnation in NYCO (a future submission should give the decided rate of impregnation and method to be used) we could estimate:

57200 cm² NYCO surface area X 0.125 mg/cm² permethrin =
estimated 7150 mg or 7.2 g permethrin/impregnated BDU/treatment

If adequate data was provided to show that only the fabric coming into direct contact with the skin contributes to potential dermal exposure, then overlapping BDU material would not be considered a contributor of dermal exposure. Assuming that overlapping material accounts for about half of the total fabric surface area, the area coming into direct skin contact, and thus, the potential exposure, should be reduced by approximately 50%, to 3.6 g per BDU, per treatment.

For treatment once a week, this would translate to:

$$\frac{3.6 \text{ g/wk} \times 52 \text{ wk/year} \times 1000 \text{ mg/g}}{365 \text{ d/yr} \times 70 \text{ kg/ave. man}} = 7.3 \text{ mg/kg/d ave. daily exposure}$$

This is only a very rough estimate for NYCO containing 0.125 mg/cm². Much additional information is needed from DOD before NDEB can provide an accurate assessment of exposure.

DOD studies (II, III, IV, V) suggest that 0.125mg/cm² to 0.200 mg/cm² of permethrin is needed to treat uniforms. Using this information, we could estimate the number of 0.5% 6 oz. spray cans which would be needed to achieve this rate of penetration. The calculation below shows that between 8.5 to 13.5 cans would be necessary.

$$\frac{0.125 - 0.200 \text{ mg/cm}^2 \text{ desired concentration}}{[0.005 \text{ conc.} \times (6\text{oz can}/16\text{oz/lb}) \times 454 \text{ g/lb} \times 1000 \text{ mg/g}] / 57200 \text{ cm}^2 \text{ BDU}}$$

$$= (0.125 - 0.20 \text{ mg/cm}^2) / [0.0146 \text{ mg/cm}^2]$$

$$= \underline{8.5 \text{ to } 13.5 \text{ cans}}$$

Because this seems like an unrealistic number of spray cans of permethrin to use on one uniform, DOD should resubmit their request and include rate and frequency information.

APPENDIX I-LIST OF INDIVIDUAL STUDIESSTUDY I

"Permethrin Fabric/Skin Contact From Wearing the Army Battle Dress Uniform" by Hubert Snodgrass Jr, 7/87, USAEHA, Aberdeen Proving Ground, MD, Study ID 75-52- 0687-88, EPA Accession #407668-12

STUDY II

Schreck, C. E., Carlson, D.E., et al., "Wear and Aging Tests with Permethrin-Treated Cotton-Polyester Fabric," conducted by the USDA in Gainesville, FL, J. Econ. Entomol. 73:451-453. 1980. EPA MRID No. 407668-18

STUDY III

"Wear and Wash Persistence of permethrin used as a clothing treatment for personal protection against the lone star tick (acarixodidae)," by Schreck, Mount, and Carlson, J. Med. Entomol., Vol 19, No 2:143-146, dated 3/24/82, EPA MRID #407668-18.

STUDY IV

"Permethrin Impregnations of Military Fabrics: An Evaluation of Application Rates and Industrial Methods by Bioassay and Gas Chromatographic Analysis" by Schreck, Kane and Carlson, reprinted from SOAP/COSMETICS/CHEMICAL SPECIALTIES, 8/82, EPA MRID # 407668-18

STUDY V

"Permethrin, The effects of laundering on the permethrin content of impregnated military fabrics" by Hubert L. Snodgrass, Jr, 3/88, Performing Lab-Aberdeen Proving Ground, MD, USAEHE, Lab Project ID 75-51-0687-88. Submitted on Coulston Intl Corp. letterhead, EPA File Symbol 50404-L, EPA Accession #407668-14.

STUDY VI

"Permethrin-Migration of 14C Permethrin From Impregnated Military Fabrics As Measured In Rabbits," by Hubert Snodgrass, Jr, Completed 3/88, USAEHA, Aberdeen Proving Ground, Lab Project 75-51-0351-87, EPA File #50404-L, Accession #407668-13.

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APPENDIX I-LIST OF INDIVIDUAL STUDIES -cont'dSTUDY VII

"Permethrin--Intirim Report-Migration of 14C Permethrin From Impregnated Military Fabric," by Hubert L. Snodgrass, Complete 2/82, USAEHA, Aberdeen Proving Ground, MD Lab Project 75-51-0351-82, EPA File #50404-L, Accession 407668-08.

STUDY VIII

"Permethrin," EPA File #50404-L, Coulston Int'l Corp., by Lawrence J. Feller, EPA Accession #407668-01

STUDY IX

"Permethrin--Pyrethrins and Pyrethroids for the treatment of Scabies and Pediculosis," by D. Taplin, 1987, Performing Lab, Univ of Miami School of Medicine, FLA, Lab Project #0278-145x/87/0602, EPA File #50404-L, Accession 407668-16.

APPENDIX II-INDIVIDUAL STUDIES

STUDY I.

"Permethrin Fabric/Skin Contact From Wearing the Army Battle Dress Uniform" by Hubert Snodgrass Jr, 7/87, USAEHA, Aberdeen Proving Ground, MD, Study ID 75-52- 0687-88, EPA Accession #407668-12

METHODS AND MATERIALS

Briefly, the Army measured the amount of fabric to skin contact by dressing a mannequin in standard issue battle dress uniform, BDU. Overlapping portions of the BDU were not included in the measurements.

STUDY RESULTS

The Army reported that the BDU (coat and trousers) contained about 5.7 m² of fabric. They further estimated that only 2.2 m² would contact the skin; and that this value would be reduced to 1.3 m² if T-shirt and briefs were worn.

DISCUSSION

Because military personnel may not always wear undergarments, we will assume that the entire BDU makes contact with the wearer. Summary of the results submitted for the complete BDU and for the single-layered, "trimmed" portions of the BDU are given below. Measurements were given for three coats and trousers.

COAT	complete	trimmed	TROUSERS	complete	trimmed
A	677g/2.77m ²	284g/1.16m ²	A	731g/3.00m ²	314g/1.29m ²
B	646g/2.65m ²	262g/1.07m ²	B	729g/2.99m ²	318g/1.30m ²
C	663g/2.72m ²	274g/1.12m ²	C	743g/3.05m ²	328g/1.34m ²

*

STUDY I CONCLUSIONS

	complete	trimmed		complete	trimmed
COAT			TROUSERS		
AVG	662g/2.71m ²	273g/1.12m ²	AVG	734g/3.01m ²	320g/1.31m ²

Assuming that the BDU consisted of coat + trousers, the sum of the individual weights (or m² area) would presumably estimate the amount of exposure through the uniform, despite the type of fabric.

APPENDIX II-INDIVIDUAL STUDIES -cont'd

STUDY I.-cont'd

The complete uniform could then be assumed to consist of an average of 1396 g of (50% nylon/cotton) NYCO material containing 5.72 m² of surface area. The uniform trimmed of overlapping NYCO material was reported to consist of an average of 602g of NYCO, containing 2.46 m² of surface area.

IF we were to assume that this measurement was satisfactory for the NYCO BDU, we would conclude the following:

Assuming this is a reasonable value for the density of BDU material and would give a fair estimate of surface area, we may make some worst-case calculations. For the complete uniform, using the lowest value reported for the density of NYCO and not eliminating overlapped material (evidence that this material may not result in further dermal exposure is only intuitive):

662g + 734g=1396g total weight, ...

1396g X 50 cm²/1.20g (worst case reported weight)=58166 cm²
 58166 cm² X 1m²/(100 cm)(100cm)=5.82 m²

STUDY I DEFICIENCIES/COMMENTS

**Calculations of surface area are based on the measurement that 50 cm² of fabric NYCO (50% nylon/cotton) weighs 1.22g, give or take 0.02g. This is a critical value for exposure assessment via the Army BDU. However, the value is simply given in a footnote, without further reference or supporting data. Insufficient data are present, therefore, to allow an evaluation of the quality assurance (QA) or reliability of this measurement.

** If the density measurement for NYCO was based on weights of 65 5 X 10 cm swatches of fabric, these data could be submitted for further method validation. We will assume, however, that this is the correct density of NYCO.

**The range of types of BDU material which the military intends to treat should be submitted.

**Measurements of material density, supported by adequate QA analyses may be necessary if materials other than NYCO are to be considered for proposed treatment, e.g., for the 100% cotton and for wool.

**The label should be amended to restrict use on NYCO fabric only if inadequate density data are not available for other fabrics to be treated.

APPENDIX II-INDIVIDUAL STUDIES -cont'dSTUDY II -cont'd

Schreck, C. E., Carlson, D.E., et al., "Wear and Aging Tests with Permethrin-Treated Cotton-Polyester Fabric," conducted by the USDA in Gainesville, FL, J. Econ. Entomol. 73:451-453. 1980. EPA MRID No. 407668-18

METHODS AND MATERIALS

As an indication of the resistance of permethrin-impregnated cloth to heat, light, rinsing and weathering, GC analyses were performed on NYCO material. Permethrin was impregnated in the NYCO at the rate of 0.125 mg/cm². Benzyl benzoate was also added at a rate of 0.25 mg/cm² because of its ability to deter chigger mites. The patches were air dried, with half of the patches stored in aluminum foil at 22C. The unstored patch was worn on the lower leg of 4 subjects, just below the knee, under the trousers, virtually for 24 hours/day, for 3 days. Analysis was completed using Gas Chromatography, GC, (0.02 mg/2cm² limit of detection) and the "knock-down" count for mosquitoes raised in the USDA laboratory.

STUDY RESULTS

Schreck, et al. reported that unworn patches stored in aluminum foil for 30 days showed "little or no detectable loss of the chemical or of biological effectiveness through the 30 days of the test." Recoveries for permethrin were good (89-100%), and "no major degradation products were observed in the chemical assays, indicating no chemical breakdown under storage." The patches were not reported to be laundered throughout the study.

The GC results (units of mg/cm²) as an average of 4 replicates are as follows:

Day	UNWORN PATCH	WORN PATCH
3	0.115	0.097
6	0.134	0.088
10	0.137	0.060
13	0.122	0.061
16	0.114	0.048
20	0.111	0.036
23	0.118	0.033
26	0.127	0.033
30	0.118	0.041

APPENDIX II-INDIVIDUAL STUDIES -cont'dSTUDY II -cont'd

Schreck, et al. reported that the amount of permethrin in worn patches decreased, but that permethrin did not degrade. Loss of biological effectiveness was also noted, confirming that the permethrin had become unavailable to the mosquitoes. Schreck, et al. continue, saying "the rate of loss was greater during the 1st 10 days than the last 20 days. From day 0 to 10 the rate of loss appeared to average ca. 0.0065 mg/cm²/day. If the differences are significant, the rate of loss is only ca. 0.002-0.003 mg/cm²/day from day 10 to 30...Overall, the time required for complete knockdown increased by a factor of ca. 5X from day 0 to 30 for both species." Although the chemical and biological data did not correlate perfectly, both indicated that permethrin available to insects decreased within the 30 days. According to the calculations provided by Schreck, et al., "although loss of permethrin occurred over the 30-day wear period, the amount remaining and unchanged after 2 weeks to 1 month (0.033 to 0.061 mg/cm², or ca. 1/4-1/2 the initial dose) appeared sufficient to effectively protect against some arthropods that attack man.

DISCUSSION

Both the chemical and the biological monitoring results using mosquito mortality showed that the apparent amount of available permethrin declined in the 30-day test period, when patches were worn. Study II concluded that although only 1/2 the initial dose of permethrin remained in the worn patches, the treatment was still biologically effective protection against mosquitoes. If the compound does not leave via washing, photolysis, evaporation, degradation, etc., we may conclude the following:

**Up to 1/2 the initial dose of the 0.125 mg/cm² patch is available for contact to the wearer, within 30 days.

**Rate of permethrin loss in the first 10 days was reported to average 0.0065 mg/cm² per day. We may estimate that this amount, at a minimum, was possibly available to the wearer via dermal exposure to the patch.

STUDY III

"Wear and Wash Persistence of permethrin used as a clothing treatment for personal protection against the lone star tick (acari:ixodidae)," by Schreck, Mount, and Carlson, J. Med. Entomol., Vol 19, No 2:143-146, dated 3/24/82, EPA MRID #407668-18.

APPENDIX II-INDIVIDUAL STUDIES -cont'd

STUDY III -cont'd

METHODS AND MATERIALS

Clothing used in these tests was worn and laundered 100% RDU, shirt and trousers. The material was treated with 0.125-0.2 mg permethrin (active ingredient)/cm² using Permanone 40% EC and Pramex 27.5% EC. The material was treated with permethrin, placed in a plastic bag for 24 hours to help penetrate the clothing and then air dried before storage in fresh plastic bags. Human subjects wore the clothing in a 0.4-ha tick-infested plot for 1 hour. Testing began intermittently from 5.5 hour of wear to 132 hours (their perceived amount of time to laundering). The results of the wash test were submitted by Schreck, et al., 1980 (II above).

Analyses of BDUs, washed and unwashed, was accomplished using GC. The wash test included unworn BDUs stored for 26 days and BDUs which were washed and assayed after each of 4 washes. Treated uniforms were washed ca. 25 min in top-loading washers with warm water and 71 g of Tide/wash load. The method sensitivity was reported to be 0.01 mg/cm² of BDU.

STUDY RESULTS

The major results are summarized in the following table for Permanone and Pramex, as performed by Gainesville, Fla, 1980. The units are "mg permethrin/cm² fabric," and values represent the average of 3 tests:

Permanone (40% EC)	132 hr (5.5 d)	%Loss	After 4 Washes	%Loss
Shirt	0.146	27%	0.093	54%
Pant	0.173	14%	0.067	67%
Pramex (27.5% EC)	132 hr (5.5 d)		After 4 Washes	
Shirt	0.207	-	0.069	66%
Pant	0.175	13%	0.147	37%

Assuming that 0.200 mg/cm² of fabric was treated (study III stated that BDU was treated at the 0.125 to 0.200 mg/cm² rate), the % loss in the above table could be calculated after 132 hr (5.5 days) and after 4 washes. Between 0 and 27% was lost after 5.5 days wear and between 37% to 67% was lost after 4 washes.

APPENDIX II-INDIVIDUAL STUDIES -cont'dSTUDY III -cont'd

DISCUSSION

The authors of Study III conclude that the GC analyses "(Table 4) show only a 5% overall loss of permethrin in clothing after 132 hr (5.5 days) of wear and a 49% overall loss after 4 washes." From this calculation, the conclusion was made that permethrin as a clothing treatment is resistant to both wear and wash stress. They further conclude that "large numbers of military or civilian personnel in a limited area might significantly reduce the tick density, ..., however, this potential for area tick control would need to be evaluated with a large number of human subjects."

**The units of the numbers in Table 4 may not be mg ai/cm² permethrin. This matter is unclear and clarification is suggested in a future submission.

**The military may wish to submit the calculations used for this study.

**Further information to document the QA/QC of the treatment of permethrin onto fabric, the degree of homogeneity, as well as the quality of the analyses, may be suggested.

STUDY IV

"Permethrin Impregnations of Military Fabrics: An Evaluation of Application Rates and Industrial Methods by Bioassay and Gas Chromatographic Analysis" by Schreck, Kane and Carlson, reprinted from SOAP/COSMETICS/CHEM. SPECIALTIES, 8/82, EPA MRID # 407668-18

METHODS AND MATERIALS

Army labs in Natick, Mass. (NLARS) and USDA labs in Gainesville, FLA cooperatively studied the treatment of NYCO with permethrin. Laboratory methods were meant to simulate commercial treatment of NYCO using hot permethrin baths. Schreck, et al., 1978, was quoted as determining that the optimum treatment rate was 0.125 mg/cm². Effect on insects was measured using biological activity. Chemical analyses using GC were also performed.

Permanone was impregnated into polyester/cotton POCO and NYCO uniforms at concentrations based on the weight of the fabric of 1.28, 0.32, 0.02 and 0.005% aqueous. Fabric was further treated by laundry extraction and oven drying. Samples were split and some were not cured, others were immersed in a durable press finish solution and oven cured at 163C for 12 minutes. Other treatments, including one with glacial acetic acid, were tested

APPENDIX II-INDIVIDUAL STUDIES -cont'dSTUDY IV -cont'd

as separate studies. The effect of washing the material in hot water (50C, 122F) using 40g of military flaked soap, followed by drip drying, was also conducted (the lab wash test). Commercial washing machines were also used for 35 min with 44C (112F) water and 71 g of Tide. These samples were also drip dried and bioassay completed. Samples were washed 15 times. The GC results are considered here and are summarized in the following table:

%bath conc. based on wt. of fabric	<u>mg/cm2 permethrin</u>	
	Mean(Uncured)	Mean(Cured)
PYCO Material		
1.28	0.139	0.004
0.3	0.026	0.003
.02	0.001	0.001
.005	0.000	0.001
PYCO treated with glacial acetic acid		
12.8	0.369	0.184
10.5	0.309	0.298
3.2	0.097	0.031
0.2	0.012	0.008
NYCO Material		
8.0	0.244	--
6.0	0.141	--
3.0	0.077	--
1.0	0.032	--

STUDY RESULTS

The conclusion was made that curing reduced the amount of permethrin in the fabric, or made it less resistant to removal by washing. The number of washes that the material "survived" and still remained as an effective insecticide (using lab-raised mosquitoes) was used to determine the best method of material treatment. This process decision is not significant except to note that the impregnation process may impact the amount of permethrin in the fabric as well as the amount available to mosquitoes and man. In terms of the current petition, and was not evaluated further. Other than the results summarized in the table above, the remainder of this paper does not appear to provide any meaningful information related to the assessment of potential dermal exposure.

APPENDIX II-INDIVIDUAL STUDIES-cont'dSTUDY IV-cont'd

DISCUSSION

**The authors of study IV did include one conclusion relevant to this petition, namely, "the data on the nylon-cotton fabric indicates that a bath emulsion containing permethrin at between 3 and 6% based on weight of fabric will provide the relatively rapid knockdown of all the species tested. In terms of treatment per unit area, this is somewhat less (Possibly up to 2/3 less ((authors' words))) than 0.125 mg/cm², a rate based on "cold" impregnation in earlier studies (Schreck et al. 1978)."

STUDY V

"Permethrin, The effects of laundering on the permethrin content of impregnated military fabrics" by Hubert L. Snodgrass, Jr, 3/88, Performing Lab-Aberdeen Proving Ground, MD, USAEHE, Lab Project ID 75-51-0687-88. Submitted on Coulston Intl Corp. letterhead, EPA File Symbol 50404-L, EPA Accession #407668-14.

METHODS AND MATERIALS

Testing was accomplished using Pounce 3.2 EC, containing 38.4% permethrin a.i., [REDACTED] xylene range aromatics, and [REDACTED] inerts, in a cis/trans isomer ratio of [REDACTED]. This formulation is not the same as the PERMANONE aerosol which the military is petitioning for use as an insecticidal spray on clothing.

Briefly, 100% cotton (CO) or NYCO swatches of fabric were laundered 1-10X using a standard Army soap. Half the material was analysed for loss of permethrin, the other half were applied to rabbits

for 7 days to assess the migration into the skin, based on radiolabelled material in excreta and the amount remaining on the skin.

A ratio of [REDACTED] cis:trans aqueous cold solution of permethrin was prepared for treatment onto CO and NYCO fabric. Swatches of fabric consisting of 50 cm² surface area were treated with about 0.65 ml of permethrin, using an autopipette. The fabric was then air dried for 4 hours and frozen until use. Samples were laundered in a 140F and then a 125F 1.2% and 0.6% bath, with three soap-free rinses. Each fabric was washed 1X, 5X or 10X. Each swatch reportedly contained 0.125 mg/cm², or 6.24 mg permethrin, and 4.73 uCi of total 14C. Direct measurements did not seem to be taken, this seems to be a calculated concentration.

APPENDIX II-INDIVIDUAL STUDIES-cont'dSTUDY V-cont'd

Fabric swatches were extracted with methanol and analyzed after laundering using liquid scintillation chromatography. This was done to monitor the cis/trans ratio after washing to determine whether one isomer was selectively removed during laundering.

Urine and feces were tested daily for ¹⁴C permethrin, and the skin analyzed similarly at the end of the test period for traces of permethrin. We do not have enough pharmacological information as to the metabolism, storage or elimination of the test compound to evaluate these data at this time (Conversation with Robert Zendzian, TB, 8/88).

STUDY RESULTS

NYCO and CO treated with radiolabelled ¹⁴C permethrin was washed 10X. Results graphically displayed in Figure 1 of this review show that the 1st washing decreases radiolabelled ¹⁴C permethrin most profoundly (to 85% of initial concentration for CO and 65% for NYCO). Losses of permethrin continues gradually at about the same rate for CO and NYCO. After the 1st wash and until the 10th wash, about 60% of the permethrin on cotton was present (40% was washed off). Similarly, after 10X of washing NYCO, about 45% of the permethrin appeared to be present (55% was washed away). This data tends to support the author's theory that permethrin binds more strongly to cotton (cellulose) fibers. No data were submitted for wool or other fabrics used in BDUs.

The protocol used for measuring the migration of permethrin from fabrics under varying environmental conditions and to determine the portion of human skin absorption was attached to this study. It is entitled, **"Migration of the insecticide permethrin from treated military fabrics under varying environmental conditions as measured in rabbits."** This protocol is dated 7/3/86, and is assigned #75-51-0351. The work was conducted in Aberdeen Proving Ground by the USAEHA; Hubert Snodgrass was the primary investigator. This protocol concerns TB and will not be included as part of this review.

Another protocol used is included as an addendum to the above-mentioned protocol #75-51-0351. It was entitled, **"Migration of the Insecticide permethrin from treated military fabrics under varying environmental conditions."** The purpose of the study was to determine the effects of laundering on permethrin-treated BDU fabrics and the potential for the insecticide to reach the skin of man. Only the effects of laundering will be considered for this review.

APPENDIX II-INDIVIDUAL STUDIES-cont'dSTUDY V-cont'd

Briefly, 50 cm² of fabric was impregnated with 6.25 mg of permethrin in a [REDACTED] cis:trans mix; treatment was made at the 0.125 mg/cm² level. Radiolabelled 14C permethrin was incorporated, the swatches frozen until use. Some of the swatches were reportedly tested to confirm the amount of impregnation. Fabric was washed 1, 5, and 10 X, using the "standard field conditions." Only the temperature 78.9F and 40% RH Environmental condition was tested.

A separate reference was given to describe the standard field condition for doing laundry. The reference was as follows, letter from B. McNally to the commander of the Army Environmental Health Agency, Herb Snodgrass, dated 3/2/87. Wash was made as follows (1) 1.18% soap (based on fabric weight) in 140F water for 5 min (2) 0.59% soap (based on fabric weight) in 110F water for 3 min (3) 3 min of a fresh 110F bath (4)-(5) 3 min of a fresh 100F bath.

A final reference in this section is a protocol modification made 4/23/87 noting an administrative change to submit the protocol under separate cover for "AFDMB."

Mass balance of radiolabelled 14C permethrin was reported to be about 98%.

Quantitative results summarized from Appendix A of this study are included in the following table:

COTTON FABRIC

NYCO FABRIC

# of Wash	Swatches Used	%loss permethrin	# of Wash	Swatches Used	%loss permethrin
0	6	0	0	6	0
1	6	17.3	1	6	33.0
2	2	23.1	2	2	39.9
3	2	27.2	3	2	42.0
4	2	30.9	4	2	45.3
5	6	37.1	5	6	47.0
6	2	38.5	6	2	49.9
7	2	35.6	7	2	51.3
8	2	42.3	8	2	49.4
9	2	41.0	9	2	55.9
10	6	39.7	10	6	55.1

APPENDIX II-INDIVIDUAL STUDIES-cont'dSTUDY V-cont'd

DISCUSSION

**NDEB defers to TB-IRS as to the conclusions concerning the transfer of permethrin through to rabbit skin. We also defer to TB-IRS as to the significance of the change of formulation on those results.

** TB-IRS will also determine the applicability of these data on the estimation of absorbance through the back of rabbit skin.

**NDEB defers to TB-IRS as to the significance of the radiolabelled material in the skin and excreta of rabbits because TB is responsible for the evaluation of the pharmacokinetics as well as the dermal penetration.

**NDEB defers to TB as to the suitability of testing conditions for the rabbits.

**There were no apparent data or actual measurements of initial permethrin or 14C permethrin on swatches. The registrants may wish to clarify this point in a future submission.

**There was no information concerning the storage time of the samples or the measurement of permethrin or 14C permethrin present after the storage.

**Insufficient data exist for the evaluation of data concerning 14C permethrin in excreta of rabbits which were dermally exposed to treated fabric. Because this is an expedited review, and because TB-IRS would need to evaluate the data pharmacologically in any case, NDEB will not consider this portion of the study at this time.

**The petitioners did not include data on losses due to laundering of wool or other fabrics used in BDUs. Such fabrics may not necessarily behave identically to cotton, although the author contends that they contain similar cellulosic fibers.

STUDY VI

"Permethrin-Migration of 14C Permethrin From Impregnated Military Fabrics As Measured In Rabbits," by Hubert Snodgrass, Jr, Completed 3/88, USAEHA, Aberdeen Proving Ground, Lab Project 75-51-0351-87, EPA File #50404-L, Accession #407668-13.

METHODS AND MATERIALS

APPENDIX II-INDIVIDUAL STUDIES-cont'dSTUDY VI-cont'd

This study was designed to measure the rate and extent of permethrin migration from military BDUs under varying climates into the skin of the wearer. Correct interpretation depends on reviewing the data with respect to permethrin pharmacokinetics and ability to dermally penetrate.

STUDY RESULTS/DISCUSSION

Because this is an expedited review, and Study VI may be more appropriately reviewed by TB, results will not be discussed at this time.

STUDY VII

"Permethrin--Interim Report-Migration of 14C Permethrin From Impregnated Military Fabric," by Hubert L. Snodgrass, Complete 2/82, USAEHA, Aberdeen Proving Ground, MD Lab Project 75-51-0351-82, EPA File #50404-L, Accession 407668-08.

METHODS AND MATERIALS

Study VII appears to be the protocol and other documentation for Study VI.

STUDY RESULTS/DISCUSSION

The protocol submitted in Study VII would be more appropriately reviewed by TB. Because this is an expedited review, Study VII will not be evaluated at this time.

STUDY VIII

"Permethrin," EPA File #50404-L, Coulston Int'l Corp., by Lawrence J. Feller, EPA Accession #407668-01

METHODS AND MATERIALS

This is a summary of tox testing and assessments performed by the US Army Environmental Hygiene Agency on the Insecticide Permethrin, compiled 4/82.

STUDY RESULTS

Abstracts of 15 reports.

APPENDIX II-INDIVIDUAL STUDIES-cont'dSTUDY VIII-cont'd

DISCUSSION

**Summary of articles are not acceptable in place of scientific data for the purposes of this review.

**If the registrant wishes to have additional data considered for Agency review, the entire study should be submitted for review.

STUDY IX

"Permethrin--Pyrethrins and Pyrethroids for the treatment of Scabies and Pediculosis," by D. Taplin, 1987, Performing Lab, Univ of Miami School of Medicine, FLA, Lab Project #0278-145x/87/0602, EPA File #50404-L, Accession 407668-16.

METHODS AND MATERIALS

Study IX amounts to a history of pyrethrums (naturally-occurring pyrethroids), their chemistry and toxicity and possible allergic reactions which occur in individuals.

A similar history of the synthetic compounds is also included, along with testimonials as to the variety of medical uses.

STUDY RESULTS/DISCUSSION

This is not applicable to the study.