



2/22/01

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Date: 2/22/01

SUBJECT: Review of Permethrin Rub-Off Trial from Astex Mattress Liners

MRID #: 452560-01
DP Barcode: D261829
PC Code: 109701
End-use Products: Astex Mattress Liners

FROM: Steven H. Weiss, Industrial Hygienist
Registration Action Branch 2
Health Effects Division (7509C)

THRU: Donna Davis, Branch Chief
Registration Action Branch 2
Health Effects Division (7509C)

TO: Arnold Layne, Branch Chief
Insecticide Branch
Registration Division (7505C)

Attached is a review of the study entitled, "*Permethrin Rub-Off Trial from Astex Mattress Liners*" submitted by Protec Health International, Ltd. (MRID 452560-01). The primary review was completed by Versar, Inc. on Feb 5, 2001, under supervision of HED. It has undergone secondary review in RAB2 and has been revised to reflect Agency policies.

Executive Summary

The purpose of this study was to measure potential rub-off transfer of permethrin residues from Astex Active Dust Mite Control Bedding Covers (specifically mattress liners) to bottom bed sheets. The Astex product consists of a polyester voile mattress liner, impregnated at a nominal rate of 550 mg permethrin/square meter of fabric. Based on the Astex label, the nominal percentage active ingredient in the mattress liners is 1.64 percent permethrin. Twelve sample sets were developed in this study. The authors found no statistical significance between permethrin rub-off as a function of bed sheet fabric type (i.e. polyester/cotton blend vs. 100 percent cotton sheeting). Therefore, within the same time interval, samples of each type of cloth were pooled, as follows:

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Chronic Exposure Samples:

First Phase Sheeting Samples: 20 samples collected after each of the first 3 weeks

Second Phase Sheeting Samples: 3 samples collected after weeks 9 and 14

Sheeting Samples Atop Additional Mattress Pads: 10 samples collected after week 4

Laundered Sheeting Samples: These may be divided into two broad sub-groups.

Group 1 (laundered once): 20 samples collected after each of weeks 1 and 3
4 samples collected after week 14

Group 2 (laundered 5 times): 4 samples collected after week 3

Acute Exposure Samples:

Group 1: 10 pairs of gloves used at the beginning of the study, to make up beds with Astex[®] mattress liners.

Group 2: "A glove" was used to directly rub an Astex mattress liner (50 firm strokes) in week 9 of the study.

The study report met some, but not all of the Environmental Protection Agency's (US-EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines. The most important deviations from EPA-OPPTS and good practice guidelines and other issues noted are summarized below:

- Residue storage stability data were not provided. The duration of time between the collection of the samples and the laboratory analysis was not reported. Data on method efficiency (residue recovery) were provided in a report entitled, "***The Recovery of Permethrin from Impregnated 100% Polyester and Polyester-Cotton Fabrics by Extraction with Ethyl Acetate***," (see Appendix C), also prepared by ENco (dated July 1998). The sensitivity of the analytical method and the effective LOD/LOQ were not clearly discussed in the Study Report, but the method used was said to be able to quantify as little as 10 mg/m². However, the report cited above states that the analytical methodology was able to measure a lower limit of 1.98 mg/m² permethrin. If the larger value is taken to be the lower limit of sensitivity (to be conservative), then many of the sample sets analyzed had values below the LOQ of 10 mg/m².
- Duplicate and control samples were not analyzed.
- Appendix B indicates that 3 samples consisting of pairs of gloves were analyzed after direct rubbing of the liners. The study report text refers to "a single glove" being used to directly rub mattress liners.
- Collection times may not be sufficient. Unlaundered sheeting samples were collected at 1, 2, 3, 9, and 14 weeks after placement of the Astex mattress liners on the beds. Average permethrin residues decreased from 32.03 mg/m² for study week 1 to 24.75 mg/m² in week 3 and 19.51 mg/m² in week 14. Using an assumed LOQ of 10 mg/m² (i.e., the higher of the 2 values cited in the report), the residue at week 14 is 2 times the LOQ. However, assuming an LOQ of 1.98 mg/m² (i.e., the lower of the 2 values cited in the report), the week-14 residue is still 10 times the LOQ. Permethrin residues in laundered

sheets declined to near LOQ levels by week 14, assuming the low LOQ of 1.98 mg/m².



MEMORANDUM

TO: Steven Weiss

cc: 1000.001.01

M. Collantes

FROM: Linda Phillips/Pat Wood

D. Forrest

DATE: February 5, 2001

SUBJECT: Review of *Supplemental Submission to the US-EPA: Permethrin Rub-Off Trial from Astex® Mattress Liners*, MRID No. 452560-01

This report reviews *Permethrin Rub-Off Trial from Astex® Mattress Liners*, submitted by Protec Health International, Ltd. as a supplemental submission in support of registration of the company's Astex® Mattress Liner products. A summary of the study and its compliance with applicable guidelines from the Environmental Protection Agency's (US-EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines is provided. The following information may be used to identify the study:

Title:	<i>Supplemental Submission to the US-EPA: Permethrin Rub-Off Trial from Astex® Mattress Liners</i> , 127 pages
Sponsor:	Lynda M. Platts, Operations Director Protec Health International, Ltd. 5 Priory Court Poulton, Cirencester, Gloucestershire, GL7-5JB, England
Analytical Laboratory:	Confederation of British Wool Textiles, Ltd. Trading as: ENco Valley Drive, Ilkley, LS29 8PB West Yorkshire, England
Study Director:	Dr. Larisa Rudenko Life Sciences Consultancy LLC 750 17th Street, NW Washington, DC 20006
Report Date:	November 1, 2000
I.D. Codes:	MRID #452560-01, File Symbol No. 71012-R, DP Barcode 27035

Executive Summary

The purpose of this study was to measure potential rub-off transfer of permethrin residues from Astex® Active Dust Mite Control Bedding Covers (specifically mattress liners) to bottom bed sheets. The Astex® product consists of a polyester voile mattress liner, impregnated at a nominal rate of 550 mg permethrin/square meter of fabric. Based on the Astex® label, the nominal percentage active ingredient in the mattress liners is 1.64 percent permethrin. Twelve sample sets were developed in this study. The authors found no statistical significance between permethrin rub-off as a function of bed sheet fabric type (i.e. polyester/cotton blend vs. 100 percent cotton sheeting). Therefore, within the same time interval, samples of each type of cloth were pooled, as follows:

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4 samples collected after week 14

Group 2 (laundered 5 times): 4 samples collected after week 3

Acute Exposure Samples:

Group 1: 10 pairs of gloves used at the beginning of the study, to make up beds with Astex® mattress liners.

Group 2: "A glove" was used to directly rub an Astex® mattress liner (50 firm strokes) in week 9 of the study.

The study report met some, but not all of the Environmental Protection Agency's (US-EPA) OPPTS Series 875, Occupational and Residential Exposure Test Guidelines. The most important deviations from EPA-OPPTS and good practice guidelines and other issues noted are summarized below:

- Residue storage stability data were not provided. The duration of time between the collection of the samples and the laboratory analysis was not reported. Data on method efficiency (residue recovery) were provided in a report entitled, "*The Recovery of Permethrin from Impregnated 100% Polyester and Polyester-Cotton Fabrics by Extraction with Ethyl Acetate*," (see Appendix C), also prepared by ENco (dated July 1998). The sensitivity of the analytical method and the effective LOD/LOQ were not clearly discussed in the Study Report, but the method used was said to be able to quantify as little as 10 mg/m². However, the report cited above states that the analytical methodology was able to measure a lower limit of 1.98 mg/m² permethrin. If the larger value is taken to be the lower limit of sensitivity (to be conservative), then many of the sample sets analyzed had values below the LOQ of 10 mg/m².
- Duplicate and control samples were not analyzed.
- Appendix B indicates that 3 samples consisting of pairs of gloves were analyzed after direct rubbing of the liners. The study report text refers to "a single glove" being used to directly rub mattress liners.
- Collection times may not be sufficient. Unlaundered sheeting samples were collected at 1, 2, 3, 9, and 14 weeks after placement of the Astex® mattress liners on the beds. Average permethrin residues decreased from 32.03 mg/m² for study week 1 to 24.75 mg/m² in week 3 and 19.51 mg/m² in week 14. Using an assumed LOQ of 10 mg/m² (i.e., the higher of the 2 values cited in the report), 4

the residue at week 14 is 2 times the LOQ. However, assuming an LOQ of 1.98 mg/m² (i.e., the lower of the 2 values cited in the report), the week-14 residue is still 10 times the LOQ. Permethrin residues in laundered sheets declined to near LOQ levels by week 14, assuming the low LOQ of 1.98 mg/m².

Study Review

Introduction

The purpose of this study was to measure potential rub-off transfer of permethrin residues from Astex® Active Dust Mite Control Bedding Covers (specifically mattress liners) to bottom bed sheets. The Astex® product consists of a polyester voile mattress liner impregnated at a nominal rate of 550 mg permethrin/square meter. Based on the Astex® label the active ingredient in the bedding covers is 1.64 percent permethrin [i.e. (3-phenoxyphenyl) methyl (+ or -) *cis-trans*-3(2,2-dichloroethenyl) 2,2-dimethylcyclopropanecarboxylate; CAS No. 52645-53-1].

A sample product label [EPA Reg. No. 71012-R] was provided. The directions for use state that users are to "fit Astex® covers over your mattress, pillow or duvet, and under your bottom sheet, pillow case, and duvet cover. After 8 weeks, all the house dust mites in your bedding will be dead. Remove the Astex® covers and vacuum your bedding thoroughly while ventilating the room. For best results, we would recommend using new filters and bag in your machine. Re-fit the Astex® covers on your bed immediately to prevent dust mites from returning, and leave the covers undisturbed for 2 years."

Protocol

The study enlisted 20 volunteers (10 males and 10 females, ranging in age from 13 to 65 years) who agreed to sleep on 20 beds fitted with Astex® Mattress Liners for three weeks, for six or seven consecutive nights. Each bed was stripped to the bare mattress, and fitted with a new mattress pad (to normalize all bottom surfaces and because some beds had been fitted with Astex® Mattress Liners previously). The Astex® Mattress Liners were then placed on top of the new mattress pads. Ten beds were fitted with all cotton sheets and 10 beds were fitted with cotton/synthetic blend bottom sheets, all placed on top of the liners. There was a slight difference in the weight per surface area of cotton/synthetic blend vs. all cotton sheeting samples. Cotton sheeting samples were slightly heavier than synthetic blend sheeting samples (144 grams/m² vs. 114 grams/m²). However, the authors found no statistical significance between permethrin rub-off as a function of the bed sheet fabric type (i.e., polyester/cotton vs. 100 percent cotton). All liners used were "from one batch impregnation that was performed by Calder Textiles Ltd. of Dewsbury, UK on 26 November 1999 (Certificate of Analysis on File)."

Twelve sample sets were developed in this study, as summarized below. Note that the first four sets relate to "chronic exposure" samples, and the final 2 sets relate to "acute exposure" samples.

Chronic Exposure Samples

- Sheeting Samples - First Three Weeks: Volunteers were "asked to follow their usual routine bed activities and keep a log of the approximate amount of time spent in bed." Once a week, the bottom sheets were collected and replaced with fresh sheets. There were three (3) one-week test periods over a period of six weeks for the entire study.

20 beds/test period * 3 1-week test periods * 1 sample/bed = 60 samples (50 cm²/sample)

- Sheeting Samples - Follow-up Sets: The main portion of the study lasted three weeks. At the end of three weeks, a few of the beds were subsequently assayed again at weeks 9 and 14.

3 beds/test period * 2 1-weeks test periods * 1 sample/bed = 6 samples (50 cm²/sample)

- Sheeting Samples - With Additional Mattress Pads: Beginning in week 4, after the first phase of the study, "10 of the beds had a new, unlaundered mattress pad placed on top of the liner, and subjects were asked to sleep on the bed for an additional week." Essentially, this sample set examined the effect of placing an additional layer of fabric between the liner and the bottom sheet.

10 beds/test period * 1 1-week test period * 1 sample/bed = 10 samples (50 cm²/sample)

- Laundered Sheetting Samples: Sheets from weeks 1 and 3 of the first study phase were laundered (i.e., washed and dried) one time. Sheets from week 14 (n=4) were also collected and laundered once. Also, four sheets from week 3 were collected and laundered five times.

20 beds/test period * 2 1-week test periods (weeks 1 and 3) * 1 sample/bed = 40 samples (50 cm²/ sample)
- washed ONCE

4 beds/test period * 1 1-week test period (week 14) * 1 sample/bed = 4 samples (50 cm²/ sample) - washed ONCE

4 beds/test period * 1 1-week test period (week 3)* 1 sample/bed = 4 samples (50 cm²/ sample) - washed FIVE times

Acute Exposure Samples

- First set: The study coordinator put on a pair of 100 percent cotton gloves "prior to opening a sealed package containing an Astex® Mattress Liner. Gloves were kept on while the liner was placed on a bed, and until the bed was completely made. Gloves were removed so that they ended up inside-out, placed into a prelabeled self-sealing plastic bag, and sent to ENco laboratories for analysis."
- Second set: Conducted in week 9 of the study, "a glove was put on and the mattress liner was rubbed with 50 firm strokes; the glove was removed, placed in a self-sealing plastic bag, and sent to ENco laboratories for analysis." [The Analytical Results presented in Appendix B (see page B- 10) seem to indicate that two gloves per sample were analyzed; the summary report (page 2) refers to "a glove" being used to directly rub the mattress liners.]

Each sheet was marked with a number in indelible ink. Beds were made up. Next, a line bisecting the sheet lengthwise was drawn down the sheet with an indelible marker. Using a 25 cm² square form, two symmetrical squares were marked onto the sheet (i.e., one on each sheet half), representing the point at which the volunteer's shoulder contacted the sheet. Then, a second set of 25 cm² symmetrical squares were marked onto the sheet, about 50 cm² below the first set, representing the point at which the volunteer's hip would contact the bed. At the end of each week, the study coordinator removed the sheets, randomly selected one top and one bottom square from either side of the midline mark, cut the two squares out, placed them in Whatman filter papers, and then placed the filter-paper wrapped packets into self-sealing plastic bags.

Analytical Methodology

Analyses were conducted by a laboratory operated by the "Environmental Technology Division (ENco)" of the Confederation of British Wool Textiles, Ltd., a British trade organization. The analytical method used in this study was attached as part of Laboratory Report ENco-738 (see Appendix C of the Study Report). The method was dated January, 1998 and was entitled "*Analytical Method for the Determination of*"

Permethrin on Treated Textiles by High Performance Liquid Chromatography or ENco Method 93A. The method was stated to be "suitable for determining the permethrin loading present on knitted or woven polyester fabrics weighing typically 35 grams per square meter and where the active substance loading is typically between 300 and 700 milligrams per square meter." Another (more detailed) copy of the same method (dated March 1998) that was also included in the Study Report, stated that "the protocol... can be used to assay fabrics with permethrin loadings in the region of 10 to 1,000 mg/m²." The method states that "Adaptations of the method are possible by varying the quantity of fabric sample assayed, the volume of the extraction solvent, and the sample dilution ratio prior to HPLC determination to yield a linear response in the range of 10 to 1,000 mg permethrin per square metre of fabric."

The method extracts a 0.5 gram portion of the textile substrate into ~10 mL methanol, with ultrasound-aided solvent extraction over 90 minutes. A 5-mL portion of the extract is filtered to remove particulates using a PTFE or polypropylene membrane to retain particles greater than 0.45 microns. The method states that "samples may be stored refrigerated at 4° C. for prolonged periods." It recommends that samples be diluted at least 100-fold in HPLC-grade methanol immediately prior to HPLC separation. HPLC is performed over a packed 5 micron Hypersil CB (MOS) column. Detection is at 230 nm. Isocratic reverse phase elution with 20:80 water/methanol is performed, and under these conditions, *trans*- and *cis*-permethrin isomers may be resolved. The retention times for the two isomers are similar; for *trans*-permethrin the retention time is estimated at 307 seconds, and for *cis*-permethrin, it is estimated to be 346 seconds.

The permethrin content of a test sample is a weighted average of individual *trans*- and *cis*- permethrin results. The second copy of Method 93A cites relative response factors (RFs) of 3.3219 for *cis*- and 1.0669 for *trans*-permethrin. The weighting factors (WF) cited are 0.244 for *cis*-permethrin and 0.756 for *trans*-permethrin. Calculation of a result uses the following equation:

$$[\text{Peak Area} - \text{trans} * \text{RF-trans} * \text{WF-trans}] + [\text{Peak Area-cis} * \text{RF-cis} * \text{WF-cis}] = \frac{\text{mg permethrin}}{\text{gram textile}}$$

No method validation data were appended to the first copy of Method 93A. However, a separate report entitled, "***The Recovery of Permethrin from Impregnated 100% Polyester and Polyester-Cotton Fabrics by Extraction with Ethyl Acetate,***" (see Appendix C), also prepared by ENco (dated July 1998), was attached. The purpose of this report was to evaluate the recovery of permethrin from fabrics using ethyl acetate. For 50:50 percent polyester:cotton sheeting, the following average permethrin loadings were tested in triplicate: 1.98; 4.93; 9.89; and 14.75 mg/m². For 100 percent polyester netting, average permethrin loadings tested were : 113.52; 155.59; 203.14; and 269.13 mg/m². All recoveries reported were within a range of 94 to 109 percent.

Results

Raw data for this study are reviewed in Appendix B of the study report. Table 1 provides a summary of the study results. The total permethrin recovered (μg) for each sample was divided by the product of the weight of each sample (in grams), as follows:

$$\text{Fabric Loading was calculated as } (\mu\text{g/g}) = \frac{\text{total permethrin recovered } (\mu\text{g})}{\text{sample weight (g)}}$$

The authors also weighed each sample analyzed, and derived two nominal fabric weight values for cotton and polycotton sheeting of 144 grams/m² and 114 grams/m², respectively. These values were used to calculate fabric loading per unit surface area by multiplying the fabric loading in µg/gram times the appropriate nominal fabric weight value (gram/m²), as follows.

$$\text{Fabric Loading } (\mu\text{g}/\text{m}^2) = \frac{\text{total permethrin recovered } (\mu\text{g})}{\text{sample weight (g)}} * \text{nominal fabric weight (g}/\text{m}^2)$$

Table 1 - Summary of Analytical Results

Sample Set Description	Study Week	Number Samples per Sample Set	Avg. Permethrin (mg/m ² ± S.D.)	Number of Samples <LOQ 10 mg/m ²
1st Phase Sheeting (unlaundered)	1	20	32.03 ± 8.87	0
	2	20	29.12 ± 10.75	0
	3	20	24.75 ± 11.64	0
2nd Phase Sheeting (unlaundered)	9	3	11.38 ± 5.03	1
	14	3	19.51 ± 1.09	0
Mattress Pad Between Liner and Sheet	4	10	1.44 ± 2.08	10
Sheeting - After ONE Laundering	1	20	9.28 ± 4.73	14
	3	20	4.51 ± 1.97	20
	14	4	2.23 ± 1.61	4
Sheeting - After FIVE Launderings	3	4	0.33 ± 0.16	4
Gloves - handling liners, while making up beds	At study initiation	10 pairs	1.96 mg ± 1.64 mg	-
Gloves - direct rubbing of liners	9	3 pairs ¹	0.10 mg ± 0.02 mg	-

¹Appendix B indicates 3 samples consisting of pairs of gloves were analyzed. The Study Report text refers to "a glove" being used to directly rub mattress liners.

Compliance with Series 875 Guidelines

- **Typical end use product of the active ingredient used.** The criterion was met. The product (polyester voile mattress liner) was impregnated with approximately 550 mg permethrin per square meter, as described in the Astex® label.
- **Material(s) tested representative of reasonable worst-case conditions expected in intended use areas.** This criterion was met. The product is said to be effective to control dust mites on mattresses, pillows, duvets for up to 2 years. In this study, treated mattress liners were used directly beneath bed sheets. This is the intended use of this product (it is not anticipated that individuals would sleep directly on these liners). In this study, subjects slept on beds with treated mattress liners for six or seven consecutive nights for three weeks or longer.
- **End use product applied by application method recommended. Application rate given and should be at the highest, label permitted, application rate.** This criterion was met. It appears that the Astex® product is manufactured using only one impregnation rate, which was identified as approximately 550 mg permethrin per square meter of fabric. All liners were from one batch impregnation. A Certificate of Analysis was said to be on file.
- **Application(s) occurred using the timing that the end-use product is normally applied to achieve intended pest control.** This criterion was met. The treated mattress liners were new at the beginning of the study. According to the label, the liners are effective for 2 years. Thus, reapplication of liners was not necessary because the study occurred over a 14-week period.
- **Residue storage stability, method efficiency (residue recovery), and limit of quantification provided.** This criterion was not entirely met. Residue storage stability data were not provided. The duration of time between the collection of the samples and the laboratory analysis was not reported. Data on method efficiency (residue recovery) were provided in a report entitled, "**The Recovery of Permethrin from Impregnated 100% Polyester and Polyester-Cotton Fabrics by Extraction with Ethyl Acetate**," (see Appendix C), also prepared by ENco (dated July 1998). The sensitivity of the analytical method and the effective LOD/LOQ were not clearly discussed in the Study Report, but the method used was said to be able to quantify as little as 10 mg/m². However, the report cited above states that the analytical methodology was able to measure a lower limit of 1.98 mg/m² permethrin. If the larger value is taken to be the lower limit of sensitivity (to be conservative), then many of the sample sets analyzed had values below the LOQ of 10 mg/m².
- **Duplicate samples collected at each collection period.** This criterion was probably not met. Duplicate samples were cut from the sheets, but it does not appear that these duplicate samples were analyzed for permethrin.
- **Control and baseline samples collected.** This criterion was not met. Results of control and baseline samples were not reported.
- **Sufficient collection times to establish dissipation curve.** It is unclear whether this criterion was met. Unlaundered sheeting samples were collected at 1, 2, 3, 9, and 14 weeks after placement of the Astex® mattress liners on the beds. Average permethrin residues decreased from 32.03 mg/m² for study week 1 to 24.75 mg/m² in week 3 and 19.51 mg/m² in week 14. Using an assumed LOQ of mg/m² (i.e., the higher of the 2 values cited in the report), the residue at week 14 is 2 times the LOQ. However, assuming an LOQ of 1.98 mg/m² (i.e., the lower of the 2 values cited in the report), the

week-14 residue is still 10 times the LOQ. Permethrin residues in laundered sheets declined to near LOQ levels by week 14, assuming the low LOQ of 1.98 mg/m².

- ***Residue data expressed as in the appropriate units.*** This criterion has been met. Permethrin residues were reported as mg permethrin per square meter of fabric
- ***Sufficient number of replicates to characterize exposure conditions for the population of interest.*** This criterion has been partially met. A total of 20 replicates were collected during the main portion of the study (i.e., during the first 3 weeks). However, during weeks 4 through 14, fewer replicates were collected.