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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Date: August 18, 2006

MEMORANDUM

SUBJECT: Secondary Review of "*Determination of Exposure to JAU 6476 (prothioconazole) and JAU 6476-desthio (SXX 0665) During Mixing/Loading and Application of JAU 6476 in Cereals.*" MRID 462464-47. PC Code 113961. DP Barcode: D303579.

FROM: Sarah Winfield, Biologist
Registration Action Branch 3
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THROUGH: Jack Arthur, ORE Assessment Team Leader
Registration Branch 3
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TO: Barry O'Keefe, Risk Assessor
Registration Branch 3
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CC: Lana Coppolino, PM
and
Bob Tomerlin, PM
Fungicide Branch
Registration Division (7505P)

Attached is a review of the worker mixer/loader and applicator exposure study for prothioconazole, submitted by Bayer CropScience LP. This review was completed by Versar, Inc. on October 4, 2004, under supervision of the Health Effects Division (HED). It has undergone secondary review in HED and has been revised to reflect current Agency policy.

The reviewed study addressed in this document involved adult human subjects who were intentionally exposed to a pesticide. This study has been determined to require a review of its ethical conduct. An ethics review is pending.

Introduction

Bayer CropScience LP submitted to the U.S. EPA the study: *Determination of Exposure to JAU 6476 (prothioconazole) and JAU 6476-desthio (SXX 0665) During Mixing/Loading and Application of JAU 6476 in Cereals* in support of the registrations for the fungicide prothioconazole and the prothioconazole formulation PROLINE 480 SC (soluble concentrate). The study objectives were:

1. To measure the exposure of workers to prothioconazole (JAU 6476) and its degradation product desthio-prothioconazole (JAU 6476-desthio) when applying prothioconazole 250 EC to cereals,

2. and to determine the proportion of conversion of prothioconazole to desthio-prothioconazole.

The first objective is standard, and requirements for this type of study are specified by the U.S. EPA Exposure Test Guidelines, Group A: 875.1100 for dermal exposure and 875.1300 for inhalation exposure. The second objective is not standard, and there are no requirements or specifications to conduct this inquiry. The study was reviewed by VERSAR (attached memo), and by the U.S. EPA. VERSAR reviewed the study according to the U.S. EPA Exposure Test Guidelines, Group A: 875.1100 for dermal exposure and 875.1300 for inhalation exposure.

Conclusions

The first objective of the study aimed to provide unit exposure information on prothioconazole and desthio-prothioconazole. The unit exposure information was determined inappropriate for use in exposure estimate calculations (and subsequent risk estimates) because of the small scale of the study, the choice of activity combinations, and the use of Bayer employees as study subjects. The best use of the study was to ascertain the likely range of percent conversion from prothioconazole to its desthio-prothioconazole metabolite/degradate during a typical agricultural workday (the second objective). Only outer dosimeters, which represent workers' clothes, detected both prothioconazole and desthio-prothioconazole, and therefore offer the most information regarding percent conversion estimates.

Study Summary

Eight worker exposure replicates (performed by 3 Bayer employees, referred to as "workers" in this review) were monitored at a test site in Monheim, Germany, during three "spray timings" (May 9th, 10th, 11th, 2000; May 30th, 31st, 2000; and June 6th, 7th, 8th, 2000 – details provided in Table 1). Each monitoring event (or replicate) consisted of a single participant performing both mixing/loading and application activities.

Table 1: Worker Exposure Replicates

Workers	Spray Timing 1*	Spray Timing 2*	Spray Timing 3§	Replicates/Worker
A	May 9, 2000		June 6, 2000	2
B	May 10, 2000	May 30, 2000	June 8, 2000	3
C	May 11, 2000	May 31, 2000	June 7, 2000	3
Replicates/Spray Timing	3	2	3	***Total Replicates* = 8**

*Applications during the first and second spray timings were conducted using equipment designed for large fields (28 m tractor mounted spray boom with a 2500 L water tank) and

§applications during the third spray timing were conducted using equipment designed for smaller fields (15 m tractor mounted spray boom with an 800 L water tank).

For each replicate, a single application of the test product was made to an approximately 50 acre field at a rate of about 0.18 lb ai/A. Due to the size of the spray tanks, two mixing/loading/application cycles were performed for each replicate during the first and second spray timings and six mixing/loading/application cycles were performed for each replicate during the third spray timing.

Dermal exposure was monitored using passive dosimetry techniques. A single layer of typical work clothing was worn over cotton underwear. Head exposure was monitored using a cap and hand exposure was monitored using hand washes. Additionally, protective gloves worn during all mixing/loading activities were analyzed. Inhalation exposure was monitored using personal air samplers connected to an IOM-sampler with a glass fiber filter, located in the breathing zone of the operator.

Analytical Method

The analytical method used in the study was a modification of method no. 00598/M001 (MR 689/99) with identical chromatographic and detection conditions. Modifications were made to accommodate the different matrices. Recoveries were within the range of 70% to 120%, and therefore, results do not need to be corrected due to the analytical method.

Field Fortifications

Field fortification results were variable. The results appeared to depend on whether prothioconazole was applied as an end-use product diluted with water, or whether prothioconazole was applied using concentrated prothioconazole, diluted with a solvent that would later be used in the extraction process. Recovery rates of prothioconazole on field fortification dosimeters treated with the diluted end-use product were lower than those treated with concentrated prothioconazole in solvent.

Field fortifications were also conducted with desthio-prothioconazole; however, they were only conducted with concentrated desthio-prothioconazole in solvent. As with prothioconazole field fortifications conducted this way, recovery rates were high. It is unknown whether recovery rates of desthio-prothioconazole, applied as an end-use product would have resulted in lower recoveries. If lower recoveries did result, the measured exposures to desthio-prothioconazole may be underestimated in this study.

Recovery rates for field fortifications with prothioconazole and desthio-prothioconazole, for all dosimeters, ranged from 54% to 104%. All results are provided below in Table 2. The bolded recovery rates were used to correct for the recovery of detected residues on particular dosimeters.

Table 2: Field Fortification Results

	[illegible]		[illegible]
Dosimeters*	Formulated, diluted with water	Concentrated, diluted in solvent	Concentrated, diluted in solvent
Outer clothing	**54%**	95%	99%
Undergarments	**66%**	88%	103%
Protective gloves	**72%**	–	26%
Hand Wash Water	–	96%	104%
*Inhalation filter, not pre-treated***	–	**54%**	–
*Inhalation filter, pre-treated w/ cysteine-HCl***	–	**87%**	96%

*Residue levels from the study were corrected for field recovery rates, when the relevant field recovery rates were less than 90%. Residues of desthio-prothioconazole were not corrected for because recovery rates were all above 90% - except for the 26% for protective gloves – this field fortification data was not used due to the fact that the standard for fortification was dissolved in organic solvent (acetonitrile), known to permeate into nitrile gloves, thereby resulting in low recoveries. Therefore glove rinse dosimeters assessed for desthio-prothioconazole were not corrected.

** Glass fiber filters (inhalation) had better recovery rates when pre-treated with cysteine-HCl. Residue levels from pre-treated and untreated glass fiber filters were corrected accordingly.

It should be noted that the percent recovery for the prothioconazole field fortifications (as noted in the above table) accounted for both recovered prothioconazole and recovered desthio-prothioconazole. By including the desthio-prothioconazole, it ensured the prothioconazole percent recovery would not be underestimated (since the desthio-prothioconazole is derived from prothioconazole). To account for desthio-prothioconazole's lower molecular weight, desthio-prothioconazole was converted to "prothioconazole-equivalents" by applying a molar ratio of the two compounds. Unfortunately, the raw data for field fortification recovery rates were not reported (only a summary table of recovery rates for different dosimeters was provided). If raw data had been provided, the proportion of prothioconazole to desthio-prothioconazole recovered from diluted end-use product (prothioconazole formulation) field fortifications could have been calculated and further informed the percent conversion estimates.

Objective 1: Exposure Estimates

Results/Unit Exposure Estimates

The following dermal and inhalation exposure values for prothioconazole and desthio-prothioconazole were calculated from the monitoring study: dermal unit exposures were 5.0

µg/lb ai handled (range 4.8 to 5.4 µg/lb ai handled) and 1.69 µg/lb ai handled (range 1.58 to 2.26 µg/lb ai handled), respectively; and inhalation unit exposures were 0.33 µg/lb ai handled (range 0.19 to 0.50 µg/lb ai handled) and 0.31 µg/lb ai handled (range 0.19 to 0.38 µg/lb ai handled), respectively. When residue levels on samples were below the LOQ, they were not corrected for, and ½ of the LOQ was used to represent these data when calculating unit exposure values. Both dermal and inhalation exposure values are presented as arithmetic means, and represent exposure from mixing/loading and application of prothioconazole (formulated as JAU 6476 250 EC) to cereals.

Discussion

HED uses unit exposure values in exposure scenarios to describe the various types of handler exposures that may occur for a specific active ingredient. The prothioconazole-specific unit exposures calculated in this study could in theory be used when calculating worker exposure estimates for mixing/loading and applying PROLINE 480 SC to cereal and similar crops. However, it was decided to use the surrogate unit exposure values from PHED for the following reasons:

- It is the policy of HED to use unit exposure data from the Pesticide Handlers Exposure Database (PHED) Version 1.1 to assess handler exposures for regulatory actions.
- The exposure scenario assessed in this study was a combination of mixing/loading and applying an emulsifiable concentrate to cereals with ground equipment, whereas, HED's policy is to separate mixing/loading and application activities when estimating exposure.
- Bayer employees were used as study subjects.
- The study was a relatively small-scale study.

In addition, there were certain guideline departures, including:

- Only 1 site was used, rather than the 3 sites suggested in *Pesticide Assessment Guidelines, Subdivision U, Applicator Exposure Monitoring,* U.S. EPA, Washington, DC, 1987.
- The formulation used in this study is approximately 2X less concentrated than the formulation Bayer has applied to register (JAU 6476 250 EC 252 g/L [25% ai] vs. PROLINE 480 SC, [41% ai])
- Breakthrough tests were not conducted on the inhalation dosimeters
- Tractor cabin conditions varied - some were closed, while others were slightly ajar, and some had filters, while others did not

It should be noted that the study resulted in prothioconazole unit exposures that are either comparable or smaller than the PHED unit exposures used by HED. It also is important to note that the unit exposure values calculated in this study mostly reflect ½ LOQ values, for there were relatively few actual measurements of prothioconazole or desthio-prothioconazole (for both prothioconazole and desthio-prothioconazole there were no hits on inner dosimeters and caps; for hand washes, there were 2 hits for prothioconazole and 1 hit for desthio-prothioconazole, for inhalation there were 2 hits during mixing/loading for prothioconazole).

Objective 2: Percent Conversion of Prothioconazole to Desthio-prothioconazole

Results/Percent Conversion Estimates
Additionally, the registrant submitted this study to determine how much prothioconazole converts to desthio-prothioconazole during the ground equipment application scenario. Prothioconazole and desthio-prothioconazole were found/measured on outer clothing dosimeters, protective glove dosimeters, and hand dosimeters (hand wash rinse water).

Outer clothing and protective glove dosimeters were the only dosimeter types where prothioconazole and desthio-prothioconazole were measured on the same dosimeter. Using only dosimeters on which both prothioconazole and desthio-prothioconazole were measured, the following percent conversion estimates were calculated:

Dosimeters	Percent Conversion Estimate Range*
Outer clothing	7 – 18%
Protective gloves	0.5 – 3.9%

*Percent Conversion (%) = [(amount desthio-prothioconazole x 1.1) / ((amount desthio-prothioconazole x 1.1) + (amount prothioconazole))] x 100, where 1.1 is the molar ratio of prothioconazole and desthio-prothioconazole, and is applied to the desthio-prothioconazole values to account for prothioconazole's higher molecular weight

Prothioconazole and desthio-prothioconazole were found in hand wash rinse water as well. However, prothioconazole and desthio-prothioconazole were not measured in the same rinses. There were also measurements on outer clothing and protective glove dosimeters on which prothioconazole and desthio-prothioconazole were found, but not on the same dosimeter. Using this set of exposure data and matching ½ LOQ values when necessary, the following percent conversion estimates were calculated for outer clothing, protective glove *and* hand dosimeters:

Dosimeters	Percent Conversion Estimate Range
Outer clothing	2 – 47%
Protective gloves	0.5 – 3.9%
Hand	13 – 61%

It should be noted that prothioconazole could degrade into components other than desthio-prothioconazole (as observed in environmental fate and effects studies). However, this study did not assay for degradates/metabolites of prothioconazole (other than desthio-prothioconazole), and therefore, these compounds were not included in the denominator of the percent conversion calculation. Had these components been detected, and subsequently included in the percent conversion estimation, it would be expected that the percent conversions would be lower than reported here.

Discussion
Analysis has indicated desthio-prothioconazole is more toxic than prothioconazole, therefore estimating the amount of desthio-prothioconazole exposure expected from application of prothioconazole is important. In theory, if the toxicological adverse effects resulting from prothioconazole and desthio-prothioconazole occupational exposure could be teased apart, one could assess risk from the chemicals separately. And desthio-prothioconazole exposure estimates could be calculated by applying a percent conversion estimate to the prothioconazole exposure estimate (see box below).

Occupational Risk from Prothioconazole:

$$\text{Occupational Risk}_{\text{PROTHIOCONAZOLE}}\ (\text{MOE}) = \frac{\text{NOAEL}_{\text{PROTHIOCONAZOLE}}}{\text{Exposure Estimate}_{\text{PROTHIOCONAZOLE}}}$$

Occupational Risk from Desthio-prothioconazole:

$$\text{Occupational Risk}_{\text{DESTHIO}}\ (\text{MOE}) = \frac{\text{NOAEL}_{\text{DESTHIO}}}{(\text{Exposure Estimate}_{\text{PROTHIOCONAZOLE}} \times \text{Percent Conversion}_{\text{PROTHIOCONAZOLE to DESTHIO}})}$$

However, it is unclear whether this would be prudent and/or feasible due to the following: in this study, neither prothioconazole, nor desthio-prothioconazole was found on most of the dosimeters representing exposure to the body (dosimeters representing the head/neck area and arms/torso/legs area). The exceptions were hand wash rinse water (representing hand exposure) and inhalation dosimeters. There were three hits in the hand wash rinses, two prothioconazole and one desthio-prothioconazole, and prothioconazole was found on inhalation dosimeters during mixing/loading activities (desthio-prothioconazole was not found on inhalation dosimeters). Percent conversion estimates were largely based on outer dosimeters and protective gloves, and not actual exposure. Additionally, although called "percent conversion estimates," these are really the proportions (desthio-prothioconazole: desthio-prothioconazole + prothioconazole) taken at a particular point in time. A study designed to specifically investigate the conversion of prothioconazole to desthio-prothioconazole would have included additional time course data.

Regardless, the study does show that the desthio-prothioconazole degradate is present during occupational use of prothioconazole formulations. In fact, even though desthio-prothioconazole is not listed as an impurity in the prothioconazole formulation, desthio-prothioconazole was found in the tank mixture in this study, and therefore, is present from the very beginning of worker exposure scenarios. Furthermore, prothioconazole has been found to quickly degrade to desthio-prothioconazole and a variety of other metabolites in other studies: a number of environmental fate and effects studies were conducted with prothioconazole to study its degradation in a variety of matrices. Radiolabeled prothioconazole was applied to a particular matrix and subsequently sampled at different time intervals, to determine how much of the prothioconazole had degraded to desthio-prothioconazole and other compounds at different points in time. From these studies, data were selected and used to calculate percent conversion estimates from prothioconazole to desthio-prothioconazole in timeframes as close to an 8-hour workday as possible. In Table 3, the selected data and percent conversion estimates are reported, and are intended to be comparable to those estimated from the worker study. The percent conversion estimates were calculated using data at durations as close to 5 to 8 hours as possible because workers in the worker study wore dosimeters for about 5 to 7 hours, and when HED estimates worker exposure, they assume workers work 8 hours/day.

Also, even though the environmental fate and effects studies measured other prothioconazole degradates/metabolites in addition to desthio-prothioconazole, these are not factored into the percent conversion estimations reported below in order to be more comparable to the percent conversions estimates from the worker study.

Table 3: Percent Conversion Estimates from Environmental Fate and Effects Studies

Study type	Soil/System type	Label	Time (hours)	# of Samples	Average Percent Conversion (%) Estimate (D/[P+D]) [4]
Aerobic soil metabolism	silt, loamy sand, sandy loam, silty clay loam	Phenyl and triazole	0	6	7.9
	silt, loamy sand, sandy loam, silty clay loam	Phenyl and triazole	24	6	**51.0**
Aerobic aquatic metabolism[1]	H-W and A total system	Phenyl and triazole	0	4	15.1
	H-W and A total system	Phenyl and triazole	24	4	33.4
Aqueous photolysis[2]	pH 7 buffer, irradiated	Phenyl and triazole	4	2	3.5
Soil photolysis[3]	silt loam, irradiated and dark	Phenyl	4	1	33.3
Hydrolysis	pH 4, pH 7, pH 9	Phenyl	6	3	**2.1**

[1] H-W = Honniger Weiher pond system (loam sediment), A = Anglerweiher lake system (loamy sand sediment);
[2] 90% of radioactivity in dark controls were parent, and it is assumed all degradation in the aqueous photolysis study is attributed to photolysis.
[3] Contrary to aqueous photolysis, all degradation in the soil photolysis studies is attributed to soil metabolism, not photolysis (degradation rate in dark control samples is slightly "faster" than irradiated samples).
[4] (D/[P+D]) = (% desthio-prothioconazole/[% prothioconazole + % desthio-prothioconazole]), measured as % radioactivity, which eliminates the need to correct for molecular weight, and convert to a percentage. **Bolded** percent conversions are the high and low values.

In the aerobic soil metabolism studies at 0 hours 7.9%, and at 24 hours 51%, of applied radiolabeled prothioconazole was converted to desthio-prothioconazole. In the aerobic aquatic metabolism study at 0 hours 15.1%, and at 24 hours 33.4%, of applied radiolabeled prothioconazole was converted to desthio-prothioconazole (for the total water system [sediment + water layer]). In the aqueous photolysis and soil photolysis studies, at 4 hours 3.5% and 33.3% of applied radiolabeled prothioconazole was converted to desthio-prothioconazole, respectively. And in the hydrolysis study, at 6 hours, 2.1% of applied radiolabeled prothioconazole was converted to desthio-prothioconazole. The average percent conversion estimates range from 2.1 to 51.0%, and are comparable (and therefore corroborative, with the range of percent conversions calculated in this study (*i.e.*, 0.5 to 61%).

In addition to the range of percent conversion estimates being corroborated, these studies corroborate the finding that prothioconazole appears to degrade to desthio-prothioconazole at t_0, in a number of different matrices (and via different mechanisms [photolysis in the aqueous photolysis studies, and soil metabolism in the soil photolysis studies]). When this is considered in light of desthio-prothioconazole's more potent toxicity (as well as the minimal data the percent conversion estimates are based on), a sound Tier 1 approach to the occupational exposure and risk assessment is to compare prothioconazole exposure estimates (which when calculated would be greater than or equal to desthio-prothioconazole exposure estimates [equal to only if there was 100% conversion]), and compare them to the more conservative quantitative hazard estimates (which currently are from the desthio-prothioconazole degradate/metabolite toxicity database). In the event refinement is needed, the percent conversion estimates reported in this review may be useful.

Versar inc.

MEMORANDUM

TO: Barry O'Keefe

cc: 11.0082.4000.001.01
Margarita Collantes

FROM: Teri Schaeffer/Karie Riley

DATE: October 4, 2004

SUBJECT: Study Review for *Determination of Exposure to JAU 6476 (prothioconazole) and JAU 6476-desthio (SXX 0665) During Mixing/Loading and Application of JAU 6476 in Cereals.* (MRID# 46246447; TAF# 4-1-23)

The attached report reviews the study *Determination of Exposure to JAU 6476 (prothioconazole) and JAU 6476-desthio (SXX 0665) During Mixing/Loading and Application of JAU 6476 in Cereals* which was submitted by Bayer CropScience LP to the U.S. EPA in support of the registration requirement for prothioconazole. The requirements for this study were specified by the U.S. Environmental Protection Agency's (U.S. EPA) OPPT Series 875, Occupational and Residential Exposure Test Guidelines, Group A: 875.1100 for dermal exposure and 875.1300 for inhalation exposure. Exposure results were provided as µg/lb-ai handled. Please feel free to contact us if you have any questions.

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Reviewer: Teri Schaeffer / Karie Riley **Date** October 4, 2004

STUDY TYPE: Mixer/Loader/Applicator Passive Dosimetry Study Using Whole Body Dosimetry and Personal Air Sampling.

TEST MATERIAL: JAU 6476 250 EC is a systemic fungicide formulated as an emulsifiable concentrate containing 25.1% active ingredient, 2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione.

SYNONYMS: Active Ingredient: prothioconazole; JAU 6476; CAS # 178928-70-6
Degradation Product: ∝-(1-Chlorocyclopropyl)-∝-(2-chlorophenyl)-methyl-1H-1,2,4-triazole-1-ethanol; JAU 6476-desthio; SXX 0665; CAS # 120983-64-4

CITATION:

Author:	Wolfgang Maasfeld -Study Director
Title:	*Determination of exposure to JAU 6476 and JAU 6476-desthio (SXX 0665) during mixing/loading and application of JAU 6476 in cereals*
Report Date:	February 28, 2002
Laboratory:	BAYER AG Business Group Crop Protection Development Department Institute for Metabolism Research and Residue Analysis 51368 Leverkusen Federal Republic of Germany
Identifying Codes:	Laboratory Project ID P 666 00 1501; Bayer AG Report MR-036/02; MRID 46246447; Unpublished.

SPONSOR: Bayer CropScience LP
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EXECUTIVE SUMMARY:

This study was conducted to measure the exposure of workers to prothioconazole (JAU 6476) and it's degradation product prothioconazole-desthio (JAU 6476-desthio) when applying prothioconazole 250EC to cereals. JAU 6476 250 EC is a systemic fungicide formulated as an emulsifiable concentrate containing 25.1% active ingredient (prothioconazole). The study was also conducted to determine the proportion of conversion of prothioconazole to prothioconazole-desthio; however, this study objective is not discussed in this report.

Eight worker exposure replicates were monitored at the test site in Monheim, Germany. Each monitoring event consisted of a single participant performing both mixing/loading and application activities. The monitoring events took place over three spray timings. Three monitoring events were performed over the first and third spray timings and 2 monitoring events were performed over the second spray timing. Applications during the first and second spray timings were conducted using equipment designed for large fields (28 m tractor mounted spray boom with a 2500 L water tank) and applications during the third spray timing were conducted using equipment designed for smaller fields (15 m tractor mounted spray boom with a 800 L water tank). For each monitoring event, a single application of the test product was made to a 20 ha (49.4 acres) field at a rate of 0.178 lb ai/A. Due to the size of the spray tanks two mixing/loading/application cycles were performed for each monitoring event during the first

and second spray timings and six mixing/loading/application cycles were performed for each monitoring event during the third spray timing.

Dermal exposure was monitored using passive dosimetry techniques. A single layer of typical work clothing was worn over cotton underwear. Exposure to head was monitored using a cap and exposure to hands was monitored using hand washes. Additionally, protective gloves worn during all mixing/loading activities were analyzed. Inhalation exposure was monitored using personal air samplers connected to an IOM-sampler with a glass fiber filter, located in the breathing zone of the operator.

Versar calculated potential and total dermal exposure for mixing/loading and application tasks combined, inhalation exposure for mixing/loading and application tasks combined and separately, and total dermal exposure. Versar corrected all residue values when field fortification recoveries were <90% and used ½ the limit of quantitation (LOQ) when residue values were reported as <LOQ. All results were reported by Versar in μg/lb ai handled. The Registrant reported potential and total ("actual") dermal exposure, inhalation exposure, and total exposure in mg/kg ai handled. The Registrant did not correct for field fortification recovery results, but did use ½ the LOQ for residue values reported as <LOQ.

Versar calculated potential dermal exposure estimates using both the inner and outer dosimeters, hand washes, protective glove rinses, and caps (representing the head). The overall average total potential dermal exposures for prothioconazole and JAU 6476-desthio were 1,446 μg/lb ai handled and 38.3 μg/lb ai handled, respectively.

Versar calculated total dermal exposure estimates from inner dosimeters, hand washes, and caps. The overall average total dermal exposures for prothioconazole and JAU 6476-desthio were 5.00 μg/lb ai handled and 1.69 μg/lb ai handled, respectively.

Inhalation exposures were calculated by Versar using the amount of residue found in the glass fiber filters and cartridges. There were no JAU 6476-desthio residues detected above the LOQon the filters and cassettes for either the mixing/loading tasks or the application tasks. There were no prothioconazole residues detected above the LOQ on the filters and cassettes for the application tasks. Versar used the NAFTA recommended inhalation rate of 0.0167 m^3/min for light activities. The total overall average inhalation exposures for prothioconazole and JAU 6476-desthio were 0.329 μg/lb ai handled and 0.306 μg/lb ai handled, respectively. Inhalation exposures were also estimated for mixing/loading and application tasks separately. For applicator tasks, the average exposures for prothioconazole and prothioconazole-desthio were 0.188 μg/lb ai handled. For mixing/loading tasks, the average exposure for prothioconazole was 0.211 μg/lb ai handled and the average exposure for prothioconazole-desthio was 0.188 μg/lb ai handled.

The total exposure estimate was calculated by taking the sum of all exposure routes (total dermal and inhalation). The overall average total exposures for prothioconazole and JAU 6476-desthio were 5.33 μg/lb ai handled and 2.00 μg/lb ai handled, respectively.

This study met most of the Group A, 875.1100 (dermal exposure) and 875.1300 (inhalation exposure) Guidelines. The major issues of concern are: (1) study took place at only one location; (2) trapping efficiency and breakthrough tests were not reported in the Study Report, (3) the study protocol was not provided with the Study Report; (4) a label specific to the test product was not provided with the study; (5) the study did not provide a description of the test site; and (6) it does not appear that laboratory fortified samples were run concurrently with the field samples.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The study sponsor waived claims of confidentiality within the scope of FIFRA Section 10(d) (1) (A), (B), or (C). The study sponsor and author stated that the study was conducted under EPA Good Laboratory Practice Standards (40 CFR part 160), Principles of Good Laboratory Practice - German Chemical Law (July 25, 1994, current version of Annex 1), and Japan's MAFF - Notification on the Good Laboratory Practice Standards for Agricultural Chemicals (JMAFF, 11 Nousan No. 6283) with the exception that recognized differences exist between the GLP principles/standards of OECD and those of FIFRA and JMAFF (for instance, authority granted Agency inspectors).

GUIDELINE OR PROTOCOL FOLLOWED: The study was reviewed using OPPTS Test Guidelines Series 875, Occupational and Residential Exposure Test Guidelines, Group A:

875.1100 (dermal exposure), and 875.1300 (inhalation exposure).

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material:

Formulation: JAU 6476 250 EC is a systemic fungicide formulated as an emulsifiable concentrate - 25.1 % ai (wt/wt) with expiration date of April 2001.

Lot/Batch # formulation: 06025/0259

Purity: The purity of the prothioconazole reference standard was verified at 99.9% with an expiration date of November, 2000. The purity of the prothioconazole-desthio reference standard was verified at 99.8% with an expiration date of September, 2000.

CAS #(s): 178928-70-6 - prothioconazole
120983-64-4 - JAU 6476-desthio (degradation product)

Other Relevant Information: This is a brand new currently unregistered, active ingredient, submitted under the new PRIA law.

2. Relevance of Test Material to Proposed Formulation(s):

The Study Report referred to the test product as JAU 6476 250 EC and the proposed label provided with the study was for a test product named PROLINE® 480 SC. The percent active ingredient for JAU 6476 250 EC was 25.1% and the percent active ingredient in the PROLINE® 480 SC product is 41%. However, they both share the same maximum single application rate of approximately 0.18 lb ai/A.

3. Packaging:

The test product was delivered to the test site in 5 L containers.

B. STUDY DESIGN

The study protocol was not provided in this Study Report. According to the Study Report, there were three deviations from the study protocol. These deviations were: (1) for field recovery, the intended quantity of field fortification to be applied to garments at the first spray time point according to the study protocol was 10 µg and 100 µg per sample for undergarments and 500 µg and 5,000 µg for outer garments. However, the applied amounts were a quarter of what was intended; (2) both torso parts of the outer clothing were not combined but analyzed separately; and (3) the flow rate of the air sampling device was measured at the start and the end of the monitoring but not in between. The Study Report also mentions that there was an amendment to the study protocol but the amendment was not defined.

1. Number and type of workers and sites:

A total of three male workers participated in the study at the one site. All of the workers were employed by Bayer AG. The ages of the workers were not provided in the Study Report. The years of experience ranged from 11 to >20 years. According to the study report, each worker was familiar with the practice of mixing/loading and application of plant protection products and they were asked to sign a worker consent form prior to the initiation of the study after being provided the proper information regarding the study.

A field, belonging to Bayer AG, located in Monheim, Germany was prepared with a cereal crop. Eight monitorings at three different spray timings were performed. For each monitoring event about 20 ha (49.4 acres) were treated. Air temperature, relative humidity, wind speed, and wind direction were recorded for each day of application. Temperatures ranged from

approximately 12°C to 27°C and relative humidity ranged from approximately 34% to 80%.

2. Replicates:

Eight monitoring replicates were conducted during three spray timings. Three monitoring events took place during the first spray timing (May 9, 10, and 11, 2000), two monitoring events took place during the second pray timing (May 30 and 31, 2000), and three monitoring events took during the third spray timing (June 6, 7 and 8, 2000). Three operators participated in the study. For each replicate, an operator would load and mix the test product in a spray tank and drive the spray equipment in the field to perform the application process. Each operator treated approximately 49.4 acres per monitoring event. For the first 5 monitoring events (first and second spray timings), the operators performed the mixing/loading and application tasks two times in order to treat the entire 49.4 acres. For the last three monitoring events (third spray timing), the operators performed the mixing/loading and application tasks six times to treat the entire 49.4 acres. An operator was monitored only once per monitoring event.

The average air pump sampling time for mixing/loading the test product was 39.5 minutes (28 to 50 minutes) and the average air pump sampling time for the application of test product to 49.4 acres was 110 minutes (87 to 150 minutes). The dosimeter clothing, except the caps and gloves, were worn additional hours for a total of approximately 7 hours (replicate A3, only 5.2 hours).

3. Protective clothing:

All the workers in this study were supplied with protective gloves which were worn during mixing/loading and any repair/maintenance procedures. Each operator wore cotton long-sleeved work shirts and cotton/polyester long pants which were worn over a long sleeved cotton t-shirt and long johns. Additionally, it appears that a tractor with a cab was used to apply the test substance; however, the Study Report was unclear.

4. Mixing/loading/application method:

The test product was applied to cereals using a tractor mounted spray boom. For the first two spray timings, equipment designed for large fields was used (28 m tractor mounted spray boom with a 2500 L water tank) and for the third spray timing, equipment designed for smaller fields was used (15 m tractor mounted spray boom with a 800 L water tank). In order to treat the entire 49.4 A field per replicate, the operators performed the mixing/loading and application tasks two times for the first two spray timings and six times for the third spray timing.

Mixing/Loading:

For the first two spray timings (encompassing the first five monitoring events), the operators performed the mixing/loading tasks in a shed. Water was filled into the tank by means of a hose connected to a water pipe. The operators put on their protective gloves and added 8 L of test product to the induction hopper. The test product came in 5 L cans, therefore beakers were used and rinsed as needed. All but the first spray timing operator (A1) added an anti-foaming agent to the tank. Then the hopper was closed and when the tank volume reached 2,400 L the hose was taken out of the tank, the tank was closed and the gloves were removed. For the second mixing/loading task, the operators unscrewed the lid, put the water hose into the tank and began to fill the tank. When about two thirds of the water volume was filled in, the operators repeated the loading process with 8 L of test product and an anti-foaming agent (with the exception of A1). When the final volume of 2,400 L was reached, the operators took another hose and rinsed the outside of the tank with water. Then the hose was taken out of the tank, the tank was closed and the gloves were removed.

For the third spray timing (encompassing the three remaining monitoring events), the operators performed the mixing/loading tasks in the field. Six mixing/loading and six application tasks were performed. For the first five mixing/load tasks, 800 L of water from a hydrant in the field was added to the tank by means of a hose along with 2.8 L of test product. The hopper was then closed and the gloves were removed. For the sixth mixing/loading task, only 2.1 L of test product with 600 L water was used. An anti-foaming agent was added at each mixing/loading task.

Application: During the first and second spray timings (encompassing the first 5 monitoring events), equipment normally used for large field sizes was used (28 m boom with a 2500 L water tank volume). After mixing/loading was finished in the shed, the operator drove the tractor with the boom sprayer in the field. The operator unfolded the boom (automatic operation) and stared the application. When the first application was finished, the boom was folded and the tractor was driven back to the shed to start the mixing/loading process again. This same procedure was repeated for each application. During the third spray timing (the last three monitoring events) equipment used for smaller field sizes was chosen (15 m boom with an 800 L water tank volume). The mixing/loading tasks were performed in the field. Therefore, once the mixing/loading task was completed the application task took place immediately after.

5. Application Rate:

The test product was applied to cereals via a spray boom at a target application rate of 200 g ai/ha (0.178 lbs ai/A) with a maximum frequency of three spray applications per season. The study did not provide information on how the application rate for each test product was determined. Calibration procedures were not discussed in the Study Report; however, the calibration date for each spray timing was provided. Table 1 provides a summary of the application rates for each monitored event.

Table 1. Prothioconazole Application Rates

Spray Timing	Operator ID	Total Amount of Active Ingredient Handled (lbs)	Total Acres Treated	Application Rate (lb ai/A)
1	A1	8.73	49.4	0.177
	B1	8.88	49.4	0.180
	C1	8.88	49.4	0.180
2	B2	8.88	49.4	0.180
	C2	8.88	49.4	0.180
3	A3	8.95	49.4	0.181
	B3	8.95	49.4	0.181
	C3	8.95	49.4	0.181

6. Exposure monitoring methodology:

Dermal: Dermal exposure was assessed using inner and outer whole body dosimeters. Inner whole body dosimeters consisted of a long sleeved t-shirt and long johns that simulated the skin. These were worn above their own underwear. An outer whole body dosimeter consisted of a pair of trousers (cotton/polyester) and a cotton shirt that represented the applicators' normal clothing. The dosimeter clothes were worn for about 7 hours (with the exception of operator A3, who wore his dosimeter clothes for approximately 5.2 hours). Each operator was taken to the Institute for Metabolism Research and Residue Analysis where his clothing was removed with the assistance of a member of the study team. The dosimeters were cut into the following seven sections after the mixing/loading/applying activities were completed:

1. Outer clothing/shirt/both sleeves
2. Outer clothing/shirt/torso
3. Outer clothing/trousers/torso
4. Outer clothing/trousers/both legs
5. Undergarments/t-shirt/both sleeves
6. Undergarments/t-shirt/torso (t-shirt and pants)
7. Undergarments/pants/both legs

Hands: Hand exposure was determined using hand washes consisting of Esemtan® lotion followed by a water rinse.

When the operator finished the last application the operator rubbed his hands together with approximately 1 mL Esemtan® hand lotion. Then the hands were rinsed with 500 ml of water. The water was collected in a bowl and an aliquot was taken and transferred into a pre-labeled 500 ml bottle and then placed in a refrigerator until analysis. For the third spray timing, a second hand wash with isopropanol was performed (200 ml per hand) directly after the Esemtan® wash. Protective gloves worn during mixing/loading and any repair/maintenance procedures were rinsed at the end of the monitoring with 200 mL acetonitrile per glove. Both rinsings were collected in one bottle which was then placed in a refrigerator until analysis.

Head: The applicators wore a cap to measure exposure to the head. After completion of the spraying, the cap was sampled like the gloves and the hand wash.

Inhalation: Inhalation exposure was assessed using personal air sampling pumps and IOM-samplers with glass fiber filters. The IOM-sampler was positioned in the breathing zone of the operator. The sampling pumps were calibrated using a "DryCal DC-Lite" primary flow meter prior to and at the end of each day of use to draw two liters per minute (Lpm). The flow rate was measured at the start and the end of the monitoring. The sampling pumps ran for the duration of each task performed. The pump start and stop times were recorded in a field log along with any pertinent comments. At the end of each sampling period the sampling device was removed and replaced with a new one. During the first and second spray timing, separate samplers were used for each mixing/loading and application. During the third spray timing one sampler for all mixing/loading steps and one sampler for all applications were used.

Field monitoring was conducted from May 9 to June 8, 2000. The individual clothing samples were removed at the Institute for Metabolism Research and Residue Analysis (MR) of Bayer AG in Leverkusen put directly into separate pre-labeled polyethylene bottles prior to the addition of the extraction solvent. Hand wash samples were transferred into a pre-labeled 500 ml bottle and placed in a refrigerator until analysis. All inhalation samplers were wrapped in aluminum foil and placed in labeled bags which were put in a cooler for temporary storage. After the last application cycle the cooler was transported to the Institute for Metabolism Research and Residue Analysis where the samplers were directly extracted. The samples were analyzed between May and September, 2000. The number of days the samples were stored from collection in the field to analysis, was not reported.

7. Analytical Methodology:

Extraction method(s): Garments, nitrile gloves, and glass fiber filters were extracted with acetonitrile, the cassette part of the IOM-sampler was extracted with isopropanol. An aliquot was taken and diluted with an isotopic standard solution. For analysis of the hand wash solutions and spray tank samples, an aliquot was taken and (after further dilution, depending on the sample) diluted with an isotopic standard solution.

Detection method(s): Analysis of prothioconazole for all matrices was by liquid chromatography with MS/MS detection using analytical method 00598/M001, MR-689/99 which was adapted to the matrices used in this study. Table 2 provides a summary of the chromatographic conditions and Table 3 provides a summary of the mass spectrometer conditions.

Table 2. Summary of Typical HPLC Conditions

HPLC Column	Superspher 60 RP-select B, 12.5 cm x 0.40 cm, 4 µm, Merck Co.
Oven Temperature	40 °C
Mobile Phase	A acetonitrile/water 1:9 (v:v) + 0.1 mL acetic acid/L B acetonitrile + 0.1 mL acetic acid/L C acetonitrile/water 1:1 (v:v) + 0.1 mL acetic acid/L
Injection Volume	50 µL
Retention Time	JAU 6476: approximately 5.5 minutes JAU 6476-desthio: approximately 4.5 minutes
Flow Rate	1.0 mL/min.
Split	150 uL/min into MS/MS from 1.0 mL/min

Table 3. Summary of Typical MS Operating Conditions

Detector	Triple Quadruple HPLC-MS/MS Mass Spectrometer API 365, PE Biosystems Deutschland GmbH, Weiterstadt,
Interface	Electrospray, Turbolon Spray® Potential: +4000 V for JAU6476-desthio -4200 V for JAU6476 Temperature: 300 °C
Gas Settings (L/min) (JAU6476 // JAU6476-desthio)	Nitrogen 5.0: Nebulizer Gas: 1.48 // 1.48 Curtain Gas: 1.25 // 1.44 Collision Gas: 1.04 // 0.87 Turbo Gas: 6.00 // 6.00
Precursor Ion (parent *m/z*)	JAU6476: 342 JAU6476-desthio: 312
Product Ion (daughter *m/z*)	JAU6476: 70 JAU6476-desthio: 100

Method validation: The analytical method 00598/M001 was adapted to the matrices of this study. According to the Study Report, released lab methods were available when the field part of the study started. The Registrant fortified samples prior to the initiation of the field phase of this study. These results are referred as method validation recoveries and as laboratory recoveries. It does not appear that any laboratory fortified samples were analyzed concurrently with the field samples.

For prothioconazole, the overall average method validation recoveries for outer and inner garments were 83% and 89%, respectively. Overall average hand wash and protective glove recoveries were 108% and 80%, respectively. The overall average glass fiber filter recovery was 78%.

For JAU 6476-desthio,the overall average method validation recoveries for outer and inner garments

were 90% and 92%, respectively. Overall average hand wash recovery was 96%. The overall average glass fiber filter recovery was 99%.

The limit of quantitation (LOQ) was 50 µg prothioconazole per sample for the outer garments, 10 µg per sample for the inner garments, 200 µg for one nitrile glove (400 µg per pair), 0.01 µg per mL hand wash solution and 0.1 µg prothioconazole for glass fiber filters. The corresponding limit of quantitation for JAU 6476-desthio was 20 µg per sample for outer garments, 2 µg per sample for inner garments, 0.004 µg/mL hand wash solution and 0.1 µg for glass fiber filters.

Instrument performance and calibration: The Study Report provided the analytical method description. Within the description, the method states that the calculation of target analyte concentrations can be done using either a multipoint calibration curve or single point calibration. The actual study did not report which method was used. There was no discussion of HPLC/MS-MS calibration.

Quantification: Residues were quantified using a standard linear regression technique.

8. Quality Control:

Lab Recovery: The Study Report refers to samples fortified and analyzed prior to the field part of the study as both method validation and as laboratory recovery. These results are provided under the section heading of Method Validation. It appears the laboratory fortified samples were not analyzed concurrently with the field samples.

Field blanks: Unfortified dermal and inhalation blank samples were prepared as described in the field fortification section of this report and were stored and analyzed in the same manner as the field samples. Prothioconazole and JAU 6476-desthio residues were not detected above the LOQ in any of the matrices used in this study.

Field recovery: Recovery samples to assess the stability of residues of prothioconazole and its conversion product JAU 6476-desthio under field conditions on dermal exposure sampling materials and air sampling media were carried out on all three spray timings. Field fortification for the determination of prothioconazole recovery was conducted using a diluted formulation of JAU 6476 EC 250 (outer garments, inner garments, and protective gloves) and/or a prothioconazole standard solution (outer garments, inner garments, hand washes, and glass fiber filters). Field fortification for all samples for the determination of prothioconazole-desthio was conducted using a prothioconazole-desthio standard solution.

Prothioconazole

At each spray timing, a defined volume of JAU 6476 EC 250 formulation was diluted in water to simulate the spray liquid and applied to parts of cotton and/or cotton/polyester representing outer garments, parts of cotton representing undergarments, and protective gloves. The quantity intended to be applied to the garments at the first spray time point according to the study protocol was 10 µg and 100 µg per sample (nominal for undergarments) and 500 µg and 5000 µg (nominal for out garments). However, only a quarter of the intended concentrations were used due to a field fortification error. At the second and third spray timings the quantities chosen were 100 µg per sample (nominal for outer garments) and 10 µg (nominal for undergarments). The samples representing the undergarments were exposed under a layer of outer clothing to ambient conditions and the samples representing the outer clothing layer were exposed directly to ambient conditions for approximately the duration the operator wore his clothes. At the end of the exposure monitoring the samples were treated and processed as previously described for the test samples. Additional second and third spray timing garment samples were fortified with prothioconazole standard solution (outer garment 100 µg nominal and undergarment 10 µg nominal).

The protective gloves were fortified at a level of 3000 µg (nominal) and were exposed directly to ambient conditions for approximately the duration of the application.

IOM samplers with glass fiber filters were fortified with a standard solution of prothioconazole at 0.2

µg/filter. The samplers were attached to sampling pumps which were operated for 1 hour and 2 hours at the first spray timing. At the second and third spray timing the pre-treated glass fiber filters were used and the sampling pumps were operated for 1 hour and 4 hours, respectively. These fortified samples were treated in the same manner as the test samples.

Hand wash water samples were fortified with a standard solution at levels of 1 µg/mL and 10 µg/mL (nominal, first spray timing) and 0.04 µg/mL (nominal second and third spray timing). These fortified samples were treated in the same manner as the test samples.

Table 4 provides a summary of the prothioconazole field fortification results for each of the matrices. The overall average percent recoveries for the outer and inner garment field fortification (diluted formulations) samples were 54% and 66%, respectively. As per discussion with EPA, the overall average percent recoveries for the diluted formulation fortification samples (outer and inner garments) were used to correct the raw data. This decision was based on the more realistic behavioral probabilities of the active ingredient in the diluted formulation samples in comparison with the actual exposure samples as opposed to the active ingredient fortified as a standard solution. The overall average recoveries for the protective gloves and hand washes were 72% and 96%, respectively. The overall average recoveries for the non-treated and pre-treated glass fiber filters were 55% and 87%, respectively.

Prothioconazole-Desthio

Field recovery samples for JAU 6476-desthio were set up at the second and third spray timing as follows: outer garments were fortified at 50 µg nominal, undergarments were fortified at 10 µg nominal, hand wash water samples were fortified at 0.04 µg/mL nominal, protective gloves were fortified at 50 µg and 500 µg nominal, and IOM samplers were fortified at 0.2 µg nominal, pre-treated filters for 1 hour and 4 hours. All spiking occurred with standard in solvent.

Table 5 provides a summary of the JAU 6476-desthio field fortification recoveries. The overall average outer and inner garment field fortification recoveries were 99% and 103%, respectively. The overall average recoveries for the protective gloves, handwashes, and non-treated glass fiber filters were 26%, 104%, and 96%, respectively. According to the Registrant, the poor protective glove recoveries were due to the use of a standard in solvent (acetonitrile) which is known to permeate into the glove material resulting in low recoveries. Therefore, recoveries for the gloves were not used to correct data.

Table 4. Field Fortification Recovery Results for Prothioconazole.

Matrix	Fortification Type	Fortification (µg/sample)	n	Mean Overall Recovery (%)	RSD
Outer garments	diluted formulation	100	4	54	0.11
		125	4		
		1250	4		
	std. in org. solvent	100	4	95	0.03
Inner garments	diluted formulation	10	4	66	0.11
		25	4		
	std. in org. solvent	10	4	104	0.05
Hand wash water	std. in org. solvent	0.04	4	96	0.07
		1	4		
		10	4		

Table 4. Field Fortification Recovery Results for Prothioconazole (continued)

Protective gloves	diluted formulation	3000	8	72	0.22
Glass fiber filters (non pre-treated -1st spray timing)	std. in org. solvent	0.2	6	55	0.16
Glass fiber filters pre-treated (2nd & 3rd spray timings)	std. in org. solvent	0.2	4	87	0.09

Table 5. Field Fortification Recovery Results for JAU 6476-desthio.

Matrix	Fortified with	Fortification (µg/sample)	n	Mean Overall Recovery (%)	RSD
Outer garments	std. in org. solvent	50	4	99	0.02
Inner garments	std. in org. solvent	10	4	103	0.02
Protective gloves	std. in org. solvent	50	2	26[a]	NA
		500	2		
Hand wash water	std. in org. solvent	0.04	4	104	0.07
Glass fiber filters	std. in org. solvent	0.2	4	96	0.05

a - Low recoveries attributed to the use of a standard in solvent which is known to permeate into glove material. Recovery data were not used.

Formulation: The formulation used for the applications was reported as being an emulsifiable concentrate having the following purity: 25.1 % ai (wt/wt) with expiration date of April 2001.

Tank mix: At each monitoring event, two samples from the spray tank were collected. The results indicate that the concentrations were 103% of nominal.

Travel Recovery: Not Reported.

Storage Stability: According to the Study Report, the field fortification samples support the stability of the active ingredient and it's metabolite in the field samples.

9. Relevancy of Study to Proposed Use:

The study design and the proposed uses for this chemical are similar.

II. RESULTS AND CALCULATIONS:

A. EXPOSURE CALCULATIONS:

The study author provided exposure values expressed as μg found per sample and mg/kg ai handled for dermal and inhalation exposure for both prothioconazole and it's metabolite, JAU 6476-desthio. Versar estimated dermal and inhalation exposure values as μg/lb ai handled for both prothioconazole and it's metabolite, JAU 6476-desthio. Versar calculated both potential dermal exposure (based on outer and inner dosimeters, cap, hand washes, and protective glove rinse) and total dermal exposure (based on inner dosimeters, cap, and hand washes). The Registrant did not correct data for overall average field fortification recoveries below 90%. For those values below the LOQ, the Registrant used ½ LOQ in their calculations. Versar corrected the raw data when field fortification recoveries were <90% using the overall average recoveries from field fortified samples prepared as a diluted formulation. Versar also used ½ LOQ for values below the LOQ in their calculations.

Potential Dermal Exposure

Potential dermal exposure estimates were calculated from both the inner and outer dosimeters, hand washes, protective glove rinses, and caps (representing the head). There were no prothioconazole or prothioconazole-desthio residues detected above the LOQ for the caps and inner dosimeters. The overall average total potential dermal exposures for prothioconazole and prothioconazole-desthio were 1,446 μg/lb ai handled and 38.3 μg/lb ai handled, respectively. Table 6 provides the Versar-calculated potential dermal exposures. Total potential dermal exposures ranged from 324 μg/lb ai handled to 3,348 μg/lb ai handled for prothioconazole and from 9.39 μg/lb ai handled to 91.6 μg/lb ai handled for prothioconazole-desthio.

Total Dermal Exposure:

Total dermal exposure estimates were calculated from inner dosimeters, hand washes, and caps (representing the head). There were no prothioconazole or prothioconazole-desthio residues detected above the LOQ for the caps and inner dosimeters; therefore, residues detected in the hand wash samples were the only detectable contributors to the total dermal exposure values. The overall average total dermal exposures for prothioconazole and prothioconazole-desthio were 5.00 μg/lb ai handled and 1.69 μg/lb ai handled, respectively. Versar's calculated total exposures are reported in Table 7. These exposures ranged from 4.78 μg/lb ai handled to 5.40 μg/lb ai handled for prothioconazole and from 1.58 μg/lb ai handled to 2.26 μg/lb ai handled for-desthio.

Inhalation Exposure

Inhalation exposures were calculated from the breathing-zone air concentrations determined from the amount of prothioconazole and it's metabolite, prothioconazole-desthio, found in the glass fiber filters and cassettes. Versar used the NAFTA recommended inhalation rate of 0.0167 m^3/min for light activities. There were no prothioconazole-desthio residues detected on the filters and cassettes for either the mixing/loading tasks or the application tasks. There were no prothioconazole residues detected above the LOQ on the filters and cassettes for the application tasks. The total overall average inhalation exposures for prothioconazole and prothioconazole-desthio were 0.329 μg/lb ai handled and 0.306 μg/lb ai handled, respectively. Inhalation exposures were also estimated for mixing/loading and application tasks separately. For application tasks, the average exposures for prothioconazole and prothioconazole-desthio were 0.188 μg/lb ai handled. For mixing/loading tasks, the average exposure for prothioconazole was 0.211 μg/lb ai handled and the average exposure for prothioconazole-desthio was 0.188 μg/lb ai handled. Tables 8 through 10 provide the Versar-calculated potential inhalation exposures for total, mixing/loading, and applicators.

Total Exposure

The total exposure estimate was calculated by taking the sum of all exposure routes (total dermal and inhalation). Total exposure across the exposure routes was calculated by Versar and are provided in Table 11. The overall average total exposures for prothioconazole and JAU 6476-desthio were 5.33 μg/lb ai handled and 2.00 μg/lb ai handled, respectively. Inhalation was of minor importance to the total exposure.

III DISCUSSION

A. LIMITATIONS OF THE STUDY:

This study met most of the Group A, 875.1100 (dermal exposure) and 875.1300 (inhalation exposure) Guidelines. The major issues of concern are: (1) study took place at only one location; (2) trapping efficiency and breakthrough tests were not reported in the Study Report, (3) the study protocol was not provided with the Study Report; (4) a label specific to the test product was not provided with the study; (5) the study did not provide a description of the test site; (6) trapping efficiency and breakthrough tests were not reported in the Study Report; and (7) it does not appear that laboratory fortified samples were run concurrently with the field samples.

B. CONCLUSIONS:

Dermal and inhalation exposure was assessed for mixing, loading, and application of the test product through ground application equipment. Average total exposure across the exposure routes was calculated as 5.33 μg/lb ai handled for prothioconazole and 2.00 μg/lb ai handled for prothioconazole-desthio. The most exposure was from mixing/loading activities. According to the Registrant, conversion of prothioconazole to prothioconazole-desthio was seen on garments, protective gloves and hands to various percentages up to about 60%.

Table 6. Potential Dermal Exposure (μg/lb ai handled)

Replicate	Inner Dosimeter Residue[a] (µg)	Outer Dosimeter Residue[a] (µg)	Cap Residue (µg)	Hands Residue[a] (µg)	Glove Rinse Residue (µg)	Potential Dermal Residue[e] (µg)	lb ai handled	Potential Dermal Exposure[f] (µg/lb ai handled)
Prothioconazole								
A1	(15.0)[b]	461	(25.0)[c]	(2.50)[c]	2322	504	8.73	324
B1	(15.0)[b]	(100)[b]	(25.0)[c]	(2.50)[c]	6858	143	8.88	788
C1	(15.0)[b]	175	(25.0)[c]	(2.50)[c]	4917	218	8.88	578
B2	(15.0)[b]	(100)[b]	(25.0)[c]	(2.50)[c]	2279	143	8.88	273
C2	(15.0)[b]	795	(25.0)[c]	7.40	19847	843	8.88	2329
A3	(15.0)[b]	726	(25.0)[c]	(5.00)[d]	14917	771	8.95	1753
C3	(15.0)[b]	252	(25.0)[c]	8.30	29667	300	8.95	3348
B3	(15.0)[b]	(100)[b]	(25.0)[c]	(5.00)[d]	19319	145	8.95	2175
Mean								1,446
Geometric Mean								1,022
Standard Deviation								1,124
Coefficient of Variation (%)								77.7
Prothioconazole-desthio								
A1	(3.00)[b]	75.0	(10.0)[c]	(1.00)[c]	11.2	89.0	8.73	11.5
B1	(3.00)[b]	(40.0)[b]	(10.0)[c]	(1.00)[c]	34.3	54.0	8.88	9.94
C1	(3.00)[b]	(40.0)[b]	(10.0)[c]	(1.00)[c]	29.4	54.0	8.88	9.39
B2	(3.00)[b]	(40.0)[b]	(10.0)[c]	(1.00)[c]	84.2	54.0	8.88	15.6
C2	(3.00)[b]	(40.0)[b]	(10.0)[c]	(1.00)[c]	200	54.0	8.88	28.6
A3	(3.00)[b]	72.8	(10.0)[c]	(2.00)[d]	479	88.0	8.95	63.3
C3	(3.00)[b]	51.4	(10.0)[c]	(2.00)[d]	753	66.0	8.95	91.6
B3	(3.00)[b]	50.2	(10.0)[c]	7.2	614	70.4	8.95	76.5
Mean								38.3
Geometric Mean								26.0
Standard Deviation								33.6
Coefficient of Variation (%)								87.7

a Outer garments were corrected for 54% overall average field fortification recovery (diluted formulation) and inner garments were corrected for 66% overall average field fortification recovery (diluted formulation). Hand wash data did not require correction.

b Each value was below the LOQ for each section which made up the total garment residue value, therefore ½ LOQ for each section was added together.

c Value was below the LOQ, therefore ½ LOQ was used in calculations.

d At the third spray timing hand washes were collected using Esemtan followed by a second wash with isopropanol. Values were below the LOQ for each type of hand wash, therefore ½ LOQs were used for both types and added together in calculations

e Potential Dermal Residue = inner dosimeter residues + outer dosimeter residues + hand residues + cap residues + glove rinse residues

f Potential Dermal Exposure = Potential Dermal Residue/lb ai handled

Table 7. Total Dermal Exposure (μg/lb ai handled)

Replicate	Inner Dosimeter Residue[a] (µg)	Cap Residue (µg)	Hands Residue[a] (µg)	Total Dermal Residue[e] (µg)	lb ai handled	Total Dermal Exposure[f] (µg/lb ai handled)
Prothioconazole						
A1	(15.0)[b]	(25.0)[c]	(2.50)[c]	42.5	8.73	4.87
B1	(15.0)[b]	(25.0)[c]	(2.50)[c]	42.5	8.89	4.78
C1	(15.0)[b]	(25.0)[c]	(2.50)[c]	42.5	8.89	4.78
B2	(15.0)[b]	(25.0)[c]	(2.50)[c]	42.5	8.89	4.78
C2	(15.0)[b]	(25.0)[c]	7.40	47.4	8.89	5.34
A3	(15.0)[b]	(25.0)[c]	(5.00)[d]	45.0	8.95	5.03
C3	(15.0)[b]	(25.0)[c]	8.30	48.3	8.95	5.40
B3	(15.0)[b]	(25.0)[c]	(5.00)[d]	45.0	8.95	5.03
Mean						5.00
Geometric Mean						5.00
Standard Deviation						0.247
Coefficient of Variation (%)						4.95
Prothioconazole-desthio						
A1	(3.00)[b]	(10.0)[c]	(1.00)[c]	14.0	8.73	1.60
B1	(3.00)[b]	(10.0)[c]	(1.00)[c]	14.0	8.89	1.58
C1	(3.00)[b]	(10.0)[c]	(1.00)[c]	14.0	8.89	1.58
B2	(3.00)[b]	(10.0)[c]	(1.00)[c]	14.0	8.89	1.58
C2	(3.00)[b]	(10.0)[c]	(1.00)[c]	14.0	8.89	1.58
A3	(3.00)[b]	(10.0)[c]	(2.00)[d]	15.0	8.95	1.68
C3	(3.00)[b]	(10.0)[c]	(2.00)[d]	15.0	8.95	1.68
B3	(3.00)[b]	(10.0)[c]	7.2	20.2	8.95	2.26
Mean						1.69
Geometric Mean						1.68
Standard Deviation						0.233
Coefficient of Variation (%)						13.8

a Inner garments were corrected for 66% overall average field fortification recovery (diluted formulation) and hand wash data did not require correction.

b Each value was below the LOQ for each section which made up the total garment residue value, therefore ½ LOQ for each section was added together.

c Value was below the LOQ, therefore ½ LOQ was used in calculations.

d At the third spray timing hand washes were collected using Esemtan followed by a second wash with isopropanol. Values were below the LOQ for each type of hand wash, therefore ½ LOQs were used for both types and added together in calculations.

e Total Dermal Residue = inner dosimeter residues + hand residues + cap residues

f Total Dermal Exposure = Total Dermal Residue/lb ai handled

Table 8. Total Potential Inhalation (Includes Mixing/Loading and Applying) (μg/lb ai handled)

Replicate	Total Residue (μg)	Replicate length (min)	Flow Rate (L/min)	Concentration[e] ($\mu g/m^3$)	lb ai handled	Respiration Rate[f] (m^3/min)	Inhalation exposure[g] (μg/lb ai)
Prothioconazole							
A1	(0.400)[a]	142	2	1.41	8.73	0.0167	0.383
B1	0.532[b]	120	2.00	2.22	8.89	0.0167	0.500
C1	(0.400)[a]	115	2.00	1.74	8.89	0.0167	0.376
B2	0.465[c]	134	2.00	1.74	8.89	0.0167	0.437
C2	(0.400)[a]	124	2.00	1.61	8.89	0.0167	0.376
A3	(0.200)[a,d]	200	2.00	0.500	8.95	0.0167	0.187
C3	(0.200)[a,d]	183	2.00	0.546	8.95	0.0167	0.187
B3	(0.200)[a,d]	175	2.00	0.571	8.95	0.0167	0.187
Mean							0.329
Geometric Mean							0.306
Standard Deviation							0.125
Coefficient of Variation (%)							37.9
Prothioconazole-desthio							
A1	(0.400)[a]	142	2.00	1.41	8.73	0.0167	0.383
B1	(0.400)[a]	120	2.00	1.67	8.89	0.0167	0.376
C1	(0.400)[a]	115	2.00	1.74	8.89	0.0167	0.376
B2	(0.400)[a]	134	2.00	1.49	8.89	0.0167	0.376
C2	(0.400)[a]	124	2.00	1.61	8.89	0.0167	0.376
A3	(0.200)[a,d]	200	2.00	0.500	8.95	0.0167	0.187
C3	(0.200)[a,d]	183	2.00	0.546	8.95	0.0167	0.187
B3	(0.200)[a,d]	175	2.00	0.571	8.95	0.0167	0.187
Mean							0.306
Geometric Mean							0.29
Standard Deviation							0.099
Coefficient of Variation (%)							32.3

a Value represents the sum of non-treated glass fiber filter (1st spray timing) or pre-treated glass fiber filter (2nd and 3rd spray timings) and cassette residues. Both types of residues were less than the LOQ, therefore ½ LOQs were used in calculations

b Non-treated glass fiber filter residue corrected for overall average field fortification recovery of 55% (1st spray timing only)

c Pre-treated glass fiber filter residue corrected for overall average field fortification recovery of 87% (2nd and 3 spray timings only).

d Only one mixing/loading and application routine performed for the third spraying event. The first and second spray timings involved two mixing/loading and application events.

e Concentration ($\mu g/m^3$) = [(Residue (μg))/(flow rate (L/min) x duration (min))]*1L/0.001m^3

f Versar used the NAFTA recommended inhalation rate of 0.0167 m^3/min for light activities.

g Exposure (μg/lb ai handled) = [(Concentration ($\mu g/m^3$) x Respiration rate (m^3/min) x duration (min)]/lb ai handled

Table 9. Mixing/Loading Potential Inhalation (μg/lb ai handled)

Replicate	Total Residue (μg)	Replicate length (min)	Flow Rate (L/min)	Concentration[e] (μg/m^3)	lb ai handled	Respiration Rate[f] (m^3/min)	Inhalation exposure[g] (μg/lb ai)
Prothioconazole							
A1	(0.200)[a]	47	2.00	2.13	8.73	0.0167	0.191
B1	(0.332)[b]	31	2.00	5.35	8.89	0.0167	0.312
C1	(0.200)[a]	28	2.00	3.57	8.89	0.0167	0.188
B2	(0.265)[c]	40	2.00	3.31	8.89	0.0167	0.249
C2	(0.200)[a]	34	2.00	2.94	8.89	0.0167	0.188
A3	(0.200)[a]	50	2.00	2	8.95	0.0167	0.187
C3	(0.200)[a]	46	2.00	2.17	8.95	0.0167	0.187
B3	(0.200)[a]	40	2.00	2.5	8.95	0.0167	0.187
Mean							0.211
Geometric Mean							0.207
Standard Deviation							0.046
Coefficient of Variation (%)							21.8
Prothioconazole-desthio							
A1	(0.200)[a]	47	2.00	2.13	8.73	0.0167	0.191
B1	(0.200)[a]	31	2.00	3.23	8.89	0.0167	0.188
C1	(0.200)[a]	28	2.00	3.57	8.89	0.0167	0.188
B2	(0.200)[a]	40	2.00	2.5	8.89	0.0167	0.188
C2	(0.200)[a]	34	2.00	2.94	8.89	0.0167	0.188
A3	(0.200)[a,d]	50	2.00	2	8.95	0.0167	0.187
C3	(0.200)[a,d]	46	2.00	2.17	8.95	0.0167	0.187
B3	(0.200)[a,d]	40	2.00	2.5	8.95	0.0167	0.187
Mean							0.188
Geometric Mean							0.188
Standard Deviation							0.002
Coefficient of Variation (%)							0.823

a Value represents the sum of non-treated glass fiber filter (1st spray timing) or pre-treated glass fiber filter (2nd and 3rd spray timings) and cassette residues. Both types of residues were less than the LOQ, therefore ½ LOQs were used in calculations

b Non-treated glass fiber filter residue corrected for overall average field fortification recovery of 55% (1st spray timing only)

c Pre-treated glass fiber filter residue corrected for overall average field fortification recovery of 87% (2nd and 3 spray timings only).

d Only one mixing/loading and application routine performed for the third spraying event. The first and second spray timings involved two mixing/loading and application events.

e Concentration (μg/m^3) = [(Residue (μg))/(flow rate (L/min) x duration (min))]*1L/0.001m^3

f Versar used the NAFTA recommended inhalation rate of 0.0167 m^3/min for light activities.

g Exposure (μg/lb ai handled) = [(Concentration (μg/m^3) x Respiration rate (m^3/min) x duration (min)]/lb ai handled

Table 10. Applicator Potential Inhalation (μg/lb ai handled)

Replicate	Total Residue (μg)	Replicate length (min)	Flow Rate (L/min)	Concentration[c] (μg/m³)	lb ai handled	Respiration Rate[d] (m³/min)	Inhalation exposure[e] (μg/lb ai)
Prothioconazole							
A1	(0.200)[a]	95	2.00	1.05	8.73	0.0167	0.191
B1	(0.200)[a]	89	2.00	1.12	8.89	0.0167	0.188
C1	(0.200)[a]	87	2.00	1.15	8.89	0.0167	0.188
B2	(0.200)[a]	94	2.00	1.06	8.89	0.0167	0.188
C2	(0.200)[a]	90	2.00	1.11	8.89	0.0167	0.188
A3	(0.200)[a,b]	150	2.00	0.667	8.95	0.0167	0.187
C3	(0.200)[a,b]	137	2.00	0.730	8.95	0.0167	0.187
B3	(0.200)[a,b]	135	2.00	0.741	8.95	0.0167	0.187
Mean							0.188
Geometric Mean							0.188
Standard Deviation							0.002
Coefficient of Variation (%)							0.823
Prothioconazole-desthio							
A1	(0.200)[a]	95	2.00	1.053	8.73	0.0167	0.191
B1	(0.200)[a]	89	2.00	1.124	8.89	0.0167	0.188
C1	(0.200)[a]	87	2.00	1.149	8.89	0.0167	0.188
B2	(0.200)[a]	94	2.00	1.064	8.89	0.0167	0.188
C2	(0.200)[a]	90	2.00	1.111	8.89	0.0167	0.188
A3	(0.200)[a,b]	150	2.00	0.667	8.95	0.0167	0.187
C3	(0.200)[a,b]	137	2.00	0.730	8.95	0.0167	0.187
B3	(0.200)[a,b]	135	2.00	0.741	8.95	0.0167	0.187
Mean							0.188
Geometric Mean							0.188
Standard Deviation							0.002
Coefficient of Variation (%)							0.823

a Value represents the sum of non-treated glass fiber filter (1st spray timing) or pre-treated glass fiber filter (2nd and 3rd spray timings) and cassette residues. Both types of residues were less than the LOQ, therefore ½ LOQs were used in calculations

b Only one mixing/loading and application routine performed for the third spraying event. The first and second spray timings involved two mixing/loading and application events.

c Concentration ($\mu g/m^3$) = [(Residue (μg))/(flow rate (L/min) x duration (min))]*1L/0.001m^3

d Versar used the NAFTA recommended inhalation rate of 0.0167 m^3/min for light activities.

e Exposure (μg/lb ai handled) = [(Concentration ($\mu g/m^3$) x Respiration rate (m^3/min) x duration (min)]/lb ai handled

Table 11. Total Exposure (μg/lb ai handled)

Replicate	Inhalation exposure (μg/lb ai)	Total Dermal Exposure (μg/lb ai handled)	Total Exposure[a] (μg/lb ai handled)
Prothioconazole			
A1	0.383	4.87	5.25
B1	0.5	4.78	5.28
C1	0.376	4.78	5.16
B2	0.437	4.78	5.22
C2	0.376	5.34	5.71
A3	0.187	5.03	5.21
C3	0.187	5.4	5.58
B3	0.187	5.03	5.21
Mean			5.33
Geometric Mean			5.33
Standard Deviation			0.202
Coefficient of Variation (%)			3.79
Prothioconazole-desthio			
A1	0.383	1.60	1.99
B1	0.376	1.58	1.95
C1	0.376	1.58	1.95
B2	0.376	1.58	1.95
C2	0.376	1.58	1.95
A3	0.187	1.68	1.86
C3	0.187	1.68	1.86
B3	0.187	2.26	2.44
Mean			2.00
Geometric Mean			1.99
Standard Deviation			0.187
Coefficient of Variation (%)			9.35

a Total Exposure (μg/lb ai handled) = Inhalation Exposure (μg/lb ai handled) + Dermal Exposure (μg/lb ai handled)

Name:
Evaluator
Occupational Exposure Assessment Section

Date

Name:
Peer Reviewer
Occupational Exposure Assessment Section

Date

Name:
Head,
Occupational Exposure Assessment Section

Date

APPENDIX A

Compliance Checklist for *Prothioconazole Mixer/Loader/Applicator Exposure Study during Mixing/Loading and Application of JAU 6476 in Cereals*

Compliance Checklist

Compliance with OPPTS Series 875, Occupational and Residential Exposure Test Guidelines, Group A: Guidelines, 875.1100 (dermal) and 875.1300 (inhalation) is critical. The itemized checklist below describes compliance with the major technical aspects of OPPTS 875.1100 and 875.1300.

Guidelines 875.1100

1. *Investigators should submit protocols for review purposes prior to the inception of the study.* It is not certain if this criterion was met. The Study Report stated that a protocol was approved by the Study Director on May 5, 2000 and the experimental phase started on May 5, 2000. The protocol was not provided in the Study Report.

2. *Expected deviations from GLPs should be presented concurrently with any protocol deviations and their potential study impacts.* This criterion was met.

3. *The test substance should be a typical end use product of the active ingredient.* This criterion was met.

4. *The application rate used in the study should be provided and should be the maximum rate specified on the label. However, monitoring following application at a typical application rate may be more appropriate in certain cases.* This criterion was partially met. The application rate used was provided. However, a label specific to the test product was not provided with the study. A label for a similar product was provided. The provided label specifies a maximum application rate of 0.18 lbs ai/A which is the same used for this study.

5. *Selected sites and indoor conditions of monitoring should be appropriate to the activity.* This criterion was met.

6. *A sufficient number of replicates should be generated to address the exposure issues associated with the population of interest. For indoor exposure monitoring, each study should include a minimum of 15 individuals (replicates) per activity.* This criterion was met. A total of 8 replicates were monitored at three different applications involving three male operators.

7. *The quantity of active ingredient handled and the duration of the monitoring period should be reported for each replicate.* This criterion was met.

8. *Test subjects should be regular workers, volunteers trained in the work activities required, or typical homeowners.* This criterion was met.

9. *Any protective clothing worn by the test subjects should be identified and should be consistent with the product label.* This criterion was met.

10. *The monitored activity should be representative of a typical working day for the specific task in order to capture all related exposure activities.* This criterion was met.

11. *Dermal exposure pads used for estimating dermal exposure to sprays should be constructed from paper-making pulp or similar material (i.e., alpha-cellulose), approximately 1 mm thick, that will absorb a considerable amount of spray without disintegrating. The alpha-cellulose material should not typically require pre-extraction to remove substances that interfere with residue analysis. This should be determined prior to using the pads in exposure tests.* This criterion was met through the use of the whole body inner dosimeter in this study.

12. *Dermal exposure pads used for estimating dermal exposure to dust formulations, dried residues, and to dust from granular formulation should be constructed from layers of surgical gauze. The pad should be bound so that an area of gauze at least 2.5 inch square is left exposed. The gauze must be checked for material that would interfere with analysis and be pre-extracted if necessary.* This criterion does not apply to this particular study review.

13. *A complete set of pads for each exposure period should consist of 10 to 12 pads. If the determination of actual penetration of work clothing is desired in the field study, additional pads can be attached under the worker's outer garments. Pads should be attached under both upper and lower outer garments, particularly in regions expected to receive maximum exposure. Pads under clothing should be near, but not covered by, pads on the outside of the clothing.* This criterion was met through the use of the whole body inner dosimeter in this study.

14. *If exposed pads are to be stored prior to extraction, storage envelopes made from heavy filter paper may be used. The envelope must be checked for material that will interfere with analysis. Unwaxed sandwich bags should be used to contain the filter paper envelopes to help protect against contamination.* This criterion does not apply to this study.

15. *Hand rinses should be performed during preliminary studies to ensure that interferences are not present. Plastic bags designed to contain 0.5 gal and strong enough to withstand vigorous shaking (i.e., at least 1 mil inch thickness) should be used. During preliminary studies, plastic bags must be shaken with the solvent to be used in the study to ensure that material which may interfere with analysis is not present.* It is not certain if this criterion was met. The study report did not discuss this process in detail.

16. *The analytical procedure must be capable of quantitative detection of residues on exposure pads at a level of 1 ug/cm^2 (or less, if the dermal toxicity of the material under study warrants greater sensitivity).* This criterion was met.

17. *The extraction efficiency of laboratory fortified controls is considered acceptable if the lower limit of the 95% confidence interval is greater than 75%, unless otherwise specified by the Agency. At a minimum, seven determinations should be made at each fortification level to calculate the mean and standard deviation for recovery. Total recovery from field-fortified samples must be greater than 50% for the study.* These criteria were met.

18. *If the stability of the material of interest is unknown, or if the material is subject to degradation, the investigator must undertake and document a study to ascertain loss of residues while the pads are worn. It is recommended that collection devices be fortified with the same levels expected to occur during the field studies. The dosimeters should be exposed to similar indoor conditions and for the same time period as those expected during field studies.* This criterion was met.

19. *Data should be corrected if any appropriate field fortified, laboratory fortified or storage stability recovery is less than 90 percent.* This criterion was met. However, field fortification spiking solutions were prepared as diluted formulation solutions and as standard solutions. The standard solution field fortified sample recoveries were >90% and corrections were not required. However, Versar corrected data for the diluted formulation recoveries which were <90%.

20. *Field data should be documented, including chemical information, area description, environmental conditions, application data, equipment information, information on work activity monitored, sample numbers, exposure time, and any other observations.* This criterion was mostly met. The study did not provide a description of the test site.

21. *A sample history sheet must be prepared by the laboratory upon receipt of samples.* It is not certain if this criterion was met.

Guidelines 875.1300

1. *When both dermal and inhalation monitoring are required, field studies designed to measure exposure by both routes on the same subjects may be used.* This criterion was met.

2. *The analytical procedure must be capable of measuring exposure to 1 ug/hr (or less, if the toxicity of the material under study warrants greater sensitivity).* This criterion was met.

3. A *trapping efficiency test for the monitoring media chosen must be documented.* It is uncertain whether this criterion was met. Trapping efficiency testing was not mentioned in the Study Report.

4. *Air samples should also be tested for breakthrough to ensure that collected material is not lost from the medium during sampling. It is recommended that at least one test be carried out where the initial trap contains 10X the highest amount of residue expected in the field.* It is uncertain whether this criterion was met. A breakthrough test was not discussed in the Study Report.

5. *If trapping media or extracts from field samples are to be stored after exposure, a stability test of the compound of interest must be documented. Media must be stored under the same conditions as field samples. Storage stability samples should be extracted and analyzed immediately before and at appropriate periods during storage. The time periods for storage should be chosen so that the longest corresponds to the longest projected storage period for field samples.* This criterion was met through field fortification tests.

6. *A personal monitoring pump capable of producing an airflow of at least 2 L/min. should be used and its batteries should be capable of sustaining maximum airflow for at least 4 hours without recharging. Airflow should be measured at the beginning and end of the exposure period.* This criterion was met.

7. *Appropriate air sampling media should be selected. The medium should entrap a high percentage of the chemical passing through it, and it should allow the elution of a high percentage of the entrapped chemical for analysis.* This criterion was met. Satisfactory fortified sample recoveries indicate the appropriate sampling media was selected.

8. *If exposed media are to be stored prior to extraction, storage envelopes made from heavy filter paper may be used. The envelope must be checked for material that will interfere with analysis. Unwaxed sandwich bags should be used to contain the filter paper envelopes to help protect against contamination.* It is not certain if this criterion was met.

9. *Personal monitors should be arranged with the intake tube positioned downward, as near as possible to the nose level of the subject.* This criterion was met.

10. *Field calibration of personal monitors should be performed at the beginning and end of the exposure period.* This criterion was met.

11. *Field fortification samples and blanks should be analyzed for correction of residue losses occurring during the exposure period. Fortified samples and blanks should be fortified at the expected residue level of the actual field samples. Fortified blanks should be exposed to the same weather conditions.* This criterion was met.

12. *Respirator pads should be removed using clean tweezers and placed in protective white crepe filter paper envelopes inside sandwich bags. The pads should be stored in a chest containing ice until they are returned to the laboratory, where they should be stored in a freezer prior to extraction.* This criterion does not apply to this study.

13. *Analysis methods should be documented and appropriate.* This criterion was met.

13544

R131998

Chemical: Dinitramine

PC Code:
102301

HED File Code: 11100 Other Chemistry Documents
Memo Date: 1/1/2001
File ID: 00000000
Accession #: 000-00-0108

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