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

**OFFICE OF**
**PREVENTION, PESTICIDES AND**
**TOXIC SUBSTANCES**

August 8, 2008

**MEMORANDUM**

**SUBJECT**: Zinc 2-pyridinethiol-1-oxide (Zinc Omadine®): Occupational and Residential Exposure Risk Assessment for New Uses (Textiles) on EPA Reg Numbers 1258-840 and 1258-841.

**P.C. Code**: 088002 **MRID's**: 47311501 and 47311502
**DP Barcode**: D350287

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## I. EXECUTIVE SUMMARY

EPA conducted an assessment for the addition of proposed new uses to the currently registered products ***Zinc Omadine® Powder (1258-840)*** and ***Zinc Omadine® 48% Dispersion Industrial Microbiostat (1258-841)***. The proposed multiple textile uses are presented in Table 1 and expand current use sites for consumer textiles. Based on the use patterns on the labels, the EPA has determined potential exposures scenarios which are: 1) handler dermal and inhalation exposure from application of zinc omadine antimicrobial to treat textiles; and, 2) residential dermal and incidental oral post application exposures to textiles (including carpets) impregnated with the active ingredient zinc pyrithione (e.g. zinc omadine).

The Agency conducted an occupational handler assessment for the new uses specified in Table 1. The Agency assessed both registered products which include both a liquid (EPA Reg #. 1258-841) and a wettable powder (EPA Reg # 1258-840) formulation. Only inhalation risks for the wettable powder formulation using an open pour application (MOE 11) exceeded the Agency's level of concern (target MOEs ≤100). However, when adding a respirator, exposure was reduced sufficiently such that estimated MOEs were no longer of concern. It should be noted that the label currently includes language that users must wear a "*NIOSH approved full face respirator equipped with a combination organic vapor/P-100 prefilter.*" Since this label restriction already exists on the current label, no other restrictions are recommended.

In developing this assessment, the Agency used toxicity endpoints from the memo entitled "*Recalculation of Toxicity Endpoints for Risk Assessment Using Additional Toxicity Studies for Zinc Omadine (New Application Method) (D351179).*" Table 2 summarizes the new toxicological endpoints developed for zinc omadine. The reader is referred to this document for additional hazard characterization.

In addition to the occupational assessment, the Agency also performed a residential post application risk assessment. In order to support the zinc pyrithione new use, the registrant submitted flux studies in order to quantify the leaching. The studies were entitled *"Measurement of Zinc Pyrithione Leached from Polyester Fabrics (MRID 47311502)"* and *"Evaluation of Zinc Omadine® in the Treatment of Textiles (MRID 47311501)."* These leaching studies were reviewed by the Agency. The Agency did not agree with the method for calculating the leach rate percentage in MRID 473115-01. In MRID 473115-01, the researchers calculated the % leach rate by dividing the concentration of leachate recovered (ppm) by the theoretical wet weight concentration of the treating solution (e.g. 0.5% or 5,000 ppm) used to impregnate the fabric. The Agency would argue that the recovered leachate should be divided by the actual dry weight (µg/gm or ppm) of active ingredient actually impregnated in the fabric textile. By dividing by the concentration of the treating solution the registrant may have underestimated the percent recovered because the concentration in the fabric is likely less than the treating solution. The Agency would recommend that the registrant completely extract the zinc pyrithione from the dry fabric to see the actual amount of zinc pyrithione originally impregnated in the sample and compare this to the weight of the impregnated fabric sample. Because of this data gap and others,

the Agency did not use the registrant reported leach rate of 0.0009% fabric treated by dipping and 0.22% fabric treated by padding provided in MRID 47311501. Other data gaps and limitations of this study are also mentioned in Section IV.B.1 and VII. It should be noted that the leach rate reported by the registrant in this study is considerably less than 5% residue transfer surrogate used in this risk assessment.

The 5% residue transfer factor used in this risk assessment is based on the default residue transfer from treated carpets and a confirmatory study from the registrant is needed to support this assumption (US EPA 2001). Using this value and other exposure assumptions, the Agency assessed both dermal and incidental oral exposures to carpet and clothing. For new uses of textiles (clothing and carpet) represented in this assessment, the calculated dermal MOEs are less than the target MOE of 100, and therefore exceed the Agency's level of concern. In addition, there are concerns with hand-to-mouth ingestion exposure for carpets. The incidental oral MOE for children for this scenario is 15.

There are some uncertainties and limitations associated with the leaching data and the characterization of exposure and risk (see Section VII). The Agency has reservations on using the leaching data from the studies provided by the registrant to provide a conservative screening estimate of the post application risks of these new uses. The Agency will require additional refinements to the submitted leaching data in order to use the leaching data in the exposure assessment.

## II. BACKGROUND

### A. Action Requested

The Agency conducted a review of expanded uses of the active ingredient zinc pyrithione as a preservative in polyester textiles/textile products. The amended textile use pattern provided on proposed labeling was submitted to the Risk Assessment and Science Support Branch (RASSB), Antimicrobials Division (AD), for review. Included in this memorandum is a non-dietary risk assessment in consideration of the expanded use pattern for this active ingredient. This assessment also reviews leaching studies (MRID 47311501 and 47311502) to support the new uses of textiles.

### B. Use Profile

***Zinc Omadine® Powder (1258-840)*** and ***Zinc Omadine 48% Aqueous Dispersion Industrial Microbiostat (1258-841)*** are industrial end-use products of the antimicrobial active ingredient zinc, 2-pyridinethiol-1-oxide (zinc pyrithione). ***Zinc Omadine® Powder*** contains 95% active ingredient (a.i.) in a powder formulation and ***Zinc Omadine® 48% Dispersion Industrial Microbiostat*** contains 48% a.i. in a liquid formulation. They are designed to be incorporated as a preservative into textiles used to manufacture non-food contact finished goods (i.e., fabricated treated article end products) prone to deterioration by algae, bacteria, fungi and

mildew.

The proposed amended use of ***Zinc Omadine® Powder (1258-840)*** is to incorporate into treating solutions at 0.07% a.i. The application rate to apparel items or clothing is not to exceed 0.2% a.i. by dry weight of the fabric. The proposed use of ***Zinc Omadine® 48% Dispersion Industrial Microbiostat (1258-841)*** is to incorporate into treating solutions at 0.067 % a.i.. The application rate to apparel items or clothing is not to exceed 0.19% a.i. by dry weight of the fabric.

The zinc omadine-impregnated textiles are used to make a variety of finished end-products. An overview of the intended uses of ***Zinc Omadine® Powder and Zinc Omadine 48% Aqueous Dispersion Industrial Microbiostat*** and types of zinc omadine-impregnated end-products are provided in Table 1.

**Table 1. New Uses of *Zinc Omadine® Powder and Zinc Omadine 48% Aqueous Dispersion Industrial Microbiostat* -Treated Textiles**

| **Proposed Textiles** |
|---|
| **Wearing Apparel:** for example slacks, shirts, underwear, sweatshirts, sweatpants, socks, oven mitts, slippers, bathrobes, gloves, hats, scarves, jackets, incontinence pad cover stock, washable incontinence briefs and panties |
| **Household products:** for example upholstery, carpet, curtains, wall coverings, mops, dishcloths, yarns, cords, toweling and blankets, sheets, pillowcases. |
| **Synthetic fiber wipes**, tissues, sponges (non-food contact) |
| **Automotive, boat, train and airplane seats and seat coverings.** |

## III. SUMMARY OF TOXICITY CONCERNS IMPACTING OCCUPATIONAL AND RESIDENTIAL EXPOSURES

Zinc omadine demonstrates low acute toxicity by the dermal, and inhalation routes (Toxicity Category III) based on animal study data on file with the Agency. There is a moderate concern for the oral route (Toxicity Category II). Zinc omadine is a severe eye irritant (Toxicity Category I). There are also limited toxicity concerns for dermal irritation (Toxicity Category IV) and sensitization. Zinc omadine demonstrates developmental toxicity as well as neurotoxicity. Based on this, a developmental endpoint was selected for the occupational and adult residential dermal exposure assessments.

Product labeling cites "DANGER" as the signal word and includes the following precautionary statements:

*"Causes irreversible eye damage; harmful if swallowed or absorbed through the skin. Do not get in eyes, on skin, or clothing; do not breathe spray mists. Users must wear protective eyewear (goggles, safety glasses, or face shield), long sleeved shirt and long pants, socks, chemical resistant gloves and chemical resistant footwear. Users must wear a fit tested, NIOSH approved full face respirator equipped with a combination organic vapor/P-100 prefilter. When*

*mixing and loading, or cleaning equipment, wear a chemical resistant apron. Wash thoroughly with soap and water, and before eating, drinking or using tobacco. Remove contaminated clothing and wash clothing before reuse."*

**Table 2. Toxicological Endpoint Selection for Zinc Omadine***

| Summary of Toxicological Non-dietary Endpoints to be used for Risk Assessment of Zinc Omadine | | | |
|---|---|---|---|
| Exposure Scenario | Dose (mg/kg/day) | Endpoint | Study |
| Incidental Oral, Short- and Intermediate-Term | Maternal NOAEL= 0.75 mg/kg/day | MOE = 100 (residential) | **Developmental Toxicity Study in Rats** LOAEL = 3.0 mg/kg/day, Based on increased salivation in maternal rats. |
| Short-, Intermediate-, and Long-Term Dermal | Dermal NOAEL = 15 mg/kg/day | MOE = 100 (residential) MOE = 100 (occupational) | **Dermal Developmental Toxicity in Rats** (MRID 46534001) Maternal LOAEL = 30 mg/kg/day, based on increased no. of dams with limited use of hindlimbs, shuffling gait, decreased body weight and body weight gain, and decreased food consumption. |
| Short-, Intermediate-, and Long-Term Inhalation | Inhalation NOAEL = 0.0005 mg/L (0.13 mg/kg/day) | MOE = 100 (residential) MOE = 100 (occupational) | **Subchronic Inhalation Toxicity Study in Rats** LOAEL = 0.0025 mg/L Based on clinical signs of toxicity, decreased activity, and increased lung weights. |

* see D351179 for more details

## IV. HANDLER AND POSTAPPLICATION EXPOSURES/ASSUMPTIONS

EPA has determined that there are potential zinc omadine handler exposures during manufacturing and also residential post application exposures to consumer use of zinc omadine-impregnated textiles. In order to determine the magnitude of occupational and residential exposures, the following exposure scenarios were considered in this exposure assessment:

- **Occupational Handlers** - Workers in a manufacturing setting who are mixing ***Zinc Omadine® Powder*** or ***Zinc Omadine® 48% Dispersion Industrial Microbiostat*** directly (open or closed pour) into a mixing vessel for incorporation as a preservative into slurries used to manufacture a variety of non-food contact finished textiles as consumer goods.

- **Residential Consumer Postapplication Exposure** - Residential consumers who are exposed to zinc omadine antimicrobial due to contact with ***Zinc Omadine® Powder*** or ***Zinc Omadine® 48% Dispersion Industrial Microbiostat*** treated consumer goods such as: clothing and carpets.

Occupational post application exposures are expected to be minimal based on the low vapor pressure and lack of aerosols generated. Compared with the handler scenarios, the Agency anticipates the exposure potential in manufacturing settings to be less of a concern after incorporation of the pesticide into the various substrates and while conducting maintenance of equipment.

Residential post application scenarios were developed for both adult/child dermal contact with treated articles and child incidental oral ingestion of pesticide residues from hand-to-mouth and object-to-mouth activity. The Agency's *Exposure Factors Handbook (USEPA, 1997a)* and *Standard Operating Procedures (SOPs) for Residential Exposure Assessments (USEPA, 1997b)* were used to derive inputs and equations for estimating potential doses.

**A. Occupational Handlers**

During manufacturing processes, occupational workers may be exposed when zinc omadine is incorporated into textiles. ***Zinc Omadine® Powder*** or ***Zinc Omadine® 48% Dispersion Industrial Microbiostat*** can be incorporated into polymers in four ways depending on the type of material:

(1) Mixing/loading/applying liquid pesticide concentrates using open pour methods. Assumes 10,000 pounds of fabric/textiles are treated per day as a high-end maximum for large commercial operations. EPA 1258-841 (48 % a.i.) indicates that the maximum application rate is to add 0.14% of this product by weight to the treating solution. Application rate to apparel items or clothing is not to exceed 0.4% product by dry weight of the fabrics to be treated (4 lb product is to be added to treat 1,000 lbs of fabric), or 1.92 lb a.i./1,000 lbs. The label indicates that application is by dipping, or exhaustion.

(2) Mixing/loading/applying liquid pesticide concentrates using metering equipment (pump liquid) ***see assumptions for (1).***

(3) Mixing/loading/applying powder pesticide concentrates using open pour methods assumes 10,000 pounds of fabric/textiles are treated per day as a high-end maximum for large commercial operations. The label (EPA Reg #1258-840 (95 % a.i.)) indicates that you can add the maximum application rate of 0.07% of this product to the treating solution. Application rate to apparel items or clothing is not to exceed 0.2% by dry weight of the fabrics to be treated (2 lb product is to be added to the "acid sour" operation to treat 1,000 lbs of fabric), or 1.9 lb a.i./1,000 lbs.

(4) Mixing/loading/applying wettable powder (water soluble packets) *pesticide concentrates using metering equipment (automatic-dispensing techniques)*
***See assumptions for (3) Note: water soluble packets represents a hypothetical closed mixing situation.***

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**1. Handler Exposure Data**

Due to the lack of product-specific/chemical-specific exposure monitoring data, surrogate data from the Chemical Manufacturers Association (CMA) antimicrobial exposure study dated December 8, 1992 (USEPA, 1999) were used for estimating unit exposures for handlers for liquids. The purpose of the CMA study was to characterize exposure to antimicrobial chemicals in order to support antimicrobial pesticide registrations (USEPA,1999). The unit exposures presented in the most recent EPA evaluation of the CMA database (USEPA, 1999) was used in this assessment. The Pesticide Handlers Exposure Database (PHED) was used to estimate exposure from wettable powders. PHED has been developed by a Task Force consisting of representatives from Health Canada, the U.S. Environmental Protection Agency (EPA), and the American Crop Protection Association (ACPA). PHED provides generic pesticide worker (i.e., mixer/loader and applicator) exposure estimates (USEPA, 1998). The dermal and inhalation exposure estimates generated by PHED are based on actual field monitoring data, which are reported generically (i.e., chemical specific names not reported) in PHED. It has been the Agency's policy to use a surrogate or a generic exposure data for pesticide applicators in certain circumstances because it is believed that the physical parameters (e.g., packaging type) or application technique (e.g., aerosol can), not the chemical properties of the pesticide, attribute to exposure levels. The unit exposures are based on using personal protective equipment (PPE) for dermal and assessing at baseline (no respirator) and with PPE (respirator with organic vapor/P-100 prefilter). For the respirator scenario, a 90% protection factor (PF) was used.

For "open pouring" liquids, dermal exposure is represented by workers wearing long-sleeve shirt and long pants with gloves was assessed only. The reported dermal unit exposure (UE) is 0.135 mg/lb a.i. for liquids. For inhalation both a baseline inhalation (no respirator) and with respirators was calculated. For baseline, the inhalation UE is 0.00346 mg/lb a.i. for liquids. With a 90% PF with respirators, the unit exposure is reduced to 0.000346 mg/lb a.i. For closed situations in which metering equipment (pump liquid) was used, the CMA study was used. The CMA dermal unit exposure was 0.00629 mg/lb a.i.. and the inhalation unit exposure was 0.000403 mg/lb a.i.

For wettable powders, the PHED data were used. The dermal PPE UE is 0.17 mg/lb a.i. and the inhalation UE is 0.0434 mg/lb a.i. For closed systems, water soluble bags were used as surrogate. The dermal UE is 0.0098 mg/lb a.i. and the inhalation UE is 0.00024 mg/lb a.i. For the respirator scenario, a 90% protection factor (PF) was used.

**2. Potential Daily Dose**

The potential daily dose to zinc omadine for occupational workers during production of zinc omadine-treated plastic products was estimated using the following equation:

$$Daily\,Dose\left(\frac{mg\,ai}{Kg/day}\right) = Unit\,Exposure\left(\frac{mg\,ai}{lb\,ai}\right) x\,Use\,Rate\left(\frac{lb\,ai}{day}\right) x\left(\frac{1}{Body\,Weight(kg)}\right)$$

The use rate is discussed above. The Chemical Manufacturers Association (CMA) unit exposure data were used to estimate exposure for handlers. The female body weight of 60 kg was used for dermal since the toxicological endpoint was based on a maternal NOAEL. For inhalation, the adult male body weight of 70 kg was used since the toxicological endpoint was not sex specific. The potential daily doses to handlers are provided in Table 3 below.

**3. Margin of Exposure (MOE)**

The Margin of Exposure (MOE) calculations for each assessed exposure scenario were derived using the following equation:

$$MOE = \frac{NOAEL\left(\frac{mg}{kg/day}\right)}{Potential\,Daily\,Dose\left(\frac{mg}{kg/day}\right)}$$

Where:

NOAEL = No Observed Adverse Effect Level (mg/kg/day).

The Target MOE for the occupational assessment was 100 or greater.

## Table 3: ST and IT Exposure Assessment to Primary Occupational Handlers

| Occupational Scenario | Dermal Unit Exposure [a] (mg/lb a.i.) | Use Rate [b] (lb a.i./100 0 lb product) | Amount Handled (lb /day) | Daily Dermal Dose [c] (mg/kg/day) | Dermal MOEs [d] Target MOE ≥100 | Inhalation Unit Exposure [a] (mg/lb a.i.) | Daily Inhalation Dose [e] (mg/kg/day) | PPE Daily Inhalation Dose [f] (mg/kg/day) | Inhalation MOEs [g] Target MOE ≥ 100 | PPE Inhalation MOEs [g] Target MOE ≥ 100 |
|---|---|---|---|---|---|---|---|---|---|---|
| **Textiles** | | | | | | | | | | |
| Mixing/loading/applying liquid pesticide concentrates using open pour methods | 0.135 | 1.9 | 10,000 | 4.3E-2 | 350 | 0.0035 | 9.5E-4 | 9.5E-5 | 140 | NA |
| Mixing/loading/applying liquid pesticide concentrates using metering equipment (pump liquid) | 0.00629 | 1.9 | 10,000 | 2.0E-3 | 7,500 | 0.00040 | 1.1E-4 | 1.1E-5 | 1000 | NA |
| Mixing/loading/applying powder pesticide concentrates using open pour methods | 0.17 | 1.9 | 10,000 | 5.4E-2 | 280 | 0.043 | 1.2E-2 | 1.2E-3 | **11** | 110 |
| Mixing/loading/applying Water soluble bags[h] | 0.0098 | 1.9 | 10,000 | 3.1E-3 | 4800 | 0.00024 | 6.5E-5 | 6.5E-6 | 2000 | NA |

a For liquids, CMA Dermal Unit Exposure data used as a surrogate for dermal and inhalation exposure (USEPA 1999). For wettable powders, PHED dermal unit exposure data was used as a surrogate (USEPA1998). Data generated on workers wearing a single layer of clothing and chemical resistant gloves using a preservative pesticide formulation

b Use rates derived from submitted product labeling and personal communication with registrant. Calculations outlined in the text.

c Daily Dermal Dose = (Dermal Unit Exposure (mg/lb a.i.) x Use Rate (lb a.i./1000 lb prod) x Amt handled (10000 lb))/ Body Weight ( 60 kg).

d Dermal MOEs = NOAEL (mg/kg/day)/ Dermal Dose (mg/kg/day). Where the dermal NOAEL is 15 mg/kg/day (UF = 100).

e Daily Inhalation Dose =(Daily Inhalation Unit Exposure (mg/lb ai) x Use Rate (lb ai/1000 lb prod) x Amt handled (10000 lb))/ Body Weight (70 kg).

f A protection factor of 90% was used to represent OVA respirators

g Inhalation MOEs = ST/IT Inhalation MOE = NOAEL (mg/kg/day)/ Inhalation Dose (mg/kg/day). Where the ST/IT NOAEL from a subchronic toxicity study is 0.13 mg/kg/day (UF = 100).

h Water soluble bags are used as an engineering control. However, it should be noted that no registered products exist that are formulated as water soluble bags.

ST Short-term exposure

IT Intermediate-term exposure

NA Not Applicable.

## B. Residential Post application Exposures

There is the potential for residential consumers to be exposed to zinc pyrithione via use of impregnated textile products. Some examples of zinc omadine-containing products are provided in Table 1. In this exposure assessment, exposures were selected as reasonable high-end scenarios:

- Post application residential exposure due to body contact with carpets and clothing;
- Post application residential exposure due to hand-to-mouth contact with carpets; and,
- Post application toddler mouthing of clothing.

Residential consumers might be exposed daily to zinc omadine from multiple sources via dermal/oral contact with one or more zinc omadine-impregnated products found in/around the home. Note that residential consumer inhalation exposure was considered insignificant since the antimicrobial is generally contained within the matrix of the textile. In addition, zinc pyrithione has a low vapor pressure (i.e., $<1.87 \times 10^{-9}$ mm Hg at 25°C) and is, therefore, not likely to generate sufficient vapor to cause an inhalation concern to occupational and residential populations performing post application tasks, or occupying recently treated areas, or from bystander contact with treated articles. Therefore, post application inhalation exposures were not assessed.

Exposures from residential scenarios were not combined with dietary and water to estimate aggregate daily exposure potential for a given adult or child across exposure routes. Note that the Agency has determined in the zinc omadine ORE that certain existing residential scenarios should be aggregated together (D308705).

### 1. Leaching Studies

In a study by Arch Chemicals Corporation, *Measurement of Zinc Pyrithione Leached From Polyester Fabrics* (MRID 473115-02), the registrant measured migration of the additive zinc omadine from polyester fabric samples. One gram textile samples were soaked in 30 mL of artificial perspiration stimulant at ambient temperature and at 37°C (to simulate body temperature) in a 1L Erlenmeyer flask and agitated for 3 hours. After 3 hours, the sample was cooled at room temperature and leaching solution was decanted. The recovered concentration of zinc omadine was performed using high performance liquid chromatography (HPLC). The HPLC was calibrated with a zinc omadine concentration of 0.05 to1.0 µg/mL. Each fabric sample weighed approximately 1 gm. The limit of detection was 0.09 µg/g. The mean recovery of zinc omadine was 96- 113% at spiking levels ranging from 0.02 to 1 µg/mL.

There were two application methods: 1) fabric samples treated by padding process with 0.5% zinc omadine and 2) fabrics treated by dipping with concentrations of 0.5% and 1.0% zinc

omadine. The zinc omadine label (1258-840) which contains 95% a.i. indicates that the application rate is not to exceed 0.07% of this product to the treating solution and the application to apparel items is not to exceed 0.2% by dry weight of the fabrics to be treated. The results of this study indicate that the fabrics treated with zinc omadine by padding process leached the average of 7.0 to11 µg/g. The levels of zinc omadine leached from fabrics treated with zinc omadine by a textile dipping process, were under the limit of detection (<0.09 µg/g). Note the dipping and padding process for textiles was not described in this study.

In another study by Arch Chemicals Corporation, *"Evaluation of Zinc Omadine in the Treatment of Textiles (MRID 473115-01)"*, Arch Chemicals, Inc. presented some calculations to convert the detected amount of zinc omadine in the leaching study to convert into % leached. Arch Chemicals, Inc. found that for padding with 0.5% zinc pyrithione, the amount leached out was 11µg/g. For fabrics treated by dipping with concentrations of 0.5% and 1.0% zinc pyrithione, the amount leached out was under the limit of detection (<0.09 µg/g). To convert to % for the padding the amount at 11µg/g was converted to11 mg/kg. The 0.5% concentration was 5,000 ppm or 5,000 mg/kg. To figure the %, the leachate (11 mg/kg) was divided by the initial concentration (5,000 mg/kg) which yields 0.22% leaching rate. For dipping, the limit of detection (0.09 mg/kg) was divided by 10,000 ppm or 10,000 mg/kg for a rate of 0.0009%.

There are limitations with both the "*Measurement of Zinc Pyrithione Leached From Polyester Fabrics* (MRID 473115-02)" and *"Evaluation of Zinc Omadine in the Treatment of Textiles (MRID 473115-01)"* studies. The Agency can not use the results of these studies to use in this risk assessment at this time based on the following limitations:

- The study (MIRD 47311502) did not provide the actual µg /gm in dry weight for the zinc pyrithione impregnated textile samples (both from "padding" and "dipping" treatments) before extraction. EPA would need the total amount of zinc pyrithione active ingredient found impregnated in the textile to obtain the percentage of active ingredient that was actually leached out. In MRID 473115-01, the researchers calculated the % leach rate by presenting just the theoretical wet weight of the treating solution (e.g. 0.5% or 5,000 ppm) and not the actual dry weight µg/gm of active ingredient recovered from impregnated in the fabric textile. The Agency believes that the actual leach rate % may have underestimated the actual amount.

- The Agency recommends that Arch Chemicals, Inc extract the active ingredient from the textile test samples to determine the dry weight µg/gm of active ingredient. The Agency is concerned that the application processes in the study may be different then the treatment processes mentioned on the proposed labels. The dry weight % should be identical to that reported on the label.

• MIRD 47311502 reported that fabrics were treated with zinc pyrithione by both "padding" and "dipping" application methods. The proposed textile uses stated on the labels (EPA Reg #'s 1258-840 and 1258-841) indicate that fabric is to be treated by "dipping" and "exhaustion" methods. The reviewer has not been able to determine if "padding" and "exhaustion" application methods presented in the study are similar to the application method in the proposed labels. Arch Chemicals Inc should submit written explanation of the "exhaustion" and "padding" and "dipping" treatment processes. The Agency is concerned that the application processes in the study may be different then the treatment processes mentioned on the proposed labels.

• An exact description of the textile "dipping and padding" processes would have been useful and how they relate "dipping" and "exhaustion" application methods should be submitted to the EPA to in order to use this study.

• The concentration (MIRD 47311502) reported in the study was 0.5% zinc pyrithione for "padding" and 0.5% and 1.0% zinc pyrithione for "dipping." The zinc omadine® wettable powder label (EPA Reg # 1258-840) which contains 95% zinc pyrithione as active ingredient should not exceed 0.07% of this product to the treatment solution (0.2% by dry weight). The zinc omadine® liquid (EPA Reg # 1258-841) which contains 48% zinc pyrithione as active ingredient should not exceed 0.14% of this product to the treatment solution (0.4% by dry weight).Although it appears that the percentage of active ingredient used in 47311502 was higher (0.5 and 1%) than the reported % on the label, it was not entirely clear whether the percentage was % active ingredient in the solution and it was not clear why the study reviewers did not use the maximum active ingredient reported in the label and whether the preservative was applied to the textile in the same way that was suggested on the label for both liquid and wettable powder formulations.

**2. Clothing Exposure**

*a. Dermal Exposure*

There is the potential for dermal exposure to adults and children from wearing clothing, sleeping in bedding, and contacting home furnishings impregnated with an antimicrobial product. The exposure from clothing will be assumed to represent the high-end exposure short-term exposure. A post application assessment assuming no laundering was conducted as a conservative measure (i.e., the effect on dislodgeable residues over time during washing is not quantifiable). It should be noted that not all articles of clothing are treated with zinc pyrithione products are worn on a continuous basis. In general, it is believed that most treated textiles used in a residential setting will result in exposures occurring over a short-term time duration (1 to 30 days) because residents are assumed to be exposed to treated textiles with varying active ingredients, not exclusively zinc pyrithione treated textiles. However, both the short- and intermediate-term exposure durations are assessed for the clothing scenarios as this scenario is

being used to represent all textile uses that may occur over time (e.g., bedding and home furnishings) where daily exposure may occur. Long-term duration was not assessed because dislodgeable zinc pyrithione residues are not expected to be available continuously.

Potential doses are calculated as follows:

$$PDD = \frac{CxSA}{BW}$$

Where:

| | | |
|---|---|---|
| PDD | = | potential (absorbed) daily dose (mg/kg/day) ; |
| SA | = | surface area of skin covered by clothing ($cm^2$); and |
| BW | = | body weight (kg). |

And

$$C = DxWF1xWF2xLR$$

Where:

| | | |
|---|---|---|
| C | = | Concentration on surface of clothing ($mg/cm^2$) |
| D | = | Density or fabric cloth weight to surface area ($mg/cm^2$); |
| WF1 | = | Weight fraction of commercial product in fabric (% in product); |
| WF2 | = | Weight fraction of zinc omadine in commercial product (% a.i.); and |
| LR | = | Leach rate (represents the amount % transferred). |

- The textile density is 10 $mg/cm^2$ based on the density of mixed cotton and synthetics (HERA 2003).
- The median surface area (SA) of clothing contacting skin for a 3-year-old toddler is 5,670 $cm^2$ (total surface area minus the head) (USEPA, 1997a). For adults, the median surface area is 16,900 $cm^2$ (total surface area minus the head) (USEPA, 1997a).
- The fraction leached per day (FL) is assumed to be 5%. The % is divided by 100 to make it a fraction. Since there are no clothing specific residue transfer factors available at this time a default of 5% was used. The 5% residue transfer factor is based on the default residue transfer from treated carpets and a confirmatory study is needed to support this assumption (US EPA 2001).
- The product contains 95% a.i. (WF2) and is used in fabrics at a dry rate of 0.2% (WF1) product by weight of material thus, the % a.i. in fabrics are 95% x 0.2% = 0.19 % Reg No. 1258-840).
- Toddlers (3 years old) body weight (BW) is 15 kg. This is the mean of the median values for male and female toddlers (USEPA, 1997b). For adults, a female body weight of 60 kg has been assumed.

The selected NOAEL is divided by the PDD to calculate MOE. A dermal NOAEL of 15

mg/kg/day is used for adults and children. The calculated dermal MOEs (**56** for adult females and **42** for toddlers) for textiles are less than the target MOE of 100, and therefore do not exceed the Agency's level of concern. The results of this assessment are presented in Table 4.

*b. Incidental Ingestion from Mouthing*

There is the potential for incidental oral exposure to children from mouthing textiles impregnated with antimicrobials.

Potential doses are calculated as follows:

$$PDD = \frac{CxSAxSE}{BW}$$

Where:

| | | |
|---|---|---|
| PDD | = | Potential Daily Dose (mg/kg/day); |
| C | = | Concentration on clothing (mg a.i. /$cm^2$); |
| SE | = | Saliva extraction Efficiency (unit less fraction); |
| SA | = | Surface Area mouthed ($cm^2$/day); |
| BW | = | Body Weight (kg). |

And

$$C = DxWF1xWF2xLR$$

Where:

| | | |
|---|---|---|
| C | = | Concentration on surface of clothing (mg/$cm^2$) |
| D | = | Density of textile (mg /$cm^2$); |
| WF1 | = | Weight fraction of commercial product in fabric (% in product); |
| WF2 | = | Weight fraction of zinc omadine in commercial product (% a.i.); and |
| LR | = | Leach rate (unit less). |

- The density of textiles is 10 mg/$cm^2$ based on the density of mixed cotton and synthetics (HERA 2003).
- The surface area of textiles mouthed by children is 100 $cm^2$/day (professional judgment).
- The saliva extraction efficiency is 50% (USEPA, 2001)
- The product contains 95% a.i. and is used in fabrics at a dry rate of 0.2% product by weight of material thus, the % a.i. in fabrics are 95% x 0.2% = 0.19 % Reg No. 1258-840).
- The fraction leached per day (FL) is assumed to be 5%. The % is divided by 100 to make it a fraction. Since there are no clothing specific residue transfer factors available at this time a default of 5% was used. The 5% residue transfer factor is based on the default

residue transfer from treated carpets and a confirmatory study is needed to support this assumption (US EPA 2001).

The selected NOAEL is divided by the PDD to calculate MOE. An oral NOAEL of 0.75 mg/kg/day is used for children. The calculated incidental oral MOE (1,180 for toddlers) for textiles using the padding leach rate are greater than the target MOE of 100, and therefore do not exceed the Agency's level of concern. The results of this assessment are presented in Table 4.

**3. Carpet Exposure**

*a. Dermal Exposure*

There is the potential for dermal exposure to adults and children from wearing clothing treated with an antimicrobial product. To determine child short- and intermediate-term exposure to zinc omadine in carpet, the following equation was used:

$$PDD = \frac{D \times CF_1 \times SA \times WF_1 \times WF_2 \times LR \times CF_2}{BW}$$

Where:

| | | |
|---|---|---|
| PDD | = | Potential daily dose (mg/kg/day) |
| D | = | Carpet weight Density (oz/yd2) |
| CF1 | = | Conversion factor (1.196x10-4 yd2/cm2) |
| SA | = | Body surface area contacting carpet (cm2/day) |
| WF1 | = | Weight fraction of commercial product in carpet (% dry weight) |
| WF2 | = | Weight fraction of zinc omadine in commercial product (% a.i.) |
| LR | = | Leach rate transferred from carpet to skin (unitless) |
| CF2 | = | Conversion factor (28,350 mg/oz) |
| BW | = | Body weight (kg) |

Assumptions

- The carpet density (D) is 36 oz/yd$^2$ based on a standard assumption (USAF 2003).;
- A conversion factor (CF1) of 1.196x10-4 yd2/cm2 is used to convert square yards to square centimeters;
- A conversion factor (CF2) of 28,350 mg/oz is used to convert mg to oz;
- The fraction leached per day (FL) is assumed to be 5%. The 5% residue transfer factor is based on the default residue transfer from treated carpets and a confirmatory study is needed to support this assumption (US EPA 2001).
- The % is divided by 100 to make it a fraction.
- The product contains 95% a.i. by weight (WF2) and is used in fabrics at a dry rate of 0.2% (WF1) product by weight of material thus, the % a.i. in fabrics are 95% x 0.2% =

0.19 % Reg No. 1258-840);

- For short- and intermediate-term exposures, it was assumed that the skin area contacting the carpet was 6570 cm2 (median SA of a toddler, US EPA 1997b); and
- The body weight of a child was assumed to be 15 kg (US EPA 1997b).

The selected NOAEL is divided by the PDD to calculate MOE. A dermal NOAEL of 15 mg/kg/day was selected for children. The Agency calculated dermal MOEs based on surrogate leach rates to represent carpets. Using the surrogate leach rate of 5%, the MOE was **3**. The results were less then the target MOE of 100, this scenario exceeds the Agency's level of concern. The results of this assessment are presented in Table 4.

*b. Hand-to-Mouth Incidental Ingestion*

There is the potential for hand-to-mouth incidental oral exposure to children from carpets.

Potential doses are calculated as follows:

$$PDD = \frac{D \times CF_1 \times SA \times WF_1 \times WF_2 \times LR \times CF_2 \times CF_2 \times TE \times SE \times FQ}{BW}$$

Where:

| | | |
|---|---|---|
| PDD | = | Potential daily dose (mg/kg/day) |
| D | = | Carpet weight density (oz/yd$^2$) |
| CF1 | = | Conversion factor (1.196x10-4 yd$^2$/cm$^2$) |
| SA | = | Surface area mouthed (20 cm$^2$/day) |
| WF1 | = | Weight fraction of commercial product in carpet (oz product/oz carpet) |
| WF2 | = | Weight fraction of zinc omadine in commercial product (% a.i.) |
| LR | = | Leach rate transferred from carpet to skin (unit less) |
| CF2 | = | Conversion factor (28,350 mg/oz) |
| ET | = | Exposure time (8 hr/day) |
| CF3 | = | Conversion factor (1 day/24 hr) |
| BW | = | Body weight (kg) |
| TE | = | Transfer efficiency object-to-hand (unit less fraction) |
| SE | = | Saliva extraction efficiency hand-to-mouth (unit less fraction); |
| FQ | = | Frequency of mouthing the hands (events per hour) (20 times/hr) |

- The carpet density (D) is 36 oz/yd$^2$ based on a standard assumption (USAF 2003);
- The product contains 95% a.i. by weight (WF2) and is used in fabrics at a dry rate of 0.2% (WF1) product by weight of material thus, the % a.i. in fabrics are 95% x 0.2% = 0.19 % Reg No. 1258-840);

- The fraction leached per day (FL) is assumed to be 5%. The % is divided by 100 to make it a fraction. The 5% residue transfer factor is based on the default residue transfer from treated carpets and a confirmatory study is needed to support this assumption (USEPA 2001).
- The surface area (SA) of carpet mouthed by children is 20 $cm^2$/day (USEPA, 1997b);
- The saliva extraction (SE) efficiency is 50% (USEPA, 2001);
- The transfer efficiency (TE) is 50% (USEPA, 2001); and,
- Toddlers (3 years old) are used to represent the 1 to 6 year old age group. For three-year olds, the median body weigh (BW) is 15 kg (USEPA, 1997a).

The selected NOAEL is divided by the PDD to calculate MOE. A developmental NOAEL of 0.75 mg/kg/day was selected for children. The calculated incidental oral MOE for toddlers was different depending on the leach rate. Using the leach rate of 5%, the MOE was **15**. The MOEs was less than the target MOE of 100, and therefore exceeds the Agency's level of concern. The results of this assessment are presented in Table 4.

## V. AGGREGATE SHORT AND INTERMEDIATE RISKS

In order for a pesticide registration to continue, it must be shown "that there is reasonable certainty that no harm will result from aggregate exposure to pesticide chemical residue, including all anticipated dietary exposures and other exposures for which there are reliable information." Aggregate exposure is the total exposure to a single chemical (or its residues) that may occur from dietary (i.e., food and drinking water), residential, and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal, and inhalation). However, this assessment only addresses non-dietary residential aggregate exposures and risks.

In performing aggregate exposure and risk assessments, the Office of Pesticide Programs has published guidance outlining the necessary steps to perform such assessments (General Principles for Performing Aggregate Exposure and Risk Assessments, November 28, 2001; available at http://www.epa.gov/pesticides/trac/science/aggregate.pdf). Steps for deciding whether to perform aggregate exposure and risk assessments are listed, which include: identification of toxicological endpoints for each exposure route and duration; identification of potential exposures for each pathway (food, water, and/or residential); reconciliation of durations and pathways of exposure with durations and pathways of health effects; determination of which possible residential exposure scenarios are likely to occur together within a given time frame; determination of magnitude and duration of exposure for all exposure combinations; determination of the appropriate technique (deterministic or probabilistic) for exposure assessment; and determination of the appropriate risk metric to estimate aggregate risk. The use patterns of the products and probability of co-occurrence were taken into account for the selection of which scenarios to incorporate into the aggregate assessment.

Short- and intermediate-term aggregate exposures and risks were assessed for adults and children that could be exposed to zinc pyrithione residues from the use of products in residential

environments. In the case of this assessment, the Agency aggregated both short- and intermediate risks together because both the exposure data and the toxicological endpoints were identical.

In the case of zinc omadine, the occupational dermal (developmental effects) and inhalation (decrease activity and lung weights) toxicity endpoints are different so occupational handler uses cannot be aggregated together and an assessment is not required for occupational post application. For residential, a handler assessment was not required.

For residential post application, both incidental ingestion and dermal are all based on developmental toxicity studies. However, the toxicological effects and NOAELs are different so the dermal and incidental oral cannot be aggregated together. For incidental oral, the toxicological effect is increased salivation in maternal rats with a NOAEL of 0.75 mg/kg/day. For dermal, the toxicological effect is increased number of dames with limited uses of hindlimbs, shuffling gait, decreased weight, decreased body weight gain and decreased body weight gain and food consumption. The reported NOAEL was 15 mg/kg/day. The following list summarize all of the resident post-application scenarios:

Adult zinc pyrithione exposures sources:
- Wearing treated clothing; and,
- Dermal contact to impregnated residues on treated carpets.

Child zinc pyrithione exposures sources:
- Wearing treated clothing;
- Dermal contact to impregnated residues on treated carpets
- Hand-to-mouth exposures to treated clothing; and,
- Hand-to-mouth exposures to impregnated residues on treated carpets.

Note that in Table 4, both dermal and incidental ingestion MOEs for adults and children were less than the target MOE of 100, and therefore exceeds the Agency's level of concern. Therefore, the Agency did not aggregate the exposure in this assessment since the individual scenarios already exceed the Agency's level of concern.

## VI. CONCLUSION

The Agency disagrees with the method for calculating the leach rate percentage in MRID 473115-01 and decided not to use the results of this leaching study. The registrant measured the leach rate of fabric by padding by measuring the concentration leached (11.1 ppm) divided by the concentration of the solution applied (5000 ppm) to get a percentage (0.22%). EPA would need the total amount of zinc pyrithione active ingredient found impregnated in the textile to obtain the percentage of active ingredient that was actually leached out. In MRID 473115-01, the researchers calculated the % leach rate by presenting just the theoretical wet weight of the treating solution (e.g. 0.5% or 5,000 ppm) and not the actual dry weight µg/gm of active

ingredient recovered from impregnated in the fabric textile. The Agency would recommend that the registrant completely extract the zinc pyrithione from the dry fabric to see the actual amount of zinc pyrithione originally impregnated in the sample.

It was necessary for the Agency to calculate risks on Table 4 using the surrogate leach rate of 5%. For new uses of textiles (clothing and carpet) represented in this assessment, the calculated dermal MOEs are less than the target MOE of 100, and therefore exceeds the Agency's level of concern. In addition, there are concerns with hand-to-mouth ingestion exposure for carpets. The incidental oral MOE for children is 15.

The residential uses that were aggregated in this assessment include the residential post application exposure from carpet and clothing uses. It is likely that these scenarios could co-occur. The Agency aggregated using a default 5% residue transfer factor since an acceptable study was not available confirmatory data will be required. There are some uncertainties and limitations with this approach (see section below). It is likely that the flux rate used in this assessment overestimates the risk. However, the Agency believes that this is assessment uses the best data available at this time and provides a conservative estimate of the risk. Since both the dermal and incidental oral MOEs exceeded the Agency's level of concern it was not necessary to aggregate the exposures.

**Table 4: Summary of New Short-, and Intermediate- Term Residential Post application Exposure and Risks**

| Scenario | Receptor | Use | PDR[a] (mg/kg/day) | Dermal MOE[b] Target MOE ≥100 | Oral MOE[b] Target MOE ≥100 |
|---|---|---|---|---|---|
| Dermal Contact to Clothing | Adults | Textiles | 0.27 | **56** | NA |
| | Children | | 0.36 | **42** | NA |
| Non-Dietary Ingestion Hand-to-Mouth Clothing | Children | Textiles | 0.00063 | NA | 1,180 |
| Dermal Contact to Carpets | Adults | Carpets | 1.3 | **12** | NA |
| | Children | | 5.1 | **3** | |
| Non-Dietary Ingestion Hand-to-Mouth | Children | Carpets | 5.15E-2 | NA | **15** |

NA = Not applicable.

[a] PDR calculations for each scenario above are outlined in the text. Most conservative leach rates used.

[b] MOE=NOAEL/PDR. Dermal NOAEL is 15 mg/kg/day; Oral NOAEL general population and children is 0.75 mg/kg/day.

## VII. UNCERTAINTIES AND LIMITATIONS

- The Agency disagrees with the method for calculating the leach rate percentage. The registrant measured the leach rate of fabric by padding by measuring the concentration leached (11.1 ppm) divided by the concentration of the solution applied (5000 ppm) to get a percentage (0.22%). EPA would need the total amount of zinc pyrithione active ingredient found impregnated in the textile to obtain the percentage of active ingredient that was actually leached out. In MRID 473115-01, the researchers calculated the % leach rate by presenting just the theoretical wet weight of the treating solution (e.g. 0.5% or 5,000 ppm) and not the actual dry weight µg/gm of active ingredient recovered from impregnated in the fabric textile. The Agency would recommend that the registrant completely extract the zinc pyrithione from the dry fabric to see the actual amount of zinc pyrithione originally impregnated in the sample.
- The registrant submitted a study where two leach rates were reported 0.0009% fabric treated by dipping and 0.22% fabric treated by padding (MRID 47311501). For the exposure routes of concern (textiles and carpets) it was not clear which leaching data set was most appropriate for textile and carpet fabrics and which treatment technique is most common in the textile industry?
- The registrant submitted leach studies for textiles using manufacturing techniques of padding and dipping. The registrant did not explain these processes. The Agency could not be certain whether all textiles in the study are treated with the same technologies (dipping or padding) as they are commonly manufactured and in the same rates as they are currently represented on the label. The label indicated that an exhaustion process is also used to impregnate the fabric of clothes. Is this process related to the padding process?
- The existing leaching study was limited in documentation (3 pg) and details, and also limited in number of replicates (8).
- For handling, the Agency assumed that 10,000 lbs of zinc omadine product was used per day based on common Agency assumptions.
- The default residue transfer factors for carpeting (5%), and clothing (5%) may not be representative of the actual transfer values. It is uncertain to what degree the residue is actually being transferred because zinc pyrithione is impregnated in the matrix and it is unknown whether or not the matrix is actually binding the zinc pyrithione thereby reducing the potential transfer.

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