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

APR - 3 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Human Exposure Considerations:**
Occupational/Residential Non-Dietary Exposure Assessment
in Support of Use Patterns for Time-Limited Registration of
Antimicrobial AlphaSan® RC 5000 **(EPA Reg. No. 11631-2).**

TO: Dennis Edwards, Chief
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DP Barcode: D286526 (S623914)

Pesticide Chemical/No.: Silver sodium hydrogen zirconium phosphate/ 072560

Registrant: Milliken Chemical

EPA Reg. No.: 11631-2

MRID No.: N/A

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Action Requested:

The Antimicrobials Division (AD), Product Management Team 33, requested that the Risk Assessment and Science Support Branch (RASSB) conduct a non-dietary exposure/risk assessment in support of registered use patterns for the time-limited registration of ***Antimicrobial AlphaSan ® RC 5000.*** This non-dietary exposure review is separate from the dietary assessment conducted in support of the amendment package submitted September 23, 2002 by ChemReg International, LLC as the agent for the registrant, Milliken Chemical. (The amendment package covered three ***Antimicrobial AlphaSan ®*** products and was submitted to meet Agency data requirements for additional toxicity studies to determine acceptability of continued registration of the indirect food contact/drinking water uses before the May 1, 2003 expiration of the time-limited registrations.)

Results Summary:

Potential occupational/residential (non-occupational) exposures were estimated for registered non-food contact uses of ***Antimicrobial AlphaSan ® RC 5000*** using "surrogate" data and Agency default assumptions in the absence of any chemical-specific exposure data. This "screening-level" assessment yielded acceptable margin of exposure (MOE) non-cancer risk estimates for both occupational and residential populations. The Agency generally is not concerned with a calculated MOE greater than or equal to the target MOE (i.e., level of concern). The Agency target MOE for this assessment is an MOE ≥ 100. The occupational assessment yielded a Dermal MOE of 301 for primary handlers and 260 for secondary handlers. The residential assessment yielded both Dermal and Incidental Oral MOEs in the E+5 thru E+6 range. **The results indicate that there is minimal potential for adverse exposure to Silver sodium hydrogen zirconium phosphate associated with the use of *Antimicrobial AlphaSan ® RC 5000* as a materials preservative.** These results are consistent with the low order of toxicity demonstrated in the animal studies conducted with this chemical.

BACKGROUND:

Antimicrobial AlphaSan ® RC 5000 is a technical source of the active ingredient Silver sodium hydrogen zirconium phosphate (99.9% a.i.), a synthetic inorganic polymer, and is registered as an antimicrobial powder for commercial use as a manufacturing-use product (MUP). It is designed to be incorporated as a preservative into various materials (plastics, films, fibers, polymeric materials and ceramics) used to manufacture food/non-food contact finished goods (i.e., fabricated treated article end products) prone to microbial deterioration. ***Antimicrobial AlphaSan ® RC 5000*** may be incorporated into finished articles at levels typically up to 2% by weight.

Antimicrobial AlphaSan ® RC 5000 was conditionally registered, May 22, 2000 under time-limited registration pending submission to the Agency of additional toxicity studies to meet FIFRA guideline requirements. At time of initial registration review, the Agency did not conduct a comprehensive exposure assessment for the proposed materials preservative use patterns since the chemical was considered relatively non-toxic. As cited in the human exposure review done by S. Mostaghimi, dated April 4, 2000 (D262981/D262982):

"According to a memorandum by Dr. Tim McMahon to Dennis Edwards dated April 4, 2000 (D262972) 'In general, the agency is not concerned with setting endpoints for risk assessment when systemic effect levels in experimental studies are above the limit dose, as this is an indication of the relative non-toxicity of the chemical in question. As the active ingredient in this case (3.8% silver sodium hydrogen zirconium phosphate) displays such behavior, a non-dietary risk assessment is not necessary at this time for the proposed uses of the product'.

As indicated in the memorandum by Dr. McMahon this chemical is relatively non-toxic and no tox end point can be identified. Also because this product is impregnated into the materials during the manufacturing process, the exposure will be minimal. Therefore, an occupational/residential exposure assessment for this chemical is not necessary at this time."

On behalf of the registrant, ChemReg International, LLC submitted September 23, 2002 additional toxicity studies for Agency review under the current amendment. The subchronic, dog feeding study (MRID 45769401) identifies a NOAEL at 400 mg/kg/day based on mortality, food consumption and body weight effects at a higher dose level; the 2-generation reproduction study in rats (MRID 45769402) identifies a NOAEL at 5000 ppm in the diet (i.e., 400 mg/kg/day) based on reductions in food consumption, body/organ weights at a higher dose level with no effects on reproductive organs/performance at any dose tested. (See review by T. McMahon dated March 14, 2003 for D286393.)

Based on the submitted additional toxicity studies, a "screening-level" assessment was conducted for representative occupational/residential scenarios using the NOAEL of 400 mg/kg/day as the toxicological endpoint and a target margin of exposure (MOE) of 100.

HUMAN EXPOSURE CONSIDERATIONS:

Use Profile

Antimicrobial AlphaSan ® RC 5000 is an antimicrobial additive for use as a preservative in a variety of materials manufactured into both food and non-food contact products. The product is supplied as a 99.9% a.i. powder for incorporation into finished goods at levels typically not exceeding 2% by weight. (An exception is in the manufacture of coatings for the inside of fire system sprinkler pipes where levels can reach 5% by weight.) Specific to this non-dietary exposure review and as per the latest accepted labeling on file dated September 26, 2002, the pesticide may be incorporated into non-food contact media such as:

1) ***Plastics, Coatings, Films and Laminates***
(intended for fabricating commercial/residential consumer goods including appliances/equipment/building fixtures/furniture/plumbing components and related industrial goods/household goods),

2) ***Fibers***
(intended for fabricating household/commercial textiles including sheets/blankets/carpets/upholstery/clothing apparel/tents/awning/sail cloth),

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3) ***Adhesives and Sealants***
(intended for fabricating adhesives for wood/wood and plastic composites/ceramic tile/paper/cardboard/rubber/plastic/window glazing/grout/sealants for pipes/plumbing and packaging adhesives/appliance and construction sealants/insulating materials),

4) ***Miscellaneous Manufactured Products***
(intended for fabricating toilets/sinks/tiles/flooring/pipes/cat litter), and

5) ***Heating, Ventilation and Air Conditioning (HVAC)***
(intended for fabricating HVAC equipment/components/ materials such as air handlers/plenums/coils/fins/insulation/ducts/filters/heat exchangers etc...).

Antimicrobial AlphaSan ® RC 5000 (99.9% a.i.) is classified under Toxicity Category III based on the acute toxicity study for primary eye irritation. All other product toxicity studies for acute oral, acute dermal, acute inhalation and dermal irritation indicate a low order of toxicity (Toxicity Category IV) for Silver sodium hydrogen zirconium phosphate when tested at 3.8% a.i.. (See T. McMahon review dated January 22, 2001 for D270044.)

Product labeling cites "CAUTION" signal word and includes the following precautionary statements: " Causes moderate eye irritation. Harmful if absorbed through the skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling. Do not breath dust." FIFRA does not require personal protective equipment (PPE) labeling statements for Toxicity Category III products.

Occupational/Residential Non-Dietary Exposure

Based on the materials preservative use patterns, the Agency has identified the following representative occupational/residential exposure scenarios for assessment:

Primary Occupational Handlers of the pesticide concentrate during mixing/loading/applying operations:

- mixing/loading/applying ***Antimicrobial AlphaSan ® RC 5000*** using open pour methods during incorporation into slurries (as representative of maximum application rates of 2.0% for adhesives/sealants);

Secondary Occupational Handlers of treated end products for which the pesticide has been incorporated during manufacturing.

- Using adhesive/sealant end products containing ***Antimicrobial AlphaSan ® RC 5000*** in construction applications (as representative of treated end product containing preservative up to 2:0% by weight);

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Residential Postapplication contact with finished consumer goods (finished treated articles) for which the pesticide has been incorporated during manufacturing.

- Dermal contact with polymeric materials incorporated with ***Antimicrobial AlphaSan® RC 5000*** (as representative of consumer goods containing preservative up to 2.0% by weight) (Adult/Child);

- Non-Dietary Ingestion from Hand-to-Mouth contact with polymeric materials incorporated with ***Antimicrobial AlphaSan® RC 5000*** (as representative of consumer goods containing preservative up to 2.0% by weight) (Child); and

- Non-Dietary Ingestion from Object-to-Mouth contact (as representative of mouthing treated consumer goods containing ***Antimicrobial AlphaSan® RC 5000*** preservative up to 2.0% by weight) (Child).

Since engineering controls/closed systems for mixing/loading/application are not cited on the ***Antimicrobial AlphaSan® RC 5000*** registered labeling, it is assumed that in industrial settings open dispensing is most likely to occur as commercial handlers load the pesticide powder into vats of manufactured emulsions/slurries. 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 (MRID 42587501) were used for estimating dermal unit exposures for primary handlers. The CMA data for "Solid Pour", which covers powder formulations used for materials preservative applications, was selected as the most appropriate best-fit for the primary handler scenario.

In lieu of actual monitoring data for secondary handlers, surrogate data from *The Pesticide Handlers Exposure Database (PHED) Version 1.1, 1998* were used to develop estimates of exposure for workers applying adhesive/sealant products. The scenario assumes that an "implement" is used to spread the sealant onto tile surfaces during commercial installation of a ceramic tile floor (as the representative scenario). CMA data are unavailable for this type of application, yet PHED offers dermal unit exposure values for application by "paint brush" which was selected as the most appropriate best-fit for the secondary handler scenario.

Both primary and secondary handler scenarios were developed as representative of potential occupational exposures in industrial/commercial settings over short-term (1 day to 1 month), intermediate-term (1 to 6 months), and long-term (> 6 months) exposure durations.

Postapplication occupational exposures will not be assessed for either primary or secondary workers since the Agency lacks appropriate exposure data with which to assess risk. 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. Also, the use of anticipated industrial safety practices will minimize potential dermal exposures.

Residential postapplication 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

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object-to-mouth activity. The Agency's *Exposure Factors Handbook (U.S.EPA, 1997)* and *Standard Operating Procedures (SOPs) for Residential Exposure Assessments (U.S.EPA, 1997)* were used to derive inputs and equations for estimating potential doses.

Reviews on file with the Agency for ***Antimicrobial AlphaSan ® RC 5000*** include a review done by A. Najm Shamim, dated October 13, 1999 (D253514) of a Milliken Chemical company migration study "Determination of Potential Migration of Silver and Zirconium from Low Density Polyethylene into Food-Simulant Solvents" (MRID 445829-24). The study determined the potential maximum levels of chemical migration from the plastic polymer into food-simulating solvents (10% and 95% ethanol) under exaggerated conditions of use as 10 ppb for silver and 20 ppb for zirconium; a combined maximum migration of 30 ppb (0.03 ppm) for the silver zirconium compound. The migration data were used for estimating dislodgeable surface residues.

Silver sodium hydrogen zirconium phosphate, the active ingredient in ***Antimicrobial AlphaSan ® RC 5000*** is non-volatile and demonstrates low acute inhalation toxicity. It is anticipated that inhalation exposures during product use/postapplication will not pose adverse risk concerns. Therefore, an inhalation exposure assessment was not conducted.

Note that RASSB did not separately assess potential dermal/inhalation exposures attributed to the incorporation of the preservative into HVAC system media/materials. ***Antimicrobial AlphaSan ® RC 5000*** is incorporated into HVAC components during their manufacture; not applied to surfaces of existing "in-service" HVAC system media. In addition, dermal exposure is expected to be minimal since the treated components are enclosed within the HVAC system and surfaces are not readily accessible for dermal contact. As noted above, the compound is non-volatile and not anticipated to off-gas into the HVAC system during operation. The registrant has not provided any air monitoring data for use in an HVAC assessment, nor can an air saturation concentration be estimated due to the lack of vapor pressure.

Adult/Child Dermal Exposure to Polymeric Materials Incorporated with Preservative

The migration study "Determination of Potential Migration of Silver and Zirconium from Low Density Polyethylene into Food-Simulant Solvents" (MRID 445829-24) was used as "surrogate data" to predict the leach rate of pesticide from treated shoe inner soles (as the representative treated article for consumer contact). The assessment assumes that 2.0 percent (20,000 ppm) of the active ingredient is incorporated into polyethylene liners during manufacture. The MRID 445829-24 study indicates that 30 ppb (0.03 ppm or 0.000003%) of silver/zirconium complex leaches out of polyethylene in the presence of ethanol solvents. For this assessment, it is assumed that 0.03 ppm of preservative will leach out from the sole liner and be available for contact. This assessment conservatively assumes that 100 percent of the residues available on the surface of the soles are transferred to the skin. Both feet will be assumed to be exposed.

The Exposure Factors Handbook indicates that the 50th percentile surface area of feet is 1,310 cm^2 for adult males (U.S. EPA, 1997). Since only the soles of the feet are expected to contact the liners, one half of the surface area of the feet is assumed. The sole liners are expected to be 1 cm thick. The density of polyurethane is close to 1 g/cm^3. Thus, the mass of the sole liners (SL) are expected to be 655 gm for male feet. The body weights (BW) of adult males is 70 kg.

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For children, the surface area of the feet is 7.1 percent of the total surface area (U.S. EPA, 1997). The total mean surface area for male and female children ages 3 to 4 is 6,565 cm^2 (U.S. EPA, 1997). Therefore, the surface area of the feet is 466 cm^2. Since only the soles of the feet are expected to contact the sole liner, one half of the surface area of the feet is assumed to contact the sole liner. The sole liners are expected to be 1 cm thick. The density of polyurethane is close to 1 gm/cm^3. Thus, the mass of the sole liners (SL) is expected to be 233 gm. The body weight used for children (ages 1 to 6) is 15 kg.

The calculation of Potential Dose Rate (PDR) is as follows:

Potential dose rate (PDR) from dermal contact (mg/kg-day) = [SL x LR x AR x CF] / [BW]

SL = Mass of sole liner (gm)
LR = Leach rate. Fraction of preservative leaching out (i.e., 0.03 ppm/20,000 ppm)
AR = Application rate is 20,000 ppm. (20 mg ai/1,000 mg polymer) incorporated into sole liners
CF = Conversion factor is 1,000 mg/gm
BW = The body weight of males is 70 kg for men and 15 kg for children.

Non-Dietary Ingestion of Preservative from Toy-to-Mouth Contact

The non-dietary ingestion of preservative from Toy-to-Mouth contact uses "surrogate" exposure estimates from Dang (1997)[1] and migration data from MRID 445829-24. In order to predict the actual amount of active ingredient several assumptions were made:

- A polyethylene highchair sample with a surface area of 12.7 cm^2 weighs 1.3072 grams (i.e., 0.1 gm/cm^2) (Dang, 1997).
- The total surface area of the impregnated material was assumed to be 500 cm^2 (i.e., the surface area of an impregnated toy) (Dang, 1997).
- MRID 445829-24 estimates that out of 20,000 ppm of active ingredient incorporated into polyethylene, only 0.03 ppm leached out under ethanol extraction test conditions .

Using these assumptions, a polyethylene sample with a surface area of 500 cm^2 weighs 50 grams (0.1 gm/cm^2 x 500 cm^2) and contains 1000 mg (i.e. 2.0 % ai as 20,000 ppm) of active ingredient. MRID 445829-24 indicates that 0.03 ppm of the silver/zirconium complex leaches out of polyethylene. Therefore, approximately 0.00015% (0.03 ppm/20,000 ppm x 100) or 0.0015 mg ai (1000 mg ai x 0.00015%) may migrate to the surface of a 500 cm^2 toy. The value of 0.00075 mg ai is a conservative estimate of the contact rate available per event (CR). It is conservative because it (1) does not account for washing of the toy or depletion of the residue after each toy-to-mouth episode, (2) assumes that 50% of the available residue (i.e., 50% of 0.0015 mg ai = 0.00075 mg ai) is transferred and ingested (Dang, 1997), and (3) assumes that the amount accumulated for the

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1 Dang. 1997. Risk Analysis for Microban Additive "B" (Triclosan/Irgasan DP300) Treated Toys for Infants. Internal Memo from Winston Dang to Frank Sanders and William Jordan, Antimicrobials Division. Dated February 24, 1997.

duration of the migration study is the amount available for contact for the each event per day. The equation for calculation of potential dose rates is as follows:

Potential dose rate (PDR) (mg/kg/day) = (CR * FQ * ET) / BW

where:

CR = Contact Rate (mg ai/event). CR of 0.00075 mg ai/event.
FQ = Frequency (events/hr). FQ of 3.05 events/hr is assumed (Dang, 1997).
ET = Estimated Exposure Time (hr/day). ET of 2 hr/day (Dang, 1997).
BW = Body weight (kg). Body weight for infants (6 months to 1 ½ year) is assumed to be 10 kg.

Non-Dietary Ingestion of Preservative from Hand-to-Mouth Contact

The non-dietary ingestion of preservative from Hand-to-Mouth contact also uses "surrogate" exposure estimates from Dang, 1997 and data from (MRID 445829-24). In order to predict the actual amount of active ingredient, several assumptions were made. The assumptions used to evaluate the surface residues (SR) were similar to the Toy-to-Mouth contact rate (CR). Only the amount of residue available for contact of 0.00075 mg ai is divided by the surface area of the toy (i.e., 500 cm^2) to obtain a value of 1.5E-6 mg/cm^2.

Potential dose rate (PDR) (mg/kg/day) = (SR * SA * FQ * ET) / BW

where:

SR = Surface Residue (mg/cm^2). 1.5E-6 mg/cm^2
SA = Surface Area of the Infant's Hand (cm^2). SA of 336 cm^2 (Dang, 1997).
FQ = Frequency (events/hr). FQ of 3.05 events/hr is assumed (Dang, 1997).
ET = Estimated Exposure Time (hr/day). ET of 2 hr/day (Dang, 1997).
BW = Body weight (kg). Body weight for infants (6 months to 1 ½ year) is assumed to be 10 kg (U.S. EPA, 1997).

Table 1: OCCUPATIONAL APPLICATION EXPOSURE ASSESSMENT FOR *Antimicrobial AlphaSan ® RC 5000* ACTIVE INGREDIENT

Exposure Scenario	Operation	Dermal UE[a] (mg/lb ai)	lbs ai/day[b]	BW (kg)[c]	Daily Dermal Dose[d] (mg/kg/day)	Short-/Intermediate-/Long-Term (ST/IT/LT) Dermal MOE[e] Agency Target MOE ≥ 100
Primary Occupational Handlers						
Mixing/loading/applying *Antimicrobial AlphaSan ® RC 5000* using open pour methods during incorporation into slurries	Industrial open loading of powder concentrate at 2.0% max. use rate to formulate adhesives/sealants. Assumes 10,000 lbs of slurry produced per day. **No PPE worn over normal work clothing.**	0.466	200	70	1.33	301
Secondary Occupational Handlers						
Using adhesive/sealant end products containing *Antimicrobial AlphaSan ® RC 5000* in construction applications.	Worker using an adhesive/sealant (as the representative treated end product containing preservative up to 2% by weight) applied to surfaces in construction project (e.g., commercial ceramic tile floor installation). **No PPE worn over normal work clothing.** Assumes 30 lbs of adhesive/sealant product used/day in commercial application.	180	0.6	70	1.54	260

Table 1. Legend:

Dermal UE = Unit Exposure values for dermal exposures were derived from: *Primary Handlers* - CMA Study Data (MRID 42587501) Pour Solid (powder) data used for Primary Handlers. Data generated on workers wearing single layer of clothing and chemical resistant gloves using a preservative pesticide formulation. In addition, some monitored workers wore dust masks . No respirators used. CMA data represent single layer work clothing and no gloves/respirator. *Secondary Handlers* - PHED , Version 1.1, 1998 Paint Brush Data as surrogate for use of implement to spread adhesive/sealant onto tile surfaces (single layer work clothing; long-sleeved shirt, long pants; no gloves, no respirator worn). (Data for interior application via Paint Brush.).

Lbs ai/day were derived as follows: *Antimicrobial AlphaSan ® RC 5000* powder concentrate contains 99.9% active ingredient. Maximum quantities of product concentrate used per day were based on Agency default assumptions for industry estimates as follows: 10,000 pounds of adhesive/sealant slurries produced/day. Handlers of treated adhesive/sealant end products assumed to use 30 lbs of adhesive/sealant product/day in commercial application based on Agency default assumptions.

At the maximum use rate of 2.0% for adhesives/sealants manufacture, the amount of active ingredient handled for the slurries scenario is: 10,000 lbs/day x 0.999 (% a.i.) x 0.02 (% product applied as use rate) = 200 lbs ai/day; and for the adhesive/sealant scenario is: 30 lbs/day x 0.02 (% a.i. by weight in end product) = 0.6 lbs ai/day

Body Weight (kg): 70 kg (since no developmental effects seen in toxicological database for a.i.)

Daily Doses were calculated as follows: Daily Dermal Dose (mg/kg/day) = [(Dermal UE (mg/lb ai) x lbs ai/day / BW (kg)] Dermal absorption assumed to be 100% as conservative estimate for lack of dermal penetration data on the a.i..

MOEs were calculated as follows: ST/IT/LT Dermal MOE = NOAEL (mg/kg/day)/ Dermal Dose (mg/kg/day). Where the NOAEL from the 90-day feeding study is 400 mg/kg/day (UF = 100).

Table 2: RESIDENTIAL POSTAPPLICATION EXPOSURE ASSESSMENT FOR *Antimicrobial AlphaSan ® RC 5000* ACTIVE INGREDIENT

Exposure Scenario	Receptor	PDR[a] (mg/kg/day)	Short-/ Intermediate-/ Long-Term (ST/IT/LT) Dermal MOE[b] Agency Target MOE ≥ 100	Short-/ Intermediate-/ Long-Term (ST/IT/LT) Incidental Oral MOE[b] Agency Target MOE ≥ 100
Residential Postapplication				
Dermal contact with polymeric materials incorporated with *Antimicrobial AlphaSan ® RC 5000* (e.g., treated shoe inner soles as representative of consumer goods containing preservative up to 2.0% by weight)(Adult/Child).	Adult	2.8 E-4	1.4 E+6	NA
	Child	4.7 E-4	8.5 E+5	NA
Non-Dietary Ingestion from Hand-to-Mouth contact with polymeric materials incorporated with *Antimicrobial AlphaSan ® RC 5000* (toy as representative of consumer goods containing preservative up to 2.0% by weight) (Infant Child)	Infant Child	3.1E-4	NA	1.3 E+6
Non-Dietary Ingestion from Object-to-Mouth contact (toy as representative of mouthing treated consumer goods containing *Antimicrobial AlphaSan ® RC 5000* preservative up to 2.0% by weight) (Infant Child).	Infant Child	4.6 E-4	NA	8.7 E+5

ble 2. Legend:

PDR calculations for each scenario above are outlined in the text. Body Weight (kg): Adult = 70 kg (since no developmental effects seen in toxicological database for a.i.); Child = 15 kg; and Infant = 10 kg.

MOEs were calculated as follows: ST/IT/LT Dermal or Incidental Oral MOE = NOAEL (mg/kg/day)/ PDR (mg/kg/day). Where the NOAEL from the 90-day feeding study is 400 mg/kg/day (UF = 100).

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Chemical File
Circulation File