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

DEC 13 1999

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: 5-Chloro-2-(2,4-dichlorophenoxy)phenol (Triclosan): Request for dietary risk assessment.

EPA Identification Numbers:

P.C. Code: 054901 MRID's: N/A
DP Barcode:D257879 Submission: S565563

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Action Requested: Dietary risk assessment from use of the active ingredient Triclosan in ice-making equipment.

Background

The registrant (Microban Products Company) has applied for use of the active ingredient Triclosan for various water contacting products as they apply to ice-making equipment. The media into which the active ingredient is being proposed to be added are polyethylene, polystyrene, and vinyl plastisol, for components including the water pan, tubing, piping, and the guard to deflect ice. RASSB has been asked to provide a dietary risk assessment for this use of Triclosan.

It is noted that the assessment of dietary risk is for this use only, and does not apply to any other existing uses of Triclosan. Dietary risk from all uses of Triclosan that result in dietary exposure has not been formally assessed.

Hazard Identification

The following Toxicology data are available for Triclosan:

3) TOXICOLOGY DATA MATRIX FOR: TRICLOSAN

Guideline Number	Data Requirement	MRID Number (Accession No.)	Core Grade (Tox. Category)
870.1100	Acute Oral Toxicity	43206501; 43206901	acceptable (IV)
870.1200	Acute Dermal Toxicity	42306902	acceptable (III)
870.1300	Acute Inhalation Toxicity	42306902	acceptable (II)
870.2400	Primary Eye Irritation	N/A	acceptable ()
870.2500	Primary Dermal Irritation	42306903	acceptable ()
870.2600	Dermal Sensitization	41008909	non-sensitizer
870.3100	Subchronic Oral Toxicity-Mice	43022605	acceptable
870.3150	Subchronic Oral Toxicity -Dogs	00133232	acceptable
870.3250	Subchronic Dermal Toxicity -Rats	43328001	acceptable
870.3700	Developmental Toxicity in Rats	43817502; 43817503	acceptable
870.3700	Developmental Toxicity in Rabbits	43022607	acceptable
870.3800	2-Generation Reproduction Toxicity in Rats	40623701	acceptable
870.4300	Chronic Toxicity / Carcinogenicity in rats	42027906	acceptable
870.4200	Carcinogenicity in Mice	FDA review	acceptable

870.4100	Chronic Toxcity in Baboons	00133230; 00133231	
870.5265	Salmonella reverse mutation assay	44389705	acceptable (neg.)
870.5300	Gene mutations in mammalian cells in culture	44389704	acceptable (neg.)
870.5385	In vivo mammalian cytogenetics:bone marrow	44389711	unacceptable (neg.)

In addition to the above guideline Toxicology studies, several non-guideline studies were submitted to and reviewed by RASSB. These studies examined the possible mechanisms involved with toxicity of Triclosan to the liver among various species. These studies form part of the database for Triclosan but are not considered in the context of the current assessment.

Toxicology Endpoint Selection

On March 10, 1998, the Health Effects Division's Hazard Identification Assessment Review committee evaluated the toxicology data base of Triclosan and selected doses and endpoints for acute dietary as well as occupational and residential exposure risk assessments, re-assessed the Reference Dose (RfD) established for chronic dietary risk assessment, and addressed the sensitivity of infants and children as required by the Food Quality Protection Act (FQPA) of 1996. For purposes of the present risk assessment, the Committee's summary conclusions regarding endpoint selection are presented in this memorandum.

The doses and toxicological endpoints selected and Margins of Exposures for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOEL = 30	diarrhea 4-6 hours after dosing	Chronic Toxicity - Baboon
	UF = 100	**Acute RfD = 0.30 mg/kg/day**	
Chronic Dietary	NOEL= 30	diarrhea 4-6 hours after dosing; hematological changes at high dose	Chronic Toxicity - Baboon
	UF = 100	**RfD = 0.30 mg/kg/day**	
Short-Term (Dermal) [a]	NOEL = 30	Diarrhea observed 4-6 hours after dosing.	Chronic Toxicity - Baboon

Intermediate-Term (Dermal) [a]	NOEL = 30	clinical signs of toxicity (vomiting, failure to eat, and diarrhea)	Chronic Toxicity - Baboon
Long-Term (Dermal) [a]	NOEL = 30	clinical signs of toxicity (vomiting, failure to eat, and diarrhea)	Chronic Toxicity - Baboon
Inhalation (Any Time Period)	NOEL = 0.05 mg/L	Increased total leukocyte count and increased serum alkaline phosphatase	21-Day Inhalation-Rat

[a] = The use of a 50% dermal absorption rate is required since an oral NOAEL was selected for these risk assessments.

As noted above, the acute and chronic Reference Dose for dietary intake is 0.3 mg/kg/day. There are no special concerns for susceptibility of infants and children to dietary exposure, as Triclosan has demonstrated no developmental or reproductive toxicity to offpsring of parental animals administered the chemical in the diet or by oral gavage. Therefore, the FQPA safety factor is **reduced to 1x** for purposes of risk assessments involving infants and children.

In a memorandum from Robert Quick, Chemist, Antimicrobials Division, to Robert Brennis, Regulatory Management Brach II, Antimicrobials Division (barcode number D257880), estimated intake of Triclosan through its presence in ice was calculated for both infants and children as well as male and female adults, using conservative assumptions regarding intake (i.e. drinks contain 50% ice). Default body weights of 60kg for adult females, 70kg for adult males, 10kg for infants, and 15kg for children were used. Intake values of 1000L and 2000L for water were used for infants/children and adults, respectively. Based upon these assumptions, the following intake values for Triclosan were calculated:

Adults (70kg): 1.13×10^{-8} mg/kg/day
Adults (60kg): 1.32×10^{-8} mg/kg/day
Children (15kg): 2.65×10^{-8} mg/kg/day
Infants (10kg): 3.98×10^{-8} mg/kg/day

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Dietary risk is typically calculated as the percentage of the Reference Dose occupied by the dietary exposure. In this case, from ingestion of Triclosan-containing ice alone, percentages of the Reference Dose occupied for 70kg and 60kg adults are 0.0000037% and 0.000004% respectively. For infants and children, the percentages of the Reference Dose occupied are 0.000013% and 0.000008% respectively.

The percentages of the Reference Dose occupied by this use for the subpopulations examined indicate that, for this use, less than 0.1% of the Reference Dose is occupied for any given group. Using the criteria established in EPA's Threshold of Regulation policy document, the fact that less than 0.1% of the Reference Dose is occupied by this use may qualify this use under the TOR policy At the very least, it is concluded that the dietary risk posed from the use of Triclosan in components of ice-making equipment is well below the Agency's level of concern.

Conclusions

RASSB has provided an estimate of the dietary risk from ingestion of Triclosan from use in ice-making equipment components. Using conservative assumptions, it is clear that, as a percentage of the Reference Dose, the risk from ingestion of Triclosan resulting from this use is below the Agency's level of concern. In addition, provided that all relevant criteria regarding residues are met per the Agency's Threshold of Regulation Policy, this use of Triclosan may be exempt from the requirement of a tolerance or tolerance exemption.