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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Terbuthylazine

FROM: Charles Frick
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c frick 10/4/94

TO: Jay Ellenberger, Chief
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THRU: Debra Edwards, Ph.D, Branch Chief
Chemical Coordination Branch
Health Effects Division (7509C)
Debra Edwards 10/13/94
and
Richard Schmitt, Ph.D, Acting Director
Health Effects Division (7509C)
Richard D Schmitt 10/13/94

Attached is the Human Health Assessment for the Terbuthylazine Reregistration Document.

Terbuthylazine is labeled for aquatic non-food industrial, commercial, and residential uses. Industrial and commercial uses are for ornamental fountains, ponds, and for water cooling systems, including evaporative condensers, heat-exchange water systems, and cooling towers. Residential uses are for ornamental ponds/aquaria. There are no food or feed uses.

Terbuthylazine was classified as to its carcinogenic potential as a "Group D Carcinogen" (inadequate evidence to determine carcinogenicity in humans) by the Health Effects Division Carcinogenicity Peer Review Committee (CPRC).

Terbuthylazine was classified as a Toxicity Category III for oral, dermal, and eye toxicity. The RFD Committee recommended an RFD for this chemical based on a no-observable effect level (NOEL) of 0.35 mg/kg/day based on a decrease in body weight, food consumption observed in male and female rats at 1.6 mg/kg/day. An uncertainty factor of 100 was used to account for the inter-species extrapolation and intra-species variability. An additional factor of 10 was used to compensate for the lack of chronic toxicity data in a non-rodent species and data on reproductive toxicity potential of this chemical. On this basis,

the RFD was calculated to be 0.00035 mg/kg/day.

Based upon a review of the toxicology database for terbuthylazine, toxicology endpoints and dose levels of concern have been identified for use in risk assessments corresponding to the categories listed below:

1. Short-term occupational exposure (1-7 days): The endpoint for short term occupational or residential exposure is the LEL from the 28-day rabbit dermal toxicity study based on clinical signs in males and females (5.0 mg/kg/day). The endpoint of 5.0 mg/kg/day is considered appropriate because toxicity (clinical signs) was minimal at that dose during the first 7 days of treatment.

2. Intermediate-term occupational or residential exposure (1 week to several months): The endpoint is 1.5 mg/kg/day (systemic toxicity) in the rabbit developmental study. This is considered to be the most appropriate endpoint based on the available data for short-term repeated exposure.

Based on available information the greatest potential for health risk is from cooling tower and commercial ornamental fountain uses as with the open-pouring application method; handlers have a calculated MOE of <100 for short and intermediate term exposure. HED recommends that the open pouring application method be disallowed. Terbuthylazine should be loaded/applied through a closed system, either using the metering-pump application method or another type of closed system. Persons using closed systems may wear a long-sleeved shirt, long pants, shoes, socks, and chemical-resistant gloves instead of any PPE required by the pesticide labeling for handlers. A chemical-resistant apron must be worn in case of a leak, spill, or other exposure to the concentrate. All other exposure scenario have calculated MOEs greater than 100.

The toxicological database for terbuthylazine is adequate and will support reregistration eligibility for current nonfood/nonfeed uses.

cc. W. Dang OREB
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HUMAN HEALTH ASSESSMENT

HAZARD ASSESSMENT

Acute and Subchronic Toxicity

The table below summarizes the results of acute toxicity studies on terbuthylazine and the toxicity categories for the different routes of administration:

ACUTE TOXICITY DATA FOR TERBUTHYLAZINE

TEST	RESULT	CATEGORY
Oral LD50 in rat (MRID 41907702)	LD_{50} 1000 - 1590 mg/kg (males); 1503 mg/kg (females)	III
4 hr inhalation LC50 in rat (MRID 41603305)	LC_{50} >5.3 mg/L	III
Dermal LD50 in rat (MRID 41907703)	LD_{50} >2000 mg/kg	III
Eye irritation in rabbit (MRID 41907704)	Mildly-to-moderately irritating	III
Dermal irritation in rabbit (MRID 41907705)	Slightly irritating	III
Dermal sensitization in Guinea pig (MRID 41907706)	Not a sensitizer	N/A

Treatment-related clinical signs reported following acute oral or inhalation exposure included piloerection, dyspnea, reduced locomotor activity and/or diarrhea.

Slightly different results were obtained in two other acute toxicity studies. In a second acute oral toxicity study (MRID 41603304) in rats, an LD_{50} of >2000 mg/kg was determined (Tox. Category III). In a second ocular irritation study in rabbits (MRID 41603306), terbuthylazine caused minimal eye irritation (Tox. Category IV). The more sensitive studies (listed in the above table) are used for regulatory purposes.

Subchronic oral toxicity: In a 28-day oral toxicity study (MRID 00161104), terbuthylazine (technical, 99.8% a.i.) was administered to male and female RAI (SPF) rats in the diet at

concentrations of 0, 25, 75, 250 or 750 ppm (corresponding to doses of 0, 2.4, 7.7, 26.6 or 68.7 mg/kg/day in males and 0, 2.3, 8.1, 27.9 or 63.4 mg/kg/day in females).

At 25 ppm (2.3 mg/kg/day) and higher, dose-related, statistically significant decreases in mean body weight compared to controls were observed in males (at termination body weight gain was 12, 18, 22 and 35% less than controls, low to high dose, respectively). Relative thymic weight was reduced (-17%, increasing to -36% at 750 ppm) and slight decrease in absolute kidney weight was also observed (-4%, increasing to -25% at 750 ppm). In females, absolute liver weights and liver:brain weights were decreased at 25 ppm and higher (about -20%, to about -30% at 750 ppm). At 250 and 750 ppm, mean body weights of females were statistically significantly reduced in females (-25 and -41%, respectively). The LEL is 25 ppm (2.3 mg/kg/day) based on decreased body weight, relative thymic weight and absolute kidney weight in males and possibly decreased liver weight in females. The NOEL is less than 25 ppm (lowest dose tested).

Subchronic dermal toxicity: In a repeated dose dermal toxicity study (MRIDs 40514802 and 42059804), terbuthylazine (technical, 97.1% a.i.) was applied daily to the intact skin of 5 male and 5 female New Zealand White rabbits for 29 consecutive days. Test material was moistened with distilled water and 0 (distilled water), 0.05, 0.5 or 500 mg/kg/day were applied for 6 hrs/day under occlusive wrap.

At 500 mg/kg/day, reduced body weight gain was observed in males (-36% of controls at Day 28) and females (-39%). Food consumption was also decreased (-76% and -89% of controls during week 1 in males and females; between -11% to -54% of controls at other times). Reduced fecal output was observed sporadically among both sexes. Mortality occurred in one female, preceded by cachexia, hypothermia and muscle wasting. The LEL of 500 mg/kg/day is based on decreased body weight gain and food consumption in males and females and, in one female, hypothermia, cachexia and mortality. The NOEL is 0.5 mg/kg/day.

The following dermal toxicity study was classified as Core-supplementary due to several study deficiencies (NOEL not determined, less than 10 animals/dose and some information lacking in study report). However,there was sufficient information for use in conjunction with other toxicity data for risk assessment purposes.

In a 28-day dermal toxicity study (MRID 00151622), male and female New Zealand White rabbits were dermally exposed to terbuthylazine (technical, 99.8% a.i.) at 0, 5, 50 or 500 mg/kg/day (10 animals/sex at 500 mg/kg/day; (5 animals/sex at all other dose levels). Doses were administered in an aqueous vehicle of 0.1% polysorbate/0.5% carboxymethylcellulose. Animals

were exposed for 6 hrs/day, 5 days/week. Five high dose animals/sex were sacrificed at 29 days and 5 after a 2-week recovery period.

At 5.0 mg/kg/day, several clinical signs classified as minimal were observed among males and females. During the first 7 days of the study, clinical signs were observed only in 1 male (dyspnea, piloerection, sedation) and 1 female (curved body position). Thereafter, all animals developed dyspnea, piloerection, sedation and curved body posture, a few developed tremors (1 male, 2 females) and 1 female had ataxia. Dermal irritation was also observed in treated animals. At 50 and 500 mg/kg/day, clinical signs occurred earlier and with greater severity (classified as moderate). At 500 mg/kg/day, body weight gain was decreased compared to controls (87% less, males and 73% less, females) and food consumption was decreased during weeks 1 and 2 (42% - 71% less than controls, males; 23% - 37%, females). The LEL of 5.0 mg/kg/day is based on clinical signs in males and females. The NOEL is less than 5.0 mg/kg/day.

Chronic Toxicity/Carcinogenicity

Mouse: In a 2-year chronic feeding/carcinogenicity study (MRID 00156487), terbuthylazine (technical, 98% a.i.) was administered in the diet to 50/sex/dose Tif:MAGF (SPF) mice at dose levels of 0, 30, 150 or 750 ppm (males - 0, 3.28, 16.99 or 86.76 mg/kg/day; females - 0, 3.22, 16.66 or 88.54 mg/kg/day).

Percent body weight gain of males in the 750 ppm group was decreased by approximately 10%, while in females it decreased by approximately 23% throughout most of the study. Food consumption in males at 750 ppm was decreased by approximately 20% throughout most of the study. The LEL for systemic toxicity is 750 ppm is based on decreased body weight in females and a possible decrease in food consumption in males. The NOEL for systemic toxicity is 150 ppm. There was no evidence that administration of terbuthylazine was associated with an increase in tumors.

Rat: In a 2 year chronic feeding/carcinogenicity study (MRID 00156486), terbuthylazine (technical, 96.8% a.i.) was administered for 24 months to a total of 80/sex/dose Tif:RAIF(SPF) rats at dose levels of 0, 30, 150 or 750 ppm (males - 0, 1.24, 6.97 or 41.47 mg/kg/day; females 0, 1.37, 7.81 or 52.80 mg/kg/day). Twenty sex/dose of these were sacrificed at 24 months and 10/sex/dose at 12 months. The remaining animals received terbuthylazine for 24 months and were then placed on untreated diet until terminal sacrifice at weeks 112 (males) or 122 (females).

At 30 ppm and above, decreased body weight gain was observed in males (10%, 28% and 49% less than controls at week 54, low to

high dose) and females (12%, 32% and 47% at week 54, low to high dose). At 30 ppm and above, food consumption was decreased in males (9%, 14% and 25% at 54 weeks) while in females only at 150 ppm and above (10% at 54 weeks). At 150 ppm and above in females, BUN and urinary specific gravity were increased while urinary volume and pH were decreased. These changes were noted in males at 750 ppm only. At 750 ppm, there were increased lesions observed in males compared to controls, including macroscopic hepatic cysts, Leydig cell nodular hyperplasia of the testes (27% vs 9%, controls) and increases in benign interstitial cell tumors of the testes (13% vs. 4%, controls) and in females, including macro- and microscopic hepatic cysts and mammary gland carcinomas (18% vs. 5%, controls). The LEL for systemic toxicity is 30 ppm (1.24-1.37 mg/kg/day) based on decreased body weight gain in males and females and food consumption in males. The NOEL is less than 30 ppm. Terbuthylazine was associated with increased incidence of testicular interstitial cell tumors in males and mammary gland carcinomas in females, but only at a dose at which excessive systemic toxicity was also observed. The HED Carcinogenicity Peer Review committee considered the systemic toxicity observed at 750 ppm to be excessive (exceeding the maximum tolerated dose or MTD) and the slight increases in tumor incidence to be of uncertain relevance to human cancer risk assessment (see "Carcinogenicity Classification", below).

In a second 2-year chronic feeding/carcinogenicity study designed to determine a NOEL for chronic systemic toxicity (MRID 00157342), terbuthylazine (technical, 98% a.i.) was administered to 80/sex/dose Tif:RAIF(SPF) rats at dose levels of 0, 6 or 30 ppm (males - 0, 0.35 or 1.6 mg/kg/day; females - 0, 0.36 or 1.6 mg/kg/day). Animals fed for 98 weeks were placed on diets lacking the test material until final sacrifice at week 118 (males) and 121 weeks (females).

At 30 ppm there were decreases in percent body weight gain in males (7% less than controls) and females (12% less) as well as decreases in food consumption in males (6% less than controls) and females (11% less). The LEL for systemic toxicity is 30 ppm based on transient decreases in body weight and food consumption consistent with another study. The NOEL for systemic toxicity is 6 ppm. Terbuthylazine administration was not associated with an increase in tumors at the doses tested.

Developmental Toxicity

Rabbit: In a rabbit developmental toxicity study (MRID 00130744), female New Zealand White rabbits were dosed by gavage from days 7 through 19 of gestation with terbuthylazine (technical, 98.5% a.i.) in 1% methylcellulose at 0, 0.5, 1.5 or 4.5 mg/kg/day. Animals were sacrificed on day 29 of gestation.

No signs of maternal toxicity were observed at any dose tested

(in a preliminary study, body weight loss was observed at 12.5 mg/kg/day but not at 5 mg/kg/day). The maternal toxicity LEL is greater than 4.5 mg/kg/day. The maternal toxicity NOEL is equal to or greater than 4.5 mg/kg/day.

No signs of developmental toxicity were observed at any dose tested. The LEL for developmental toxicity is greater than 4.5 mg/kg/day. The NOEL for developmental toxicity is equal to or greater than 1.5 mg/kg/day. Although a LEL was not established, this study is considered adequate for regulatory purposes since (1) the data indicates that the rabbit is not more sensitive than the rat for developmental toxicity (rat NOEL = 5.0 mg/kg/day) and (2) the rabbit preliminary study indicated that maternal toxicity was observed at 12.5 mg/kg/day.

Rat: In a rat developmental toxicity study (MRID 41962701), female Tif:RAI (SPF) rats were administered 0, 1, 5 or 30 mg/kg/day terbuthylazine (technical, 96.4% a.i.) by gavage in an aqueous 3% corn starch vehicle (10 ml/kg) on days 6 through 15 of gestation, inclusive. Animals were sacrificed on Day 19 of gestation.

Maternal toxicity was observed at 30 mg/kg/day as significantly reduced body weight gain (60% less than controls) during the treatment period compared to controls and food intake was also reduced (-18%). The maternal toxicity LEL is 30 mg/kg/day based on decreased body weight gain and food intake. The maternal toxicity NOEL is 5 mg/kg/day.

Developmental toxicity was also observed at 30 mg/kg/day as dose-related increased incidence of absent ossification of the posterior phalanx of anterior digit 2 (30% litter incidence vs 10%, controls). The developmental toxicity LEL is 30 mg/kg/day based on absent ossification in anterior digit 2. The developmental toxicity NOEL is 5 mg/kg/day.

Reproductive Toxicity

Acceptable data on reproductive toxicity is not available to the Agency at this time. A 2-generation reproduction study in rat is not required to support reregistration of terbuthylazine unless food uses are added.

Mutagenicity

Terbuthylazine was negative for reverse gene mutation in Salmonella typhimurium strains in reverse gene mutation assays when tested with or without metabolic activation up to limits of solubility (5 mg/ml) in two independently conducted studies (MRIDs 00108817 and 00140816; MRID 41634001).

In a mouse L5178T/TK+/- assay terbuthylazine did not cause

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increased mutation frequency with or without metabolic activation when tested up to 1 mg/ml (MRID 00151618).

In a mouse micronucleus assay, terburthylazine did not cause increased micronuclei formation in bone marrow of mice following administration to mice up to the limit dose of 5000 mg/kg (MRIDs 41418102 and 42059805).

Terbuthylazine did not induce unscheduled DNA repair in cultured rat hepatocytes at test concentrations up to 125 μg/ml or 1000 μg/ml in two independently performed studies (MRIDs 41391801 and 42059806; MRID 00151619). Terbuthylazine was also negative when tested for unscheduled DNA repair at concentrations of up to 125 μg/ml in cultured human fibroblasts (MRID 00151620).

Metabolism

Although a guideline metabolism study has not been submitted, adequate information is available from two published metabolism studies to provide a general characterization of metabolism of terbuthylazine in rats. These studies have not been formally reviewed. Metabolism of terbuthylazine in rats is similar to other chloro-s-triazine herbicides. The major routes of metabolism are hydrolysis of the chlorine moiety and mono or didealkylation. Hydroxylation of one or both of the dealkylated NH_2 groups may also occur (MRID 00055672).

In a rat metabolism study (MRID 00038018), ^{14}C-terbuthylazine (3.6 mg) was administered orally to Wistar rats. Terbuthylazine was rapidly (50% excreted by 16-17 hrs) and completely metabolized and did not accumulate in tissues. Radioactivity was excreted equally in urine and feces in males, but in females about 2/3 of the radiolabel was excreted in the urine. Urine and feces contained up to 25 and 15 identified metabolites, respectively, most of which were polar. Degradation of the triazine ring did not occur. Ammeline and ammelide, 2 dechlorinated and dealkylated/hydroxylated metabolites common to all triazines, were identified in low amounts in the feces.

Carcinogenicity Classification

On May 25, 1994 (Peer Review Document dated August 24, 1994), the HED Carcinogenicity Peer Review Committee classified terbuthylazine as a Group D Carcinogen (inadequate evidence to determine carcinogenicity in humans). The incidence of benign interstitial tumors in testes of male rats and of mammary gland carcinoma in female rats was increased, but the increase was only observed at a dose at which excessive toxicity was observed (750 ppm). The classification was assigned because although terbuthylazine is structurally related to other s-triazines that induce similar types of tumors, tumors were only observed at a

dose that exceeded the maximum tolerated dose (MTD) and were only seen in one species.

Chronic exposure - Reference Dose (RfD): On April 7, 1994, the HED RfD/Peer Review Committee recommended establishing an RfD of 0.00035 mg/kg/day for terbuthylazine. This was based on a NOEL of 0.35 mg/kg/day from the chronic toxicity study in rats, where effects on body weight, food consumption were observed in males and females at 1.6 mg/kg/day. An uncertainty factor of 100 was used to account for inter- and intra-species variability, with an additional factor of 10 to compensate for lack of non-rodent chronic toxicity data and reproductive toxicity data. The RfD has not yet been reviewed by the Agency RfD.

EXPOSURE ASSESSMENT

Occupational and Residential Exposure

Terbuthylazine is a microbicide/microbiostat (slime-forming fungi and bacteria) formulated as a flowable concentrate.

Terbuthylazine is labeled for aquatic non-food industrial, commercial, and residential uses. Industrial and commercial uses are for ornamental fountains, ponds, and for water cooling systems, including evaporative condensers, heat-exchange water systems, and cooling towers. Residential uses are for ornamental ponds/aquaria. Applications are made as continuous feed or intermittent slug treatments.

An occupational and/or residential exposure data assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to mixers, loaders, or applicators during use or to persons entering treated sites after application is complete. HED has determined that an exposure assessment is required for terbuthylazine, since it triggers the toxicological criteria and that the normal use-patterns identified for terbuthylazine products potentially expose persons associated with its use.

The Agency has identified potential exposure to loaders and applicators during commercial and industrial applications of terbuthylazine. The Agency also has identified potential post-application exposure to persons cleaning or maintaining water cooling towers and to persons, especially children, wading or swimming in commercial or residential fountains or ornamental ponds.

Mixer/Loader/Applicator (Handler) Exposure:

Requirements for mixer/loader/applicator (i.e., handler) exposure study are addressed by Subdivision U of the Pesticide Assessment Guidelines. Mixer/loader/applicator (M/L/A) exposure data for terbuthylazine were not required during Phase IV of the reregistration process, since no toxicological criteria had been triggered at that time. However, toxicological data submitted to support reregistration indicate that short term exposures to terbuthylazine may cause health effects, and therefore, an occupational and/or residential exposure assessment is warranted.

No terbuthylazine specific M/L/A exposure data were available for the exposure assessment. However, terbuthylazine is an antimicrobial and the Agency issued in March 4, 1987, a data call-in notice for subchronic and chronic toxicological data for antimicrobial pesticide active ingredients. The Agency sought to use data submitted in response to the data call-in to complete this exposure assessment. That data, "Chemical Manufacturers Association Antimicrobial Exposure Assessment Study," has been evaluated by HED and found to meet the requirements of Subdivision U of the Pesticide Assessment Guidelines and to be appropriate for use in estimating human exposure to antimicrobial. Since FMC was not an original participant in the CMA study, use of that study to support reregistration of terbuthylazine requires data compensation issues to be resolved before the Terbuthylazine RED is released by EPA.

Exposure assessments of terbuthylazine were done for industrial water cooling tower systems, and commercial fountains, and homeowner ornamental fountain uses (e.g., Trade name such as Belclene 329, 44.7% a.i.) for control of algae in recirculating water cooling towers and decorative/ornamental fountains.It is assumed the quantity of active ingredient used in ornamental fountain is less than one-tenth of industrial site based on smaller volume of heated water.

I. Open-Pouring Application Method

Belclene 329 is applied at the point in the system where there is good mixing such as in the cooling tower sump near the recirculating pump or near the fountain recirculatory pump. 8 fluid ounces of Belclene 329 (44.7% a.i.) is applied into 10,000 gallon of water in the system (0.8 fluid ounces for 1,000 gallon of water for ornamental fountain, this dosage is equivalent to 3 ppm of a.i.). Assuming one gallon of Belclene 329 is equivalent to 11 pounds, a total amount of product equal to 0.31 lb of a.i. is added into the system each time (or 0.031 lb of a.i. to

ornamental fountain).

OPEN POURING LIQUID				
Setting	MCS* (ug/lb ai)	lb ai/used	BW** (kg)	Daily Exposure (ug/kg/d)
Cooling Tower & Commercial Ornamental Fountain	27130	0.31	60	140.17
Non-Commercial & Homeowner Ornamental Fountain	27130	0.031	60	14.02

* MCS = Maximum Credible Sum was derived from CMA Study.
** BW = Body Weight

Daily Exposure (ug/kg/day) = (MCS X lb ai/used) / BW=140
ug/kg/day = 0.14 mg/kg/day exposure to commercial applicators
or
0.0142 mg/kg/day exposure to homeowner users

II. Metering-Pump Application Method

METERING-PUMP LIQUID				
Setting	MCS* (ug/lb ai)	lb ai/used	BW** (kg)	Daily Exposure (ug/kg/d)
Cooling Tower & Commercial Fountain	930	0.31	60	4.81
Non-Commercial & Homeowner Ornamental Fountain	930	0.031	60	0.48

* MCS = Maximum Credible Sum was derived from CMA Study.
** BW = Body Weight

Daily Exposure (ug/kg/day) = (MCS X lb ai/used) / BW = 4.81
ug/kg/day = 0.00481mg/kg/day exposure to commercial applicators
or
0.000481 mg/kg/d exposure to homeowner users

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Post-Application Exposure:

Post-application exposure study requirements are addressed by Subdivision K of the Pesticide Assessment Guidelines. Based on the existing use patterns of terbuthylazine, post-application exposure criteria are not met for requesting post-application exposure data. Because of the use patterns and the dilution factors in the water cooling tower systems and ornamental fountains, post-application exposure will be minimal and data are not required.

RISK CHARACTERIZATION

Toxicological Endpoints

Short-term occupational exposure (1 - 7 days): The endpoint for short-term occupational or residential exposure risk assessment is the LEL (5.0 mg/kg/day; LDT) from the 28-day rabbit dermal toxicity study (MRID 00151622; NOEL was not determined in this study). The endpoint of 5.0 mg/kg/day is considered appropriate because toxicity (clinical signs) was minimal at that dose during the first 7 days of treatment (1 male and 1 - 2 females affected; dyspnea, piloerection, sedation and/or curved body posture observed). This endpoint is further supported by the NOELs of developmental studies (gavage) in rabbit (4.5 mg/kg/day; LEL not determined) and rat (5 mg/kg/day; LEL = 30 mg/kg/day).

Intermediate-term occupational or residential exposure (1 week-several months): The endpoint for intermediate term occupational or residential exposure risk assessment is 1.5 mg/kg/day (mid-dose in the rabbit developmental study) and is based on systemic toxicity observed at 5 mg/kg/day in the 28-day rabbit dermal toxicity study (clinical signs). Although not a study NOEL, it is considered to be the most appropriate endpoint, based on consideration of available short-term repeated exposure studies (two 28-day rabbit dermal toxicity studies, rat 28-day gavage toxicity study, rabbit and rat developmental toxicity studies). Although no toxicity was observed in the rabbit developmental toxicity study up to 4.5 mg/kg/day or at 5 mg/kg/day in the rat developmental toxicity study, toxicity was observed in a rabbit dermal study at 5 mg/kg/day, and in the rabbit gavage studies at 2.3 mg/kg/day. A NOEL of 0.5 mg/kg/day was established for rabbit dermal toxicity, but no intermediate doses were tested between 0.5 and 5.0 mg/kg/day. The rabbit developmental study mid dose (1.5 mg/kg/day) was therefore considered a more realistic endpoint for risk assessment.

OCCUPATIONAL/RESIDENTIAL RISK

HED has a concern for systemic toxicity. Because handlers may be at risk for toxic effects from exposure to terbuthylazine, margins of exposure (MOE) are calculated by this equation:

$$MOE = \frac{\text{Toxic endpoint (mg/kg/day)}}{\text{Daily exposure (mg/kg/day)}}$$

Based on the endpoint for short-term occupational or residential exposure (5.0 mg/kg/day) and the endpoint for intermediate term occupational or residential exposure (1.5 mg/kg/day) and assuming 100% dermal absorption the Margin of Exposure (MOE) are calculated.

1. Open Pouring Application Method

Commercial	
short term	= 5.0 (mg/kg/day) / 0.14 (mg/kg/day)
	= 36
intermediate term	= 1.5 (mg/kg/day) / 0.14 (mg/kg/day)
	= 11
Non-commercial	
short term	= 5.0 (mg/kg/day) / 0.014 (mg/kg/day)
	= 360
intermediate term	= 1.5 (mg/kg/day) / 0.014 (mg/kg/day)
	= 110

2. Metering - pump

Commercial	
short term	= 5.0 (mg/kg/day) / 0.0048 (mg/kg/day)
	= 1000
intermediate term	= 1.5 (mg/kg/day) / 0.0048 (mg/kg/day)
	= 310
Non-commercial	
short term	= 5.0 (mg/kg/day) / 0.00048 (mg/kg/day)
	= >10,000
intermediate term	= 1.5 (mg/kg/day) / 0.00048 (mg/kg/day
	= 3000

Post-Application Exposure:

Because of the use patterns and the dilution factors in the water

cooling tower systems and ornamental fountains, risk from post-application exposure is expected to be minimal.

Restricted Entry Interval:

To HED's knowledge, at this time there are no registered uses of terbuthylazine within the scope of the Worker Protection Standard for Agricultural Pesticides, i.e., no uses registered for use in the production of food, feed, fiber, ornamental, turf, or tree crops (even though the worker may clean water tower after a period of time). Therefore, there is no existing reentry or restricted-entry interval assigned to this active ingredient through WPS. Based on the assessment that the potential for post-application exposure to workers entering treated sites is minimal for the currently registered (non-WPS) uses, HED recommends that no restricted-entry interval or other restriction on entry following application be established at this time. HED notes a restricted-entry interval should be established if uses within the scope of the Worker Protection Standard are registered in the future.

Personal Protective Equipment (PPE) Requirements:

1). OCCUPATIONAL USES

WPS Uses: To HEDs knowledge, at this time terbuthylazine has no registered uses within the scope of the Worker Protection Standard for Agricultural Pesticides (WPS). If uses within the scope of the WPS are registered in the future, the definitive personal protective equipment required for such uses should be based on the acute toxicity for the end-use product as established through PR Notice 93-7 or more recent Agency guidance. However, the minimum PPE requirement for any end-use product, regardless of its acute toxicity, should be a long-sleeved shirt, long pants, shoes, socks, and chemical-resistant gloves. Closed mixing/loading systems should be considered, instead of allowing open pouring application methods.

NonWPS Occupational Uses at Commercial or Industrial Sites: The exposure assessment for mixers/loaders/applicators participating in the application of terbuthylazine in water cooling towers and commercial ornamental fountains indicated that the potential exposure resulting from the open pouring application method was unacceptable. The potential exposure resulting from the metering-pump application method was acceptable. HED recommends that the open pouring application method be disallowed. Terbuthylazine should be loaded/applied through a closed system,

either using the metering-pump application method or another type of closed system. Persons using closed systems may wear a long-sleeved shirt, long pants, shoes, socks, and chemical-resistant gloves instead of any PPE required by the pesticide labeling for handlers. A chemical-resistant apron must be immediately available during loading and application and must be worn in case of a leak, spill, or other exposure to the concentrate.

NonWPS Occupational Uses at Residential Sites: The exposure assessment for mixers/loaders/applicators participating in the application of terbuthylazine at residential sites (non-commercial ornamental pools and fountains) indicated that the potential exposure resulting from the either the metering pump or open pouring application method is acceptable, based on the lower quantity of chemical used (i.e., one-tenth volume of water treated). However, the minimum PPE for professionals (non-homeowners) at residential sites who mix, load, or apply terbuthylazine using the open pouring application method is long-sleeved shirt, long pants, shoes, socks, and chemical-resistant gloves.

2). HOMEOWNER USES

The potential exposure to homeowners resulting from either the metering pump or open pouring application method was judged as acceptable based on the same reason of less quantity of chemical used. However, the recommended PPE for homeowners who mix, load, or apply terbuthylazine using the open pouring application method is long-sleeved shirt, long pants, shoes, socks, and chemical-resistant gloves.

REFERENCE

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