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

11/4/83

003689

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Richard Mountfort, PM #23
Registration Division (TS-767)

THRU: Robert B. Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769)

11/4/83

SUBJECT: Simazine Registration Standard

Submission of the Toxicology Branch evaluation of Simazine toxicity data consists of:

1. Reviews of previously unreviewed studies.

2. Data Evaluation Reports for each relevant toxicity study.

3. "One-Liners" for the Data Base.

4. Data Summary, a bibliography indicating the toxicological data gaps and measures taken to fill them.

5. Policy discussion and tolerance assessment.

Toxicology Chapter

Acute Testing:

There are no available acute studies on the technical grade of the active ingredient. Acute studies submitted in MRID #00023965 were previously reviewed and Core classified by C. Frick (memo, 9/20/77 and TOX Doc. #001892). Simazine is a chlorotriazine herbicide and algaecide which has low toxicity from acute exposure.

81-1 Oral LD_{50}

The oral administration of Princep 80W to male and female rats produced no deaths at a dosage level as high as 15,380 mg/kg BW (TOX Doc. #001892). After 14 days of observation necropsy did not reveal any gross pathological lesions related to simazine. The LD_{50} is greater than 15,380 mg/kg BW. The data are sufficient to place simazine in toxicity category IV and are adequate for registration requirements.

81-2 Dermal LD_{50}

Simazine 80W was in contact with the skin of male and female rabbits for 24 hr. at dosage levels of 4.6, 6.8, and 10.2 gm/kg BW. No deaths occurred but extreme paralysis of the hindquarters, moderate tremors and convulsions were observed in the high dose group. Paralysis persisted throughout the 14-day observation period (MRID #0002395). Dermal toxicity results place simazine in category III and satisfy this registration requirement.

81-3 Inhalation LC_{50}

No data are available for review and, therefore, presents a data gap for inhalation toxicity.

81-4 Skin Irritation

A dose of 500 mg of Simazine 80W on abraded and intact skin sites of rabbits was slightly irritating at 72 hours (MRID #00023965). Results of this study place simazine in toxicity category IV and are adequate for registration requirement.

81-5 Eye Irritation

Exactly 50 mg of undiluted Simazine 80W was instilled into the conjunctival sac of the right eye of each of 5 test rabbits. Moderate irritation which was observed at 72 hours was reversible in 7 days (MRID #00023965). No corneal opacity was observed. Study data adequately place simazine in toxicity category III and satisfy registration requirements.

Subchronic Testing

82-2 21-Day Dermal

Study Type: 21-Day Subacute Dermal Toxicity in Rabbits.

MRID Number: 00057567

Sponsor: Ciba-Geigy Corp.

Contracting Lab: Bio-Resarch Laboratories, Ltd., Canada
Project No. 12017 Dated: 1/14/80

Test Material: Simazine Technical, 97.6% purity

Methods and Experimental Design:

New Zealand White rabbits from Canadian Breeding Farms and Laboratories were individually housed in cages under temperature-controlled conditions and acclimatized for two weeks. Eighty rabbits were equally divided into 4 test groups of 10 males and 10 females to receive Simazine Technical at doses of 0, 10, 100 and 1000 mg/kg. All animals were shaved 24 hours prior to initial testing and at necessary intervals thereafter. In addition, the skin of 5 rabbits/sex/dose were abraded and again once each week. All animals were weighed once prior to the initial application and twice weekly thereafter with dosing volume adjusted to the most recent body weight. Test material was weighed out in appropriate volumes on each day of dosing, slightly moistened with physiological saline and topically applied to intact and abraded skin sites with occlusive wrapping (10% body surface area). The control group was administered physiological saline concurrently. Applications were maintained for a period of six hours at each dosing after which the impervious wrap was removed and the skin wiped to remove any residual test material. Each animal received applications 5 days a week for a total of 15 applications over a period of 21 days. Viability and toxicity checks were made once each morning and late afternoon. Scoring for erythema and/or edema according to the technique of Draize was made daily. Estimates of food consumption were made twice weekly during the study.

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Blood samples for biochemical and hematological analyses were withdrawn on days 0 and 21. The following were performed on each blood sample:

1. Complete blood count consisting of hemoglobin, hematocrit, WBC with differential, RBC, platelet and reticulocyte count, and

2. Analyses for BUN, glucose, alkaline phosphatase activity, S.G.P.T., S.G.O.T., calcium, potassium, lactic dehydrogenase, direct and total bilirubin, total cholesterol, total protein, albumin, globulin and A/G ratio.

On day 21 of the study each rabbit was sacrificed and immediately subjected to a complete gross necropsy. In addition, the liver, kidneys, heart, gonads, thyroid (with parathyroid), adrenals, and pituitary were examined and weighed.

Histopathological examination was performed on multiple sections of treated and untreated skin, on any gross lesion present (along with normal contiguous tissue), on representative samples of liver, kidney, brain (3 levels, from cerebellum, cerebrum and pons), heart, pituitary, thyroid with parathyroid, adrenals and gonads.

Results:

Dermal application of simazine technical to abraded and intact skin sites did not appear to produce any dose-related systemic toxicity in rabbits. Nonspecific intermittent episodes of lacrimation and pulmonary congestion occurred in control and treated groups. One high dose female died on day 11 of the study and gross necropsy revealed generalized congestion in most visceral organs.

Slight erythema was seen on the intact skin of one high dose male during the first seven days of the study. One low dose female exhibited very slight erythema on 3 nonsuccessive days on intact skin. Signs of erythema and/or edema were absent in all other rabbits throughout the study. Ulcerative dermatitis which was localized at abraded skin test sites occurred in 2 mid dose males and 1 high dose female.

Incidental differences occurred in both pre-treatment and post-treatment hematology and blood chemistry analyses. No significant differences were revealed between test groups. Miscellaneous subclinical lesions were observed at necrospy in control and test groups which were unrelated to simazine dosage.

Conclusion:

Fifteen dermal applications of technical simazine over 21 days at doses up to 1 g/kg produced no systemic toxicity nor any dose-realted alterations of the skin. Ulcerative dermatitis observed in 3/80 rabbits was most likely due to technical handling. NOEL > 1000 mg/kg

Classification: Core-guidelines

This study satisfies the registration requirement.

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83-1 Chronic Testing
Chronic Toxicity - Rodent

Study Type: Two-Year Dietary Feeding Study - Albino Rats

MRID Numbers: 00037752, 00025441, 00025442, 00042793 and 00080626.

Sponsor: Geigy Agricultural Chemicals

Contracting Lab: Hazleton Laboraties, Date: 1/15/60

Test Material: Simazine 50W, a wettable powder containing 49.9% active compound.

Experimental Design:

Weanling male and female albino rats of the Charles River Strain were assigned in groups of 30 per sex to the following test material concentration groups: 0 (control), 1.0, 10.0 and 100 ppm. Rats in the control group were fed the basal laboratory diet, Purina Laboratory Chow. Rats in the test groups were fed the basal laboratory diet containing the appropriate amount of test material on a weight/weight basis. All dosages were expressed as 100% of the active ingredient. Water and feed were offered ad libitum to these rats which were housed individually in wire mesh cages. Individual body weights and food consumption were recorded weekly.

At the initiation of the study, 5 rats of each sex were chosen at random from the control and each test group to be sacrificed after 26 weeks of feeding. Similar groups of 5 rats of each sex were chosen at random for sacrifice at 52 weeks of feeding. After 26 weeks and one year, respectively, of feeding Simazin 50W, survivors of these selected groups were sacrificed. Gross necropsies were performed on each animal and the following tissues were preserved for histological examination: brain, thyroid, lung, heart, liver, spleen, pancreas, kidney, adrenal, stomach, small and large intestines, gonads and bone marrow. Prior to sacrifice urine samples from 3 rats of each sex from each selected group were collected, pooled from each sex separately, and submitted for analysis for sugar, protein, and bile pigment, and for the determination of pH, specific gravity, and gross and microscopic appearance.

Microhematocrit and differential leukocyte determinations were performed on blood from all the animals sacrificed and enough additional animals to make a total of 5 males and 5 females from each group. The weights of liver, kidneys, and adrenals of all animals and of the testes of all males sacrificied at 26 and 52 weeks were recorded, and organ-to-body-weight ratios were determined for those rats sacrificed at 26 weeks.

After completion of 104 experimental weeks, all surviving control and test rats were sacrificed and necropsies were performed. The following tissues from each animal were preserved in 10% Formalin: brain, pituitary, thyroid, heart, lungs, liver, spleen, kidneys, adrenals, small and large intestine, stomach, pancreas, bladder, gonads, skeletal muscle, peripheral nerve, bone and bone marrow (sternum and rib junction). Microhematocrits and differential leukocyte counts were performed on 5 rats of each sex from the control and each test group. Urinalysis, consisting of sugar, protein, bile pigments, pH and specific gravity determinations, appearance, and microscopic examination of the sediment were performed on pooled samples from representative rats of each sex in each group.

From each rat in control and high dose groups, the following tissues were examined microscopically: thyroid, heart, lungs, liver, kidneys, adrenals, spleen, stomach, small and large intestines, pancreas, gonads, and bone marrow. The remaining tissues from these rats, and from rats in low- and mid-dose groups were held for possible future histological study. The weights of liver, kidneys and adrenals of all animals sacrificed and of the testes of all males sacrificed were recorded, and organ-to-body-weight ratios were determined.

Gross necropsies were performed on the rats which died during the course of the study, and representative tissues were preserved in 10% Formalin for possible future histological study.

The criteria chosen for statistical analysis were survival at 26, 52 and 104 weeks; body weight gains from 0-52 weeks; total food consumption from 0-13 weeks, from 39 to 52 weeks, and from 91 to 104 weeks; and terminal body weights, organ weights and organ-to-body weight ratios for those animals sacrificed at 26 and 104 weeks.

Survival was analyzed by the Chi-square method at the 95% probability level. Before conducting the F-test, the variances were tested for homogeneity by Bartlett's method. If, upon completion of the F-test, a significant F-value was obtained, the significantly different groups were determined by Scheffe's test.

Results:

No differences in general physical appearance, behavior, clinical signs and symptoms were observed among control and treated groups of animals of either sex. Respiratory involvement was the most common syndrome seen in all groups and was unrelated to the dietary feeding of Simazine 50W. Chorea, ataxia and "spinning" were observed sporadically in a few control and test rats which usually had middle or inner ear infections.

Food consumption was similar in control and test groups of both sexes throughout the 104 week period. Females, however, consumed a greater amount of food than males in terms of g/Kg body weight. Therefore, compound dosages (mg/kg/day) for each female test group were higher than that of comparable male test groups. There was a steady decrease in compound dosages in male and female test groups during the first 32 weeks, a period of high growth rate; compound dosages leveled off thereafter.

No meaningful differences in mean body weights were observed in control and test groups of either sex during the study. Survival in mid- and high-dose females was greater than in controls (male and female) and treated males.

Hematological findings were similar in test and control groups at 26, 52 and 104 weeks with one exception. At 26 weeks an unexplained high percentage of eosinophils was observed among females fed 10 ppm. Urinalysis of pooled samples at these intervals did not reveal any meaningful differences among test and control groups of either sex.

Detailed gross necropsy findings were presented for each individual rat which died, time of death, gross signs observed prior to death, and for each inidividual rat sacrificed at 26, 52 and 104 weeks. Most of the deaths appeared to be associated with respiratory infection, although incidental pathological changes were observed in older rats. No consistent pattern of gross pathology was observed in test and control rats sacrificed at 26, 52 and 104 weeks. At terminal sacrifice gross necropsy findings in test and control rats were typical for lesions frequently observed in old rats.

Histopathological findings in test (high dose) and control rats sacrificed at 26 and 52 weeks revealed no consistent pattern of lesions in the examined tissue sections. Lesions observed in microscopic examination of tissues from control and treated animals sacrificed after 104 weeks were similar, except an unexplainable excess of thyroid and mammary tumors in high-dose females (thyroid adenoma, carcinoma and adenocarcinomas; mammary adenoma and adenofibromas). There were 4/15 (26.7%) thyroid tumors in females at 100 ppm compared to 1/8 (12.5%) in female controls, and 5/15 (33.3%) mammary tumors in females compared to 1/8 (12.5%) in female controls. These tumors were listed in a tabular summary of microscopic pathology, but were not described in a supplemental detailed histopathologic evaluation of the thyroid, kidney and adrenals. A descriptive detailed histopathologic evaluation of other tissues/organs, including mammary glands, was not provided. Data were either lacking or too contradictory to derive any biological or statistical significance of tumor incidence or dose related effect.

Conclusion:

There were no dose related pathological changes detected in this study. Mortality was due primarily to respiratory infections with very few males in test and control groups surviving at 104 weeks; survival of high-dose females was approximately twice that of control females. Histopathologic evaluation was not provided for animals that died during the study affording no comparison with the fewer animals present at termination. Chronic toxicity and oncogenic potential could not be determined in this study from the feeding of Simazine 50W to rats at dosages up to 100 ppm for 104 weeks.

Classification: Core-Supplementary

This study does not fulfill registration requirement for oncogenic or chronic toxicity in the rodent (rat) and is considered to be a data gap.

83-1 Chronic Testing
Chronic Toxicity - Non-Rodent

Study Type: Two-Year Dietary Feeding - Dogs

MRID Numbers: 00023364 and 00080627

Sponsor: Geigy Chemical Corp.

Contracting Lab: Woodard Research Corp.

Test Material: Simazine 80W, a putty colored powder.

Methods:

Twenty-four purebred beagle dogs were assigned to 4 groups of 6 dogs each (3 males, 3 females) at the following dietary levels of Simazine 80W: 0 (control), 15, 150 and 1500 ppm. Test material and dry Dietrich and Grambrill dog meal were mixed mechanically to obtain a dosage level of 1500 ppm and further diluted to 150 ppm and 15 ppm dosage levels. The amount and method of provision of food to these experimental animals was not described. Animals were housed individually with water ad libidum.

General daily observations were made on all animals during the first 52 weeks of the study. During the remainder of the study to 104 weeks, daily observations included food intake, fecal consistency and urinary output. Detailed physical examinations and body weights were recorded weekly throughout the study.

Hematological and clinical chemistry determinations were obtained at various intervals during the study. Qualitative urinalysis were made on cage-collected samples at similar intervals.

One male and one female from each dosage level were sacrificed at the 52 week interval. The remaining animals (2 males, 2 females) were sacrificed at 105 weeks. All animals were subjected to necropsy and gross pathological lesions were recorded. The following organs from sacrificed animals were weighed: liver, lungs, heart, thyroids, adrenals, kidneys, spleen, gonads, prostate, uterus, brain and pituitary gland. Weighed organs plus esophagus, duodenum, ileum, colon, cecum, stomach, parotid salivary gland, thymus, trachea, gall bladder, pancrease, mesenteric lymph node, skin, femoral bone marrow and spinal cord were fixed and stained for histopathological examination.

Results:

No dogs died during the 104-week study. Good normal body weight gain was observed in control and low-dose (15 ppm) dogs, but body weight gain was somewhat less in dogs dosed at 150 ppm during the first 52 weeks. A net loss of 6% in body weight occurred in dogs dosed at 1500 ppm during the same period. In the second half of the study body weights stabilized with variable weight gain and loss at various intervals among individuals in all test and control groups.

Hematological values were similar in control and test groups although variations were observed in individual animals at different sampling intervals. Qualitative urinalyses were similar in treated and control groups throughout the study.

Reported gross pathological observations of dogs sacrificed at 52 and 105 week intervals revealed no dose/test material related lesions. Also, no changes attributable to the administration of the test material were indicated in histopathologic examinations of tissues from these animals.

Conclusion:

All dogs survived the two-year study with no signs of toxicity due to dietary administration of Simazine 80W at 15, 150 and 1500 ppm, except net weight loss at 1500 ppm and less weight gain at 150 ppm. These differences cannot be accounted for since the reports lacked individual feeding records (food consumption) and weight gain differences did not occur during the second half of the study. Ages of individual dogs used in the study and individual observation records were lacking. Neither chronic toxicity nor oncogenic potential could be determined from this study.

Classification: Core-Supplementary

This study does not satisfy the registraton requirement and is considered to be a data gap for non-rodent chronic toxicity.

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83-2 Oncogenicity Study

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Rat

Refer to chronic toxicity-rodent above. The rat study does not fulfill oncogenicity requirements for registration and is considered to be a data gap.

Second Species (Mouse)

An oncogenicity study in a second species has not been received for review. A data gap exists for this registration requirement.

83-3 Teratogenicity - 2 species

No data were available for review. A data gap exists for this requirement in 2 species.

83-4 Reproduction

Study Type: Three-Generation Reproduction Study in the Rat.

MRID Numbers: 00023365 and 00080631

Sponsor: Geigy Chemical Corp.

Contracting Lab: Woodard Research Corp. Dated: 9/16/65

Test Material: Simazine 80W

Experimental Design:

Weanling albino rats from Charles River Breeding Laboratories were individually housed in temperature-controlled quarters and acclimatized for one week. Eighty rats, comprising the F_0 Generation, were assigned to 2 groups of 40 rats each (20 males, 20 females) at dietary levels of Simazine 80W as follows: 0 ppm (Control) and 100 ppm. Test material was mecnanically mixed and fed to F_0 rats until sacrifice at 26 weeks. All rats were weighed every two weeks except during mating periods; females were not weighed during gestation and lactation. After 74 days on the compound, males and females were paired and mated for 10 days.

At the birth of each litter (F_{1a} generation), observations recorded were: numbers of live and still born pups, live pup mean weight, physical condition of the dam and pups, and presence of external malformations.

At weaning, the number and mean weight of survivors in each litter were recorded. The pups were examined, sacrificed, and necropsied. F_0 generation parent rats were remated as different pairs within each group and the second (F_1b) litters were observed at birth as described above for the F_1a litters. Male and female weanlings from F_1b litters were weighed and examined and selectively assigned to study groups as follows: 30 rats (10 M, 20 F) from control litters became the control group at 0 ppm; 30 rats (10 M, 20 F) from 100 ppm simazine treated litters were placed in each of 2 test groups at 50 ppm and 100 ppm dietary simazine.

After 12 days on control diet, the simazine groups were fed the test compound for 28 weeks. After 81 days on the compound, the males in each group were paired and mated with the first 10 females and then mated with the second 10 females. Each resulting F_2a litter was observed and examined at birth and at weaning as described above and weanlings were sacrificed. F_1b parents were remated and produced second litters (F_2b) from which 30 representative weanlings (10 M, 20 F) each were assigned to study groups to receive the same dietary levels of simazine at 0, 50 and 100 ppm. Rats were fed their respective diets from 26 days after weaning until termination of the study. Mating of the F_2b rats and observations at birth and weaning of the F_3a and F_3b litters followed the same format as described above. At weaning both the F_3a and F_3b litters were weighed and sacrificed. The F_3b litters were autopsied and heart, liver and kidneys from 2 males and 2 females from each litter were weighed; and these tissues plus spleen, adrenals, thyroid, gonads and bone marrow were fixed in formalin. Tissues of 1 male and 1 female from each litter were examined histologically. Sacrifice of the F_2b parent rats terminated the study.

Results:

Growth rates of simazine-treated and control rats were comparable in both sexes of all 3 generations, with one exception. Treated F_1b males had somewhat lesser body weight gain than controls throughout the study period. A few sporadic deaths of undetermined causes occurred among control and simazine-fed groups in all generations.

Obervations of reproductive performance in control and simazine-fed groups of rats from each of two matings per generation were as follows: number of litters per group, live births per litter, mean birth weight, live weanlings per litter, and mean weanling weight. These data indicated that litters produced by rats fed simazine at 100 or 50 ppm were basically similar to those of untreated control rats, both

within each generation and among the 3 generations. Birth defects and/or teratological changes were not detected in this study.

At termination no gross pathology nor dose-related differences in organ weights or body weights were observed in F_3b litters. Histopathological examination revealed no differences between control and treated groups, except for somewhat greater glycogen depletion and hepatic cell size irregularity at 100 ppm and a slightly higher incidence of round cell foci in the hepatic parenchyma in both of the treated groups. Mean absolute liver weights and mean liver/body weight ratios were slightly higher in both of the treated groups than in the control group. Mean terminal body weights increased progressively by dosage levels such that treated weanling rats outweighed control weanlings as follows: +1 g in both sexes at 50 ppm, and +5 g and +4 g in males and females, respectively, at 100 ppm. Since terminal sacrifices were conducted over a period of 2 weeks following weaning, differences in body weights suggest that sacrifices may have occurred first in controls, next at 50 ppm, and lastly at 100 ppm. Glycogen depletion and accompanying liver cell changes may be a consequence of the amount of elapsed time since weaning during a period of drastic dietary adjustment. The significance of these minor changes is questionable.

Conclusion:

Simazine 80W had no adverse effects on reproductive performance in rats at a dietary level of 100 ppm for three generations over a total study period of 93 weeks.

Reproductive NOEL > 100 ppm

Classification: Core - Minimum Data

This study satisfies the registration requirement.

Mutagenicity Testing

84-2 Gene Mutation
84-2 Chromosomal Aberration
84-2 Other Mechanisms of Mutagenicity

Mutagenicity studies were not available for review. Data gaps exist for the entire category of mutagenicity testing required for registration.

Special Testing

85-1 General Metabolism

General metabolism studies allowing adequate determination of metabolite moieties were not available for review. A data gap exists for a required general metabolism study which identifies and quantitates metabolites formed in the exposure of the mammalian species.

Tolerance Assessment

Tolerances have been established for Simazine in a variety of food and forage crops, meat and poultry, milk and dairy products, and shellfish. The Maximum Permissable Intake (MPI) of 3 mg/day for a 60 kg human, derived from an Acceptable Daily Intake (ADI) of 0.05 mg/kg/day, was based on a 2-year rat feeding study with a no-observed-effect-level (NOEL) of 100 ppm (5 mg/kg) (memo, PP #0F0855, C.H. Williams, 7/6/71). The Agency has since reevaluated the existing data base which revealed significant deficiencies and, therefore, the ADI was withdrawn pending receipt of acceptable data. Published tolerances account for a theoretical maximum residue contribution of 0.2890 mg/day to the 1.5 kg diet of a 60 kg human or 0.0048 mg/kg/day. Evaluation of acute toxicity data did not reveal any adverse acute effects of Simazine. Data are either lacking or insufficient to determine long-term chronic effects, oncogenicity potentials, teratogenicity and mutagenicity. These data are crucial and necesary for the continuation of existing tolerances and for the consideration of additional tolerances. Additionally, information specifying sameness or differences between metabolites formed in plants and animals is necessary.

Toxicology Branch recommends that a statutory requirement or deadline be placed on the registrant(s) for submission of such data before revocation of existing tolerances or withdrawal of existing registrations is considered necessary.

George W. Robinson 11/4/83

George W. Robinsor, D.V.M.
Review Section #1
Toxicology Branch/HED (TS-769)

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Tox Chem No. Simazine #740 File Last Updated _____ Current Date _____

Study/Lab/Study #/Date	Material	MRID No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
Acute oral, rats (M & F) IBT, #8530-09517 11/9/76	Princep 80W	TOX Doc.	LD50 > 15,380 mg/kg (HDT)	IV	Minimum 001892
Acute dermal, rabbits (M & F) IBT, 6/4/65	Simazine 80W	00023965	LD50 > 10.2 gm/kg (HDT) slight to mild erythema and edema, moderate tremors and convulsions, paralysis of hindquarters	III	Guidelines 001892
Primary Eye Irritation, Rabbits IBT, 6/4/65	Simazine 80W	00023965	Moderately irritating with 50 mg instilled into conjunctival sac of right eye; irritation reversible within 7 days.	III	Minimum 001892
Primary Skin Irritation, Rabbit IBT, 6/4/65	Simazine 80W	00023965	500 mg test material used on abraded and intact skin sites; slightly irritating; score = 1/4 in scoring table of 0/4	IV	Minimum 001892
21-day dermal, rabbit Bio-Research #12017 1/14/80	Simazine Technical 97.6% a.i.	00057567	No systemic toxicity nor dose related skin effects from 15 applications at 1 g/kg (HDT) NOEL > 1000 mg/kg	N/A	Guidelines
2-Yr. Feeding, Rat (M & F) Hazleton, 1/15/60	Simazine 50W 49.9% a.i.	00037752 00025441 00025442 00042793 00080626	100 ppm (HDT) gave no evidence of drug toxicity; chronic toxicity and oncogenic potential could not be determined	N/A	Supplementary
2-Yr. Feeding-dog (M & F) Woodard, 1965	Simazine 80W	00023364 00080626	No overt signs of toxicity at 1500 ppm (HDT); chronic toxicity and oncogenic potential could not be determined (too few animals used). Body wt. changes at 150, 1500 ppm not evaluatable.	N/A	Supplementary
3 Generation Reproduction, Rat Woodard, 1965	Simazine 80W	00023365 00080631	Reproductive NOEL > 100 ppm	N/A	Minimum

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TABLE A
GENERIC DATA REQUIREMENTS FOR Simazine

Data Requirement	Composition 1/	Use Patterns 2/	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 3/
§158.135 Toxicology					
ACUTE TESTING:					
81-1 - Oral LD_{50} - Rat	TGAI	A,B,C,D,H	YES	TOX Doc. 001892	NO
81-2 - Dermal LD_{50}	TGAI	A,B,C,D,H	YES	MRID#00023965	NO
81-3 - Inhalation LC_{50} - Rat	TGAI	A,B,C,D,H	NO	-	NO
81-7 - Acute Delayed Neurotoxicity - Hen	TGAI		NO	-	NO
SUBCHRONIC TESTING:					
82-1 - 90-Day Feeding - Rodent, Non-rodent	TGAI	A,B,C,D,H	NO	-	NO
82-2 - 21 Day Dermal	TGAI	A,B,C,D,H	YES	MRID#00057567	NO
82-3 - 90-Day Dermal	TGAI	A,B,C,D,H	NO	-	NO
82-4 - 90-Day Inhalation - Rat	TGAI	A,B,C,D,H	NO	-	NO
82-5 - 90-Day Neurotoxicity-Hen, Mammal	TGAI	A,B,C,D,H	NO	-	NO

1/ Composition: TGAI = Technical grade of the active ingredient.
2/ The use patterns are coded as follows: A=Terrestrial, Food Crop; B=Terrestrial, Non-Food; C=Aquatic, Food Crop; D=Aquatic, Non-Food; E=Greenhouse, Food Crop; F=Greenhouse, Non-Food; G=Forestry; H=Domestic Outdoor; I=Indoor.
3/ Data must be submitted no later than _____.

TABLE A
GENERIC DATA REQUIREMENTS FOR Simazine

Data Requirement	Composition	1/ Use 2/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)?3/
§158.135 Toxicology (continued)					
SPECIAL TESTING					
85-1 - General Metabolism	PAI or PAIRA	A,B,C,D,H	No	None	YES
85-2 - Domestic Animal Safety	Choice				
Acute Testing (continued)					
81-5 Primary eye irritation	TGAI	A,B,C,D,H	Yes	MRID#00023965	NO
81-4 Primary skin irritation	TGAI	A,B,C,D,H	Yes	MRID#00023965	NO

1/ Compositions: PAI = Pure active ingredient; PAIRA = Pure active ingredient, radiolabelled; Choice = Choice of several test substances determined on a case-by-case basis.
2/ The use patterns are coded as follows: A=Terrestrial, Food Crop; B=Terrestrial, Non-Food; C=Aquatic, Food Crop; D=Aquatic, Non-Food; E=Greenhouse, Food Crop; F=Greenhouse, Non-Food; G=Forestry; H=Domestic Outdoor; I=Indoor.
3/ Data must be submitted no later than _____

TABLE A
GENERIC DATA REQUIREMENTS FOR Simazine

Data Requirement	Composition 1/	Use 2/ Pattern	Does EPA Have Data To Satisfy This Requirement? (Yes, No or Partially)?	Bibliographic Citation	Must Additional Data Be Submitted Under FIFRA Section 3(c)(2)(B)? 2/
§150.13[5] Toxicology (continued)				MRID# 00037752 00025441 00025442 00042793	
CHRONIC TESTING:					
83-1 - Chronic Toxicity - 2 species: Rodent and Non-rodent	TGAI TGAI	A,B,C,D,H A,B,C,D,H	rodent-no non-rodent-no	00080626 00023364 00080627	YES YES
83-2 - Oncogenicity Study - 2 species: Rat and Mouse preferred	TGAI TGAI	A,B,C,D,H A,B,C,D,H	rat-no mouse-no	MRID# 00080626 None	YES YES
83-3 - Teratogenicity - 2 species	TGAI	A,B,C,D,H	No	None	YES
83-4 - Reproduction, 2-generation	TGAI	A,B,C,D,H	Yes (rat)	MRID# 00023365 00080631	NO
MUTAGENICITY TESTING					
84-2 - Gene Mutation	TGAI	A,B,C,D,H	No	None	YES
84-2 - Chromosomal Aberration	TGAI	A,B,C,D,H	No	None	YES
84-2 - Other Mechanisms of Mutagenicity	TGAI	A,B,C,D,H	No	None	YES

1/ Composition: TGAI = Technical grade of the active ingredient.
2/ The use patterns are coded as follows: A=Terrestrial, Food Crop; B=Terrestrial, Non-Food; C=Aquatic, Food Crop; D=Aquatic, Non-Food; E=Greenhouse, Food Crop; F=Greenhouse, Non-Food; G=Forestry; H=Domestic Outdoor; I=Indoor.
3/ Data must be submitted no later than _____
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