

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DODECYLGUANIDINE HYDROCHLORIDE

Chemical Code # 001047, Tolerance # 50281
SB 950 # 662

January 14, 2003

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, no study on file.
Chronic toxicity, dog:	Data gap, no study on file.
Oncogenicity, rat:	Data gap, no study on file.
Oncogenicity, mouse:	Data gap, no study on file.
Reproduction, rat:	Data gap, no study on file.
Teratology, rat:	Data gap, unacceptable study, no adverse effect indicated
Teratology, rabbit:	Data gap, no study on file.
Gene mutation:	No data gap, acceptable study, no adverse effect
Chromosome effects:	No data gap, acceptable study, no adverse effect
DNA damage:	No data gap, acceptable study, no adverse effect
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 135232 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T030114

Prepared by Green & Silva, 1/14/03

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study on file.

CHRONIC TOXICITY, RAT

Subchronic, dermal:

50281 - 018, 023 97109, 115208 "A 21-Day Dermal Toxicity Study in Rats with CT-334-87", (Auletta, C.S., Bio/Dynamics, Inc., East Millstone, NJ, Report # 4932-88, 7/7/89). CT-334-87 (purity and lot # not given) was administered dermally to Sprague-Dawley (CD[®]) rats (5/sex/dose) at 0 (distilled water), 12.5, 25.0 and 50.0 mg/kg/day (occluded exposure, clipped, intact skin) for 6 hours/day, 5 days/week for 3 weeks. Systemic NOEL > 50 mg/kg/day (There were no systemic effects from treatment at any dose.) Dermal NOEL < 12.5 mg/kg/day (There was an increase in eschar and exfoliation in males at 50 mg/kg. There was an increase in edema and necrosis in both sexes at 50 mg/kg. There was an increase in superficial necrosis in females at 50 mg/kg. There was a dose-related increase in desquamation, atonia, erythema and fissuring in both sexes at ≥ 12.5 mg/kg.

Histopathologically there was an increase at 50 mg/kg in surface accumulation of inflammatory cells/cell debris, hyperkeratosis, parakeratosis, spramous cell hyperplasia, erosions/ulcers, subacute (chronic active)/chronic inflammation (F) and necrosis (M.) Possible adverse dermal effect. Not acceptable (missing pages 7, 8, 9 & 11; information on test article) upgradeable. (Green & Silva, 1/13/03).

50281 - 023 115250 (duplicate of 022 115207) "Analysis of Cyttox[®] 2014," (Anderson, R.H., Cyanamid, Chemical Research Division, Wayne, NJ, ID #: 1402, 1/16/89). This volume had an analysis of the dosing material used in the subchronic dermal, rat study (50281 - 023 115208) and the developmental rat rangefinding study (50281 - 022 115206). No worksheet. Silva, 1/14/03.

CHRONIC TOXICITY, DOG

Subchronic Study:

50281 - 017, 024 097108, 115210 "A Subchronic (3 Month) Oral Toxicity Study in the Dog with CT-334-87 via Capsule Administration," (Auletta, C.S.; Bio/Dynamics, Inc., Mettlers Road, East Millstone, NJ. 08875, Report # 88-3311, 10/16/89). CT-334-87 (assumed 100% pure but actual content of a.i. not provided) was fed in gelatin capsule to Beagle dogs (4/sex/dose) at 0, 5, 25 and 100 mg/kg/day for 90 days. NOEL = 5 mg/kg/day (Males at ≥ 25 mg/kg showed increased excessive salivation and thinness/emaciation and at 100 mg/kg emesis and watery stool were increased. Females at ≥ 25 mg/kg showed increased thinness/emaciation and at 100 mg/kg there was increased excessive salivation, emesis, dehydration and lethargy. Bodyweight at 100 mg/kg was decreased 5 to 17% in both sexes.) Unacceptable but possibly upgradeable (purity of test article for DGH; whether doses were corrected; missing pages in the report). No adverse effect indicated. (Green & Silva, 1/8/03)

50281 - 024 115211 "Analysis of Cytos[®] 2014," (Anderson, R.H., Cyanamid, Chemical Research Division, Wayne, NJ, ID #: 1402, 1/16/89). This volume had an analysis of the dosing material used in the subchronic dog study (50281 - 024 115210). No worksheet. Silva, 1/14/03.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

Range-finding Study:

50281 - 022 115206 "A Range-finding Study to Evaluate the Toxicity of CT-334-87 in the Pregnant Rat," (Schroeder, R.E.; Bio/Dynamics, Inc., East Millstone, NJ, Report # 88-3308, 9/28/89). CT-334-87 (assumed 100% pure; Lot #: W7718, but purity not stated) was administered by gavage to mated CD[®] (Sprague-Dawley derived) rats (5/dose) at 0 (distilled water), 125, 250, 500, 750 and 1000 mg/kg/day on gestation days 6 through 15. Maternal NOEL < 125 mg/kg (All died at 750 (5/5) and 1000 mg/kg (5/5), 4/5 died at 500 mg/kg and 2/5 died at 250 mg/kg. Body weight gain during treatment was lower (45 grams), compared with control (66 grams) at 125 mg/kg. At 250 mg/kg, 1 surviving pregnant female lost 45 grams over the GD 6 - 15 treatment period. Food consumption was decreased during treatment in surviving animals at \geq 125 mg/kg. Excessive salivation was observed at 0 (0/5, 0%), 125 (1/5, 20%), 250 (2/5, 40%), 500 (5/5, 100%), 750 (4/5, 80%) and 1000 mg/kg (4/5, 80%) during treatment. At \geq 250 mg/kg brown/yellow staining of skin/fur in the ano-genital area, moist rales, brown staining about the mouth and nares and soft stool were observed during treatment.) Developmental NOEL = 125 mg/kg (Fetal body weights and litter size were decreased at 250 mg/kg.) Effects in fetuses were primarily considered to be due to excessive toxicity in dams. These data are supplemental. (Green & Silva, 1/10/03)

Definitive Study:

50281 - 019, 021 097110, 115205 "A Teratogenicity Study in Rats with CT-334-87," (Schroeder, R.E.; Bio/Dynamics, Inc., East Millstone, NJ, Report # 88-3309, 10/9/89). CT-334-87 (assumed 100% pure, but not stated) was administered by gavage to mated CD[®] (Sprague-Dawley derived) rats (24/sex/dose) at 0 (distilled water), 45, 90 and 180 mg/kg/day on gestation days 6 through 15. Maternal NOEL = 45 mg/kg/day (There was decreased food consumption in dams at \geq 90 mg/kg.) Developmental NOEL = 90 mg/kg (There was a slight increase in fetal visceral variations, fetal skeletal malformations and fetal skeletal variations at 180 mg/kg.) No adverse effect indicated. Not

acceptable (no analyses of dosing solutions; upgradeable for a.i., no purity of test article). (Green & Silva, 1/10/03).

TERATOLOGY, RABBIT

No study on file.

GENE MUTATION

** 50281 - 029 135232 "*Salmonella/Escherichia Coli* Plate Incorporation Mutagenicity Assay," (San, R.H.C, Baublitz, J.C.; Microbiological Associates, Inc., Rockville, MD., Study # G94BN75.502; 1/24/95). *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *Escherichia coli* strain WP2 μ vrA were exposed to Metasol DGH (35% a.i.) at 0 (DMSO), 3.3, 10.0, 33.0, 100.0, 333.0 and 1000.0 μ g per plate (in triplicate) both with and without metabolic activation (Aroclor 1254 induced rat liver S9) for 48 - 72 hours. There were no treatment-related effects at any dose with any strain. Positive controls functioned as expected. No adverse effect indicated. (Green & Silva, 1/7/03).

CHROMOSOME EFFECTS

Preliminary Dose Assessment:

50281 - 025 134950 "Single Acute Exposure Dose Selection Study on CT - 334 - 87," (Ivett, J.L., Hazleton Laboratories America, Inc., Kensington, MD, HLA Study #: 11071-0-459-PO). CT-334-87 (Lot # WI-2524, purity not stated) was administered by gavage to ICR mice (3/sex, 8 weeks old) at 1500 mg/kg in a single dose. Doses were based on LD₅₀ for rats, dogs and rabbits (1400 mg/kg). All animals were examined after dosing and periodically throughout the duration of the study (3 days) for toxicity and mortality. All mice appeared normal immediately after dosing; however 2 hours after dosing 1 female (#3983) was found dead and all males were languid with squinted eyes. The remaining 2 females appeared normal and remained healthy for the 72 hour observation period. Within 26 hours of dosing males developed rough haircoats. Approximately 44 ½ hours after dosing males had rough haircoats and squinted eyes and 2 males (#'s 3936 & 3963) had hunched backs. Approximately 67 ½ hours post-dosing males had rough haircoats and #'s 3936 and 3963 still had hunched backs. These conditions remained unchanged at the completion of the 72 hour observation. The results were sufficient to select doses of 140, 467 and 1400 mg/kg for the definitive mouse bone marrow micronucleus assay. (Silva, 1/7/03).

Definitive Study:

** 50281 - 016, 025, 026, 027 097107, 115213, 118448, 131202 "Mutagenicity Test on Dodecylguanidine Hydrochloride *In Vivo* Mouse Micronucleus Assay," (Ivett, J.L., Hazleton Laboratories America, Inc., Kensington, MD, Report # 11071-0-455, 3/5/90). CT-334-87 (Lot # WI-2524, purity not stated) was administered by gavage to ICR mice (5 - 20/sex/dose) at 0 (deionized water), 140, 467 and 1400 mg/kg in a single dose. Samples were harvested at 24, 48, or 72 hours after treatment. No treatment-related results were observed at any dose. The positive control functioned as expected. Although there were some deficiencies in the study, none inhibited the evaluation of whether or not dodecylguanidine hydrochloride induced genotoxicity. No adverse effect. Acceptable. (Green & Silva, 1/3/03)

DNA DAMAGE

** 50281 - 016, 025, 026, 027 097106, 115212, 118442, 131201 "Mutagenicity Test on CT-334-87 in the *In Vitro* Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay", (Cifone, M.; Hazleton Laboratories America, Inc., Kensington, MD, Report # 11071-0-447, 3/8/90). CT-334-87 technical (purity not stated) was used on primary hepatocytes from adult male Fisher 344 (F344/CDF) rats (3 cultures/dose for UDS; 2 cultures/concentration for cytotoxicity) at 0 (DMSO), 0.05, 0.10, 0.25, 0.5, 2.5 and 5.0 ug/ml for 19.4 hours. There were no treatment-related effects at any dose. Although there were too few repetitions, according to FIFRA Guidelines, there was no indication of a positive response at any dose (although cytotoxicity was observed). Acceptable. No adverse effect. Green & Silva, 1/02/03.

NEUROTOXICITY

Not required at this time.