

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
SODIUM CHLORATE

Chemical Code # 536 Tolerance #1020
SB 950 # 317

DECEMBER 8, 1998

I. DATA GAP STATUS

Chronic toxicity, rat:	No study on file (An acceptable 90-day gavage study is on file)
Chronic toxicity, dog:	No study on file (An acceptable 90-day gavage study is on file)
Oncogenicity, rat:	No study on file.
Oncogenicity, mouse:	No study on file.
Reproduction, rat:	No study on file.
Teratology, rat:	No data gap, no adverse effect.
Teratology, rabbit:	No study on file.
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, possible adverse effect
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers for the above study types through 098079 (Document No.050) and above 900000 were examined. This includes all relevant studies indexed by DPR as of December 9, 1998.

In the 1-liners below:

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T981208.wpd prepared by J. Gee.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

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

CHRONIC TOXICITY, RAT

No study on file.

SUBCHRONIC, RAT

** 1020-047 098072 "A subchronic (3 month) oral toxicity study of sodium chlorate in the rat via gavage" (D. S. Barrett, Bio/dynamics, Project 86-3112, 12/4/87) Sodium chlorate, 100% white granular solid, was given to 15 Sprague-Dawley CD® rats/sex/group at 0 (distilled water), 10, 100 or 1000 mg/kg/day by gavage, 7 days per week for 90 days. Hematology, clinical chemistry and ophthalmology were conducted at appropriate intervals but no urinalysis was done. The clinical chemistry/hematology included sodium and chloride levels in the blood and percent methemoglobin found at the end of treatment. There were no treatment-related effects on any of these parameters. The most significant finding was a suggestion of anemia, especially in female rats with slightly lower red blood cell counts, hematocrit and hemoglobin levels. There were no histological findings after 90 days due to treatment. NOEL = 100 mg/kg/day (hematology). ACCEPTABLE. (Gee, 11/10/98)

1020-019 954557 "90-Day subacute oral toxicity of sodium chlorate." (IBT No. B5664, 3/19/68) Invalid study. No worksheet. (Gee, 12/10/98)

CHRONIC TOXICITY, DOG

No study on file.

SUBCHRONIC STUDIES

** 1020-048 098073 "A subchronic (3 month) oral toxicity study in the dog via gavage administration with sodium chlorate" (D. S. Barrett, Bio/dynamics, NJ, 86-3114, 10/19/87) Four beagle dogs/sex/group were given sodium chlorate, 100%, by oral gavage at 0 (distilled water), 10, 60 or 360 mg/kg/day for 3 months. Clinical signs included emesis in 1/4 females during the first 3 weeks of dosing. No other clinical signs or effects on hematology, clinical chemistry (including methemoglobin), ophthalmology, or histopathology were reported. No urinalysis was done. Range-finding study was not included for dose selection but the report contains a statement that doses higher than 360 resulted in emesis. NOEL = 60 mg/kg/day. ACCEPTABLE. (Gee, 11/12/98).

1020-019 954558 "Ninety-day subacute oral toxicity of sodium chlorate - Beagle dogs." (IBT No. C5665, 3/12/68) Invalid study. No worksheet. (Gee, 12/10/98)

1020-027 024093 "Subchronic toxicity of chlorine dioxide and related compounds in drinking water in the nonhuman primate." (J. P. Bercz *et al.*, Environmental Health Perspectives 46: 47-55 (1982)) Sodium chlorate solutions equivalent to 25, 50, 100, 200 and 400 mg/l of ClO₂, was available to African Green Monkeys for 30 - 60 days. Hematology parameters were measured. Red cell count and hemoglobin were slightly decreased with "dose dependence" with treatment. Other parameters were reported as "no response". No worksheet. (Gee, 11/12/98).

1020-034 039955 "The effects of repeated administration of the chlorates and chlorides of potassium and sodium in massive doses." (I. S. Kleiner and L. B. Dotti, Bulletin of N. Y. Medical College and Flower Hospital, 3: 309 - 322 (1940)) Rabbits were given 1 g/kg 6 days/week for 4 weeks by gavage. There was no consistent effect on methemoglobin or body weight. Rats were fed diets containing 2.5% salt with a slight inhibition of growth. No inhibition of growth at 0.85% extra salt. No worksheet. (Gee, 11/12/98).

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOGENICITY, RAT

** 1020-049 098074 "A teratogenicity study in rats with sodium chlorate." (R. E. Schroeder, Bio/dynamics, Project 86-3117, 9/24/87) Sprague-Dawley CD® rats, 24/dose group, were given sodium chlorate, 100% purity, at 0 (distilled water), 10, 100 or 1000 mg/kg/day by oral gavage in 5 ml/kg, days 6 - 15 of gestation. No treatment-related effects were reported on body weight, food consumption, clinical signs or developmental parameters. Maternal and developmental NOEL = 1000 mg/kg/day. No adverse effects. ACCEPTABLE. (Gee, 11/12/98).

TERATOGENICITY, RABBIT

No study on file.

GENE MUTATION

** 1020-050 098075 "Sodium chlorate: Investigation of mutagenic activity at the HGPRT locus in a Chinese hamster V79 cell mutation system." (G. Hodson-Walker, Life Science Research, UK, Report No. 89/SKR002/0631, 9/18/89) Chinese hamster V79 4-1 clone 9 3/12 cells were exposed for 3 hours with and without rat liver activation to concentrations of 0 (distilled water), 8, 40, 200, 1000 or 5000 ug/ml. There were triplicate cultures per concentration with two trials. EMS was the positive control without activation and DMBA, the positive control with activation. Both were functional. There was no concentration-dependent cytotoxicity as determined by plating efficiency compared with the solvent control. There was no increase in the mutation frequency as measured by resistance to 6-thioguanine after a 7-day expression period. No adverse effect. ACCEPTABLE. (Gee, 11/12/98)

** 1020-050 098077 "Sodium chlorate: Assessment of mutagenic potential in histidine auxotrophs of *Salmonella typhimurium* (the Ames test)." (K. May, Study Director, Life Science

Research Limited, UK, LSR report 89/SKR001/0285, 8/14/89) Sodium chlorate, 99.9%, was tested with and without Aroclor 1254-induced rat liver activation at 0 (distilled water), 50, 158, 500, 1580 and 5000 ug/plate in two trials, triplicate plates per trial. *Salmonella* strains used were TA1535, TA1537, TA1538, TA100 and TA98. Positive controls were functional. There was no evidence of cytotoxicity or induction of revertants at any concentration tested under conditions of the assay. No adverse effect. ACCEPTABLE. (Gee, 12/8/98)

CHROMOSOMAL EFFECTS

** 1020-050 098076 "Sodium chlorate: Assessment of clastogenic action on bone marrow erythrocytes in the micronucleus test." (J. M. Mackay, Life Science Research Limited, UK, LSR 89/SKR003/0253, 8/25/89) CD-1 mice, 5/sex/group, were given an oral dose of 0 (distilled water), 200, 1000 or 5000 mg/kg. Chlorambucil, 30 mg/kg, was the positive control at 24 hours. Animals were sacrificed at 24, 48 or 72 hours after dosing. 2000 polychromatic erythrocytes were scored per animal and the ratio of polychromatic:mature cells was calculated for each animal. Five males at 5000 mg/kg had clinical signs of hunched posture and piloerection on day 4. The frequencies of micronucleated erythrocytes in treated animals was similar to controls. No adverse effect. ACCEPTABLE. (Gee, 12/7/98).

DNA, OTHER

** 1020-050 098078, 098079 "Unscheduled DNA synthesis (UDS) in HeLa S3 cells in vitro." (A. H. Seeberg, Study Director, Life Science Research, Roma Toxicology Centre, Report 102002-M-02289, 9/27/89) HeLa S3 cells in monolayer were treated with sodium chlorate (99.9%) for three hours in the presence of hydroxyurea and tritiated thymidine. Concentrations were 0 (distilled water), 100, 316, 1000, 3160 and 10000 ug/ml. There were triplicate cultures and two independent trials with and without rat liver activation (phenobarbital and beta-naphthoflavone induced). DNA was extracted from the cells and quantitated as ug. Radioactivity was determined by liquid scintillation counting and the results were expressed as DPM/ug DNA. 4-Nitroquinoline-N-oxide and benzo(a)pyrene were functional as positive controls. The incorporation of thymidine decreased with increasing concentrations of sodium chlorate indicating toxicity. There was no evidence of the induction of UDS with treatment. ACCEPTABLE. (Gee, 12/9/98)

** **1020-050 No record number assigned** "Sodium chlorate: Assessment of its ability to cause lethal DNA damage in strains of *Escherichia coli*." (K. May, Life Science Research Limited, LSR report no. 89/SKR004/0341, 9/5/89) Sodium chlorate, 99.9%, was tested with *Escherichia coli* strains WP2 (repair proficient), WP67 (repair deficient) and CM871 (repair deficient) with and without rat liver activation. Cells were incubated for 2 or 18 hours in liquid culture with shaking, then diluted and plated for viable colony counts. Concentrations of sodium chlorate were 0 (distilled water), 100, 316, 1000, 3160 or 10000 ug/ml. Positive controls were mitomycin C (- S9) and 2-aminoanthracene (+ S9), and ampicillin as a negative control for toxicity without DNA damage. The coefficients of survival (C_s) were calculated, comparing survival of treated cultures with relevant controls and repair proficient cells with repair deficient cells. Values less than 0.3 were considered indicative of DNA damage. The results indicated that sodium chlorate caused DNA damage without (as well as with) activation after 2 hours of incubation at ≥ 1000 ug/ml but not after 18 hours. Mitomycin C was effective with both repair deficient strains but 2-aminoanthracene was effective only with CM871. The absence of

differential toxicity at 18 hours was suggested as due to a "feeder" effect of lysing cells in nutrient-exhausted medium. Possible adverse effect. ACCEPTABLE. (Gee, 12/8/98).

NEUROTOXICITY

Not required at this time.