

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
SUMMARY OF TOXICOLOGICAL DATA
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DALAPON
(Grouped with Dalapon)

SB 950-503, Tolerance #

August 8, 1986

I. DATA GAP STATUS

Chronic rat: Data gap, inadequate study, no adverse effect indicated.

Chronic dog: Data gap, inadequate study, possible adverse effect indicated.

Onco rat: Data gap, no study on file.

Onco mouse: Data gap, inadequate study, no adverse effect indicated.

Repro rat: Data gap, inadequate study, no adverse effect indicated.

Repro dog: Data gap, inadequate study, no adverse effect indicated.

Terato rat: Data gap, inadequate study, possible adverse effect indicated.

Terato rabbit:Data gap, no study on file.

Gene mutation: Data gap, inadequate study, no adverse effect indicated.

Chromosome: Data gap, inadequate study, no adverse effect indicated.

DNA damage: Data gap, inadequate study, no adverse effect indicated.

Neurotox: Not required.

Note, Toxicology one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

File name 3b: sb059dal.jrg

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DALAPON, MAGNESIUM SALT
(Grouped with Dalapon)

SB 950-502, Tolerance #

August 8, 1986

I. DATA GAP STATUS

Chronic rat: Data gap, no study on file.

Chronic dog: Data gap, no study on file.

Onco rat: Data gap, no study on file.

Onco mouse: Data gap, no study on file.

Repro rat: Data gap, no study on file.

Terato rat: Data gap, no study on file.

Terato rabbit: Data gap, no study on file.

Gene mutation: Data gap, no study on file.

Chromosome: Data gap, no study on file.

DNA damage: Data gap, no study on file.

Neurotox: Data gap, no study on file.

Note, Toxicology one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

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MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

DALAPON, SODIUM SALT
(Grouped with Dalapon)

SB 950-503, Tolerance

July 29, 1986

I. DATA GAP STATUS

Chronic rat: Data gap, no study on file.

Chronic dog: Data gap, no study on file.

Onco rat: Data gap, no study on file.

Onco mouse: Data gap, no study on file.

Repro rat: Data gap, no study on file.

Terato rat: Data gap, no study on file.

Terato rabbit: Data gap, no study on file.

Gene mutation: Data gap, no study on file.

Chromosome: Data gap, no study on file.

DNA damage: Data gap, no study on file.

Neurotox: Data gap, no study on file.

Note, Toxicology one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

File name 3b: sb059dal.jrg

GROUPED WITH: Dalapon, Magnesium Salt and Dalapon, Sodium Salt

CHRONIC, RAT

005 036524 (1956, Hazleton Labs) JRG 4/29/86 One liner: Dalapon, purity not stated; 24 males and 20 females were fed 0, 0.01 or 0.03% in the diet, 24 males only fed at 0.1% over two years; NOEL not established; no adverse effect reported; incomplete, unacceptable (missing data, number of animals, no diet analysis, age of animals not given, no justification of dose selection, no purity of test article, limited number of animals for histopath, no individual body weights, food consumption).

001 031108 (Date and lab not given) JS 3/21/85 Very brief summary of 005 036524.

006 036531 (1960, Journal article) JRG 4/28/86 Summary of 005 036524. Journal article - Ag. and Food Chemistry 8: 47 (1960).

CHRONIC, DOG

005 036522 (1956, Hazleton Labs) JRG 4/29/86 One liner: Dalapon, purity not given; female and two males per group were given 0, 15, 50, or 100 mg/kg by capsule for 52 weeks; NOEL: not established; no chronic effects due to treatment are reported; incomplete, unacceptable (number of animals).

No justification of dose and no good evidence mtd was approached; inadequate number of tissues for histopath and no purity for test article. Soft feces on occasion at 50 and 100 mg/kg.

001 031107 (Date and lab not given) JS 3/21/85 Very brief summary of 005 036522. Insufficient information for review.

006 036530 (1960, Journal article) JRG 4/28/86 Summary of 005 036522. Ag. and Food Chemistry 8: 47 (1960).

005 036523 (1975, Mellon Institute) JRG 4/29/86 One -liner: Dalapon, ~90%; four males and six female Beagle dogs were fed 0, 15, 45, or 90 mg/kg over two years; NOEL: 45 mg/kg; an increase in liver wt. and in animals with vacuoles in the spinal cord with dose is reported; unacceptable (missing data), incomplete, upgradeable. Need justification of high dose - study 36522 showed no toxic effects over 52 weeks at 100 mg/kg. No analysis of diet; only a stability check; no individual histopath. No body weights, organ weights/dog, no food consumption. Histopathology showed no findings in the liver to support the increase in weight so this is probably not of biological significance. The vacuoles in the spinal cord (and possibly the sciatic nerve) need further evaluation. The 1-year study above does not include the spinal cord or sciatic nerve among the tissues examined.

ONCOGENICITY, RAT

No studies on file

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ONCOGENICITY, MOUSE

8.

005 036525 (1983, Dow Chemical) JRG 4/29/86 One liner: Dow, 1983; dalapon 75.2% acid equiv.; 86/sex/group as controls and 50/sex/group as test animals were fed 0, 2, 60, or 200 mg/kg over two years; NOEL: 60 mg/kg (liver weight). No oncogenic effect was reported. Incomplete (missing data), unacceptable. Ten/sex/group were sacrificed at 1 year. Doses reportedly based on a 14-day tolerance study and a 90-day subchronic. Better justification, however, is needed in that the LD50 is 4 g/kg and there is a lack of clinical observations at 200 mg/kg. The pilot studies suggest a higher dose should have been used. Also, no individual histopath, body weights, time to death, food consumption, other. No histopath. to confirm increased liver weight at 200 mg/kg so significance is questionable. The total number of males with benign tumors (pg. 56) is statistically higher in the high dose group but the higher number (11/50) of males with lacrimal (Harderian) gland tumors compared with controls (6/86) contributes to this total. The significance of this tumor type to man is questionable because the gland is vestigial, unlike in rodents. The overall conclusion is that the test article is not oncogenic in this study.

REPRODUCTION, RAT

006 036532(1960,Journal article) JRG 4/28/86 Reviewed with 036542

006 036542 (1960, Journal article) JRG 4/28/86 One liner: publication, 1960; Ag and Food Chemistry 8: 47 (1960); dalapon, no purity stated; four males and 12 females were fed 0, 0.03, 0.1 or 0.3% (3000 ppm) for three generations, two litters each; no evidence of a repro effect; NOEL - not established; incomplete (missing data), unacceptable. No description of the test article, no analysis of diet, no age, no justification of dose levels with no indication an adequate dose was used, no individual data so cannot

evaluate any effects on weight at weaning, husbandry (gang housed for mating), others.

REPRODUCTION, DOG

006 036533 (1962, Dow Chemical) JRG 4/28/86 One liner: Dalapon, no purity stated; two controls, six at 50 mg/kg, three at 100 mg/kg and one at 200 mg/kg fed in diet after breeding; NOEL - not established; no obvious repro effects but insufficient info; incomplete, unacceptable. No purity of test article, no diet analysis, females were already already bred when dosing started.

TERATOLOGY, RAT

006 036526-7 (1971, Dow Chemical) JRG 4/28/86 One liner: Dalapon, no purity stated, lot MM072301; 25/group were given 0, 500, 1000, or 1500 mg/kg, days 6-15 by oral gavage; NOEL (maternal wt. gain): 1000 mg/kg; fetus, not clear; some evidence of dev. tox. without a maternal effect; skeletal effects at all doses; incomplete, unacceptable. No individual data,

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test article not described for purity, inadequate fraction (1/3) subjected to visceral exam, starting weights were not well matched. Without individual litter data, an evaluation is most difficult but there appears to an effect on skeletal development at all doses. Fetal weight significantly decreased at 1000 and 1500. Maternal tox. marginal at 1500 mg/kg/day.

TERATOLOGY, RABBIT

Rabbit teratology due Nov. 1, 1986

MUTATION, GENE

006 036535 (1972, Journal article) JRG 4/28/86 Summary, J. Agr. Food Chemical 20: 649-656 (1972). 110 pesticides were screened with Salmonella and T₄ phage. No adverse effect reported with dalapon.

006 036536 (1977, Journal article) JRG 4/28/86 Summary, Mutation Res. 46: 395-402 (1977). Aspergillus nidulans was tested for induction of point mutations to 8-azaguanine resistance, mitotic crossing-over and mitotic non-disjunction with 13 pesticides. No activation. No adverse effect with dalapon.

006 036537 (1978, Journal article) JRG 4/28/86 Ames Assay - Summary, Mutation Res. 57: 277 (1978). TA1535-38 strains were tested with and without activation at 2000 ug in a spot test. No increase in revertants reported. Dalapon at 85% purity.

006 036540 (1983, Journal article) JRG 4/28/86 Summary, Mutation Res. 116: 185-216 (1983). Summary of 228 pesticides tested in Ames assay. Negative in TA98 and TA100.

MUTATION, CHROMOSOME

006 036539 (1984, Microtest Research Ltd.) JRG 4/28/86 One liner:
- CHO in vitro aberrations; Dalapon, no purity stated; CHO were exposed without S-9 for 24 hours or with S-9 (2 hours) at 0, 125, 250, 500 or 1000 ug/ml, duplicate cultures, harvested at 24 hours only with no justification given; no increase in aberr; incomplete, unacceptable, upgradeable. Need description of test article and justification of a single time of sampling. Should have a shorter sampling time as well. At 24 hours, the cells would be in M₂ assuming treatment did not delay cell cycling significantly. Cells with aberrations might have died in the interim between treatment and 24 hours.

006 036541 (1979, Journal article) JRG 4/28/86 Summary, Environmental Health Perspectives 31: 81-95 (1979). Tested for non-disjunction in Aspergillus nidulans diploid strain to 800 ug/ml. No effect reported.

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MUTATION, DNA

006 036536 (1977, Journal article) JRG 4/28/86 Summary (see above).

NEUROTOXICITY, HEN

No studies on file; not required

GROUPED COMPOUNDS

Dalapon is grouped with Dalapon, magnesium salt (SB950# 502; Tolerance # 50718) and Dalapon, sodium salts (SB950# 503; Tolerance# 50719). Neither of these compounds have worksheets or data on file in Med. Tox. or indexed by the library as of May 19, 1986.

EPA ONE-LINERS

EPA one-liners not available for Dalapon or its salts as of May 15, 1986.