

Table 1. Health Effect Levels of Naled in Laboratory Animals

Route	Duration	Species	NOAEL	LOAEL	Organ/Effect	Comments	Reference
ACUTE DURATION TOXICITY							
dermal	once	rat (M)		800 mg/kg	LD ₅₀		Hayes 1982, Kidd and James 1991
dermal	once	mouse		600 mg/kg	LD ₅₀		NIOSH 2000
dermal	once	rabbit		1,100 mg/kg	LD ₅₀		Kidd and James 1991
oral	once	rat (M)		250 mg/kg	LD ₅₀		Hayes 1982
oral	once	rat (F)		281 mg/kg	LD ₅₀		Hayes 1982
oral	once	rat		430 mg/kg	LD ₅₀		Zenz et al. 1994
oral	once	mouse (M)		375 mg/kg	LD ₅₀		Hayes 1982
oral	once	mouse (F)		360 mg/kg	LD ₅₀		Hayes 1982
oral	once	mouse		222 mg/kg	LD ₅₀		NIOSH 2000
inhalation	6 hours	mouse		1,500 mg/m ³	LC ₅₀		Hartley and Kidd 1986
Intermediate Duration Toxicity							
dermal	28 days	Sprague-Dawley CD rat	1 mg/kg/day	20 mg/kg/day	Dermal irritation (erythema, edema, necrosis, and exfoliation). After 4 weeks, effects included acute ulcerative inflammation, necrosis, and epidermal hyperplasia. Systemic toxicity included plasma, erythrocyte, and brain cholinesterase inhibition and body weight gain and depression.	Most treatment-related effects resulted from 80 mg/kg/day. No treatment-related histopathologic changes other than skin effects were observed.	EPA 1999a (Based on unpublished data submitted to EPA)
oral	84 days	rat	100 ppm diet		No toxic effects	Technical-grade naled, given in diet, 99% pure	Worthing and Walker 1983
oral	27 days	rat	30 ppm diet			No depression of plasma, erythrocyte, or brain cholinesterase activities	ACGIH 1991

Table 1. Health Effect Levels of Naled in Laboratory Animals (continued)

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oral (gavage)	28 days	rat	1 mg/kg/day	10 mg/kg/day	Cholinergic effects: 10 mg/kg/day produced mild cholinergic signs and reduction of plasma and brain cholinesterase by 50%; 1 mg/kg/day produced cholinesterase inhibition in plasma (no clinical signs)	Supplemental study, 100 mg/kg/day produced mortality and more significant cholinergic signs.	EPA 1999a (Based on unpublished data submitted to EPA)
inhalation	13 weeks, 6 hrs/day, 5 days/wk.	Fischer-344 rat	0.2 mg/m ³	1 mg/m ³	Cholinesterase inhibition	Based on 25%–30% depression of plasma during study and depression of erythrocyte cholinesterase (50%–60% early and 25%–20% at end of study)	EPA 1999a (Based on unpublished data submitted to EPA)
inhalation	13 weeks, 6 hrs/day, 5 days/wk.	Fischer-344 rat		6 mg/m ³	Tremors, salivation, nasal discharge, abnormal respiration, and anogenital staining. Inhibition of brain, plasma, and erythrocyte cholinesterase	No other effects related to treatment.	EPA 1999a (Based on unpublished data submitted to EPA)
inhalation	5 weeks, 6 hrs/day, 5 days/week,	guinea pig and rat		42 mg/m ³	Decreased cholinesterase activity, discomfort, inactivity	Aerosol composed of 65% naled, 25% xylene, and 10% emulsifier-surfactant	ACGIH 1991
Inhalation	3 weeks, 6 hrs/day, 5 days/week	rat		3.4 mg/m ³	Dose-dependent inhibition of the brain, erythrocyte, and plasma cholinesterase, effects noted at 7.2 and 12.1 mg/m ³	Effects observed at all concentrations and in both sexes.	ACGIH 1991
Chronic Duration Toxicity							
oral (gavage)	Lifetime, 1 dose/day	rat		2 mg/kg	Dose-related reduction in plasma, brain, erythrocyte cholinesterase	No other adverse effects; incidence of neoplastic lesions similar to that of controls.	ACGIH 1991
oral (gavage)	Lifetime, 1 dose/day	rat	0.2 mg/kg/day		No recordable effect	Incidence of neoplastic lesions similar to that of controls.	ACGIH 1991

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oral (gavage)	1 year	beagles	0.2 mg/kg/day	2 mg/kg/day	Plasma, erythrocyte, and brain cholinesterase activity depressed. Clinical signs included emesis, diarrhea, mineralization of lumbar spinal cord (M and F), anemia, erythrocyte count reduced, hemoglobin and hematocrit lowered.	Kidney and liver affected only at high dose (20 mg/kg/day)	EPA 1999a (Based on unpublished data submitted to EPA)
oral (gavage)	2 year	Sprague-Dawley CD rats	0.2 mg/kg/day		Cholinesterase inhibition, systemic toxicity	No effect.	EPA 1999a (Based on unpublished data submitted to EPA)
oral (gavage)	2 year	Sprague-Dawley CD rats		2 mg/kg/day	Cholinesterase levels lowered in plasma (4%–33%), erythrocytes (54%–60%), and brain (24%)	LOAEL for cholinesterase inhibition. No other treatment-related effects	EPA 1999a (Based on unpublished data submitted to EPA)
oral (gavage)	2 years	Sprague-Dawley CD rats		10 mg/kg/day	See above	LOAEL for systemic toxicity	EPA 1999a (Based on unpublished data submitted to EPA)
Developmental/Reproductive Toxicity							
oral (gavage)	gestation days 6–19	Sprague-Dawley rats	10 mg/kg/day	40 mg/kg/day	Maternal toxicity, tremors, hypoactivity, discharge from mouth and eyes, dyspnea	Dams sacrificed on day 20 of gestation, no developmental toxicity related to treatment. Resorption may have occurred at high dose that produced maternal toxicity.	EPA 1999a (Based on unpublished data submitted to EPA)

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oral (gavage)	gestation days 6–19	Sprague-Dawley rats			Maternal toxicity	.	Beaudoin and Fisher 1981; EPA 1999a (Based on unpublished data submitted to EPA)
oral (gavage)	gestation days 7–19	New Zealand rabbits	8 mg/kg/day		No maternal toxicity, pilot study used to determine dose level. 2 mg/kg/day produced mild cholinergic effects; 10 mg/kg/day produced high cholinergic effects.	Highest dose tested, no maternal or developmental toxicity related to treatment.	EPA 1999a (Based on unpublished data submitted to EPA)
oral (gavage)	2 generations	rats	6 mg/kg/day	18 mg/kg/day	Systemic effects in males of both generations; reproductive indices unaffected. Decreased body weight in both generations, survival of pups reduced, consistent decrease in pup weight during lactation, F0 and F1.	Parental systemic effects	EPA 1999a (Based on unpublished data submitted to EPA)