

Table 2. Health Effect Levels of DEET in Laboratory Animals

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|--------------------------------|----------------|------------|------------------------------|-----------------------------|---|---|--------------------------------------|
| ACUTE DURATION TOXICITY | | | | | | | |
| dermal | 5 minutes | rabbit | 0.05 mL | | no skin irritation, no signs of toxicity | DEET, AI3-37220 and ethyl alcohol used in 25:25:50 formulation. | Metker 1996; Snodgrass & Harvey 1996 |
| dermal | 24 hours | rabbit | 0.5 mL | | no skin irritation, no signs of toxicity | DEET, AI3-37220 and ethyl alcohol used in 25:25:50 formulation. | Metker 1996; Snodgrass & Harvey 1996 |
| dermal | once | guinea pig | 2000 mg a.i./kg | | no signs of toxicity | DEET, AI3-37220 and ethyl alcohol used in 25:25:50 formulation. | Metker 1996; Snodgrass & Harvey 1996 |
| dermal | not specified | rabbit | | not specified | mild irritation to abraded skin | No sensitization potential shown. | Harvey 1987 |
| dermal | not specified | guinea pig | | not specified | mild irritation to abraded skin | No sensitization potential shown. | Harvey 1987 |
| dermal | once | rat | 400 mg/kg | | increased release of cytochrome c. | Treatment with DEET and 1.3 mg/kg of permethrin caused toxicity. DEET alone had no effect. | Abu-Qare and Abou-Donia 2001a |
| dermal | once | rat | | 400 mg/kg | increased urinary excretion of 6 β -hydroxycortisol. | Effect noted from treatment with DEET alone and in combination with 1.3 mg/kg permethrin. May suggest CYP3A4 induction. | Abu-Qare and Abou-Donia 2001b |
| dermal | once | rat | | 400 mg/kg | elevated ratio of 3-nitrotyrosine and tyrosine at 48 hours, marker for oxidative stress | DEET alone and in combination with PB (13 mg/kg oral). | Abu-Qare et al. 2001 |
| dermal | 4 days, 2x/day | rat | | 15 μ L | mild erythema | Mild erythema found only in 20% of test animals, ongoing experiment at date of publication. | Olson 1999 |
| dermal | once | dog | | 2-40% can/kg 1 can=198g | restlessness | Cans contained 9.0% DEET and 0.9% fenvalerate. Effects only noted in one dog. All recovered within 72 hours. | Mount et al. 1991 |
| dermal | once | cat | | 10-40% can/kg 1 can=198g | encephalopathy, restlessness, hypersalivation, vomiting, depression, tremors. | Cans contained 9.0% DEET and 0.9% fenvalerate. 1 cat euthanized 22 hours after 20% exposure, 1 cat died 2 hours after exposure. | Mount et al. 1991 |
| dermal | once | horse | 75 g (3.75-75% DEET aerosol) | | no adverse effects noted | | Palmer 1969 |

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| Route | Dura- tion | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|--------------|-----------------------|----------------|--------------|---|--|--|--------------------------------------|
| eye drop | once | rabbit | | 0.1ml DEET or CHF1 (50% DEET, 25% Dow Corning 200 Fluid, and 25% isopropyl alcohol) | corneal toxicity, mild iritis, vascularization of the eye | Animals whose eyes were washed exhibited shorter opacity duration, vascularization was irreversible, CHF1 was most potent of solutions used. | Kellner et al. 1982 |
| oral | once | rat | | 2000 mg a.i./kg | lethargy, ataxia, death in 2/5 females (25:25 formulation), 1/5 females (50:50 formulation) | DEET, AI3-37220 and ethyl alcohol used in 25:25:50 formulation, 50:50 formulation of DEET and AI3-37220 used. | Metker 1996; Snodgrass & Harvey 1996 |
| oral | once | rat | 50-200 mg/kg | 500 mg/kg | neurotoxicity | Effect on response time, decrease in activity. | Schoenig et al.1993 |
| oral | once | rat | 0-200 mg/kg | 500 mg/kg, 100 mg/kg with 5 mg/kg PB or 15 mg/kg permethrin | locomotor behavioral | DEET alone reduced speed of females in met-estrus; permethrin/DEET, PB/DEET lowered speeds more than DEET alone. | Hoy et al. 2000a |
| oral | daily for 7 days | rat | 200 mg/kg | 100 mg/kg with PB or permethrin | locomotor | Male rats had lower speed with PB + DEET, higher speed with DEET + permethrin; female rats had lower speed with PB + DEET, increased center time with DEET + permethrin. | Hoy et al. 2000b |
| oral | once | dog | | 0.66-2% can/kg 1 can=198g | encephalopathy, ataxia, seizure, hypersalivation | Cans contained 9.0% DEET and 0.9% fenvalerate, all dogs recovered within 72 hours. | Mount et al. 1991 |
| oral | once | cat | | 0.5-1% can/kg 1 can=198g | encephalopathy, depression, hypersalivation, ataxia, respiratory distress, seizure, muscle tremors | Cans contained 9.0% DEET and 0.9% fenvalerate. 1 cat euthanized after 28 hours, 1 cat died after 8 hours. | Mount et al. 1991 |
| ip | once | rat | | 200 mg/kg (given with 1-3 mg/kg PB) | DEET had no effect alone, DEET+PB inhibited whole brain cholinesterase activity | DEET did not facilitate entry of PB into central nervous system. | Chaney et al. 1998 |
| ip | once | rat | 200 mg/kg | | neurotoxicity | DEET + PB (3 mg/kg) in combination inhibited cholinesterase activity, DEET alone had no adverse effect. | Chaney et al. 2000 |
| ipl | once | rat | 56 mg/kg | 113-225 mg/kg | blood pressure and heart rate decreased | Reduction significant at 225 mg/kg, but not at 113 mg/kg. Hypotension and bradycardia significantly reduced by DEET. | Leach et al. 1988 |

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| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|---------------------------------------|---------------------|------------|-------------------------------|--|--|--|--------------------------|
| ip | once | mouse | | 200 mg/kg | seizure | Toxicity dominated by DEET, DEET and PB (5 mg/kg) caused anticonvulsant-resistant seizures. | Chaney et al. 1999 |
| ip | once | mouse | | 0.5 g/kg | increased ammonia levels | Urea cycle may have been affected by use of DEET. | Heick et al. 1988 |
| ip | once | beagle dog | | 225 mg/kg | blood pressure and heart rate decreased, decreased cardiac output | Hypotension and bradycardia significantly reduced by DEET, significant increase in P-R and Q-T intervals from ECG test. | Leach et al. 1988 |
| INTERMEDIATE DURATION TOXICITY | | | | | | | |
| dermal | 60 days | rat | | 4-400 mg/kg, alone and with 0.013-1.3 mg/kg/day permethrin | neurotoxicity | Decreased uptake of [3H]hexamethonium iodide in brainstem, decline in sensorimotor performance; also decrease in blood-testis barrier permeability. | Abou-Donia et al. 2001 |
| dermal | 60 days | rat | | 40 mg/kg | premature neuronal cell death, neural degeneration, neuron health deficiency | DEET + permethrin (0.13 mg/kg) caused cell death, DEET alone caused degeneration, all groups caused health deficiency. | Abdel-Rahman et al. 2001 |
| dermal | 5 days/wk, 9 weeks | rat | 100-1000 mg/kg/day | | | 98.3% DEET was used. Slight but insignificant increase in liver and kidney weight at highest dose. | Lebowitz et al. 1983 |
| dermal | 60 days | horse | 31 g (3.75-7.5% DEET aerosol) | 31 g (15-75% DEET aerosol) | dermatosis, excessive sebaceous secretion, skin cracked and inflamed | Adverse effects were dose-dependent. | Palmer 1969 |
| sc | daily for 30 days | rat | | 500 mg/kg/day | increased blood-brain barrier permeability | DEET given in combination with PB and Permethrin; PB able to cross blood-brain barrier and have cholinesterase-inhibiting effect. | Abou-Donia et al. 1997 |
| sc | 5 days/wk, 2 months | hen | | 500 mg/kg/day | neurotoxicity | Increased neurotoxicity due to combination with PB and permethrin. | Abou-Donia et al. 1996a |
| sc | 5 days/wk, 2 months | hen | | 500 mg/kg/day | neurotoxicity | Elevated excitability, weight loss, decrease in plasma cholinesterase activity, intermittent diarrhea, shallow breathing, decreased motor activity, neuropathological changes. | Abou-Donia 1996b |

Table 2. Health Effect Levels of DEET in Laboratory Animals, cont.

| Route | Duration | Species | NOAEL | LOAEL | Organ/Effect | Comments | Reference |
|--|--|--------------|-------------------|---|--|---|---------------------------|
| CHRONIC DURATION TOXICITY | | | | | | | |
| oral | cont. for 2 gens, then 9 mos. straight | rat | 500-2000 mg/kg | 5000 mg/kg | neurotoxicity | Increase in motor activity, increase in initial activity. | Schoenig et al. 1993 |
| DEVELOPMENTAL/REPRODUCTIVE TOXICITY | | | | | | | |
| sc | 5 days/wk, 9 weeks | rat (male) | | 0.3-1.8 mL/kg/day | death in all but low dose group; decline in rotorod test scores, skin lesions at injection sites | no surviving males in high dose group; no reproductive toxicity noted. | Wright et al. 1992 |
| dermal | gestation days 1-29 | rabbit | | 50-1000 mg/kg/day | moderate to severe skin irritation | No teratogenic effects noted. Skin irritation dose-dependent. | Angerhofer and Weeks 1981 |
| oral | gestation days 6-18 | rabbit | 30-100 mg/kg/day | 325 mg/kg/day | decreased body weight gain, food consumption. | No evidence of fetal toxicity, no external abnormalities. | Schoenig et al. 1994 |
| oral | gestation days 6-15 | rat | 125-250 mg/kg/day | 750 mg/kg/day | maternal toxicity, neurotoxicity, fetal toxicity | Toxicity included: hypoactivity, ataxia, decreased muscle tone, decreased maternal food consumption/body weight, decreased fetal body weight. | Schoenig et al. 1994 |
| sc | gestation days 6-15 | rat (female) | | 0.5-1.2 mL/kg/day | death, decline in rotorod test scores | All females died after 10 days of treatment; no developmental or reproductive toxicity noted. | Wright et al. 1992 |
| sc | gestation days 6-15 | rat (female) | 0.30 mL/kg/day | | | Only one skeletal malformation observed in control animal. | Anon 1984 |
| topical | once | chick | | 1.27 µmoles in 10 µL of DEET/mineral oil solution | cardiovascular, musculoskeletal, central nervous system effects | Developmental study on chick embryos treated topically on chorioallantoic membrane during incubation. | Kuhlmann et al. 1981 |

LEGEND

a.i. = active ingredient
ECG = electrocardiogram
ip = intraperitoneal
PB = pyridostigmine bromide
sc = subcutaneous