8. REGULATIONS AND ADVISORIES

ATSDR has derived an acute-duration inhalation MRL of 0.02 mg/m^3 for guthion based on a NOAEL of 1.24 mg/m^3 for significant reductions in erythrocyte AChE activity in male rats exposed to guthion aerosols 6 hours/day, 5 days/week for 2 weeks (Kimmerle 1976). The MRL was derived by dividing the $NOAEL_{[HEC]}$ of 0.50 mg/m^3 by an uncertainty factor of 30 (3 for extrapolation from animals to humans using dosimetric adjustment and 10 for human variability).

ATSDR has derived an intermediate-duration inhalation MRL of 0.01 mg/m^3 for guthion based on a NOAEL of 1.24 mg/m^3 for significant reductions in erythrocyte AChE activity in male and female rats exposed to guthion aerosols 6 hours/day, 5 days/week for 12 weeks (Kimmerle 1976). The MRL was derived by dividing the $NOAEL_{[HEC]}$ of 0.37 mg/m^3 by an uncertainty factor of 30 (3 for extrapolation from animals to humans using dosimetric adjustment and 10 for human variability).

The intermediate-duration inhalation MRL of 0.01 mg/m^3 was adopted for use as the chronic-duration inhalation MRL.

ATSDR has derived an acute-duration oral MRL of 0.01 mg/kg/day for guthion. The MRL is based on a BMDL of 1.04 mg/kg/day for inhibition of erythrocyte AChE activity in pregnant rats administered guthion by gavage on gestation days 6–15 (Astroff and Young 1998) and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

ATSDR has derived an intermediate-duration oral MRL of 0.003 mg/kg/day for guthion. The MRL is based on a BMDL of 0.29 mg/kg/day for inhibition of erythrocyte AChE activity in dogs exposed to guthion in the diet for 26 weeks (Allen et al. 1990) and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

ATSDR has derived a chronic-duration oral MRL of 0.003 mg/kg/day for guthion. The MRL is based on a BMDL of 0.30 mg/kg/day for inhibition of erythrocyte AChE activity in dogs exposed to guthion in the diet for 52 weeks (Allen et al. 1990) and an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

EPA has not derived an inhalation reference concentration (RfC) or an oral reference dose (RfD) for guthion.

The EPA Office of Pesticide Programs calculated an acute oral reference value of 0.003 mg/kg/day based on a LOAEL of 1.0 mg/kg/day from an acute neurotoxicity study in rats in which inhibition of plasma ChE and erythrocyte and brain AChE activities were observed (EPA 2001b). The uncertainty factor used in this assessment was 300 (10 for interspecies extrapolation, 10 for intraspecies variation, and 3 for the use of a LOAEL).

The EPA Office of Pesticide Programs calculated a chronic oral reference value 0.00149 mg/kg/day based on a NOAEL of 0.149 mg/kg/day from a 1-year chronic toxicity study in dogs in which erythrocyte AChE inhibition was observed (EPA 2001b). The uncertainty factor used in this assessment was 100 (10 for interspecies variation and 10 for intraspecies variation).

Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), tolerances for residues on raw agricultural commodities for guthion range from 0.2 to 5 ppm (EPA 2006i); see 40 CFR 180.154 for a complete listing of tolerances for residues and the corresponding raw agricultural commodities. EPA has further upheld these tolerances for residues in an order denying objections from the Natural Resource Defense Council (NRDC) to the issuance of these tolerances (EPA 2004b). Guthion is a pesticide classified for restricted use and is limited to use by or under the direct supervision of a certified applicator (EPA 2006e).

Guthion is currently registered for use on the following crops (EPA 1999a): almonds; apples/crabapples; blueberries, lowbush and highbush; Brussels sprouts; cherries, sweet and tart; nursery stock; parsley; pears; pistachios; and walnuts. On June 9, 2006, EPA proposed the cancellation of guthion usage for apples, blueberries, cherries, parsley, and pears by 2010 and a phase out of its uses on almonds, Brussels sprouts, pistachios, walnuts, and nursery stock by 2007 (EPA 2006l).

The international and national regulations and guidelines regarding guthion in air, water, and other media are summarized in Table 8-1.

Table 8-1. Regulations and Guidelines Applicable to Guthion

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification	No data	IARC 2007
WHO	Air quality guidelines	No data	WHO 2000
	Drinking water quality guidelines	No data	WHO 2004
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)[a,b,c]	0.2 mg/m^3	ACGIH 2007
EPA	AEGL	No data	EPA 2006a
	Hazardous air pollutant	No data	EPA 2006c 42 USC 7412
NIOSH	REL (10-hour TWA)[d]	0.2 mg/m^3	NIOSH 2005
	IDLH	10 mg/m^3	
OSHA	PEL (8-hour TWA) for general industry[e]	0.2 mg/m^3	OSHA 2005c 29 CFR 1910.1000
	PEL (8-hour TWA) for construction industry[e]	0.2 mg/m^3	OSHA 2005b 29 CFR 1926.55, Appendix A
	PEL (8-hour TWA) for shipyard industry[e]	0.2 mg/m^3	OSHA 2005a 29 CFR 1915.1000
b. Water			
DOT	Marine pollutant	Yes	DOT 2005 49 CFR 172.101, Appendix B
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	Yes	EPA 2006b 40 CFR 116.4
	Drinking water standards and health advisories	No data	EPA 2006m
	National primary drinking water standards	No data	EPA 2003
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	1 pound	EPA 2006f 40 CFR 117.3
	Water quality criteria for nonpriority pollutants		EPA 2006d
	Fresh water (CCC)	0.01 µg/L	
	Salt water (CCC)	0.01 µg/L	
c. Food			
EPA	Tolerances for residues (see 40 CFR 180.154 for a complete listing of tolerances for residues on raw agricultural commodities)	Range: 0.2–5 ppm	EPA 2006i 40 CFR 180.154

Table 8-1. Regulations and Guidelines Applicable to Guthion

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
FDA	Order denying objections to issuance of tolerance	Yes	EPA 2004b 69 FR 30042
	Bottled drinking water	No data	FDA 2005 21 CFR 165.110
d. Other			
ACGIH	Carcinogenicity classification	A4[f]	ACGIH 2007
	Biological exposure indices (for acetyl-cholinesterase inhibiting pesticides)		
	Cholinesterase activity in red blood cells (sampling time is discretionary)	70% of individual's baseline	
EPA	Carcinogenicity classification	No data	
	RfC	No data	
	RfD	No data	
	Pesticide classified for restricted use[g]	All liquids with a concentration >13.5%	EPA 2006e 40 CFR 152.175
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance	Yes	EPA 2006g 40 CFR 302.4
	Reportable quantity	1 pound	
	Extremely hazardous substances and their threshold planning quantities	10/10,000 pounds	EPA 2006h 40 CFR 355, Appendix A
DHHS	Carcinogenicity classification	No data	NTP 2004

[a]Inhalable fraction and vapor
[b]Skin notation: refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, either by contact with vapors, liquids, and solids.
[c]Sensitization: refers to the potential for an agent to produce sensitization, as confirmed by human or animal data.
[d]Skin designation: indicates the potential for dermal absorption; skin exposure should be prevented as necessary through the use of good work practices, gloves, coveralls, goggles, and other appropriate equipment.
[e]Skin designation
[f]A4: not classifiable as a human carcinogen
[g]Pesticide classified as restricted use: limited to use by or under the direct supervision of a certified applicator for agricultural crop uses. Criteria influencing restriction includes inhalation hazard to humans.

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = Acute Exposure Guideline Level; CCC = Criterion Continuous Concentration; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DHHS = Department of Health and Human Services; DOT = Department of Transportation; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; STEL = short-term exposure limit; TLV = threshold limit values; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization