Dioxathion

(CAS No: 78-34-2)

Health-based Reassessment of Administrative Occupational Exposure Limits

Committee on Updating of Occupational Exposure Limits,
a committee of the Health Council of the Netherlands

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1 Introduction

The present document contains the assessment of the health hazard of dioxathion by the Committee on Updating of Occupational Exposure Limits, a committee of the Health Council of the Netherlands. The first draft of this document was prepared by E Meijer, M.D. (Wageningen University and Research Centre, Wageningen, The Netherlands)*.

The evaluation of the toxicity of dioxathion has been based on reviews published by the American Conference of Governmental Hygienists (ACG99) and in the 'Handbook of Pesticide Toxicology' (Gal91). Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. In addition, in February 2000, literature was searched in the on-line databases Medline, Toxline, and Chemical Abstracts, covering the period 1964-1966 until February 2000, and using the following key words: dioxathion and 78-34-2. Data of unpublished studies were generally not taken into account. Exceptions were made for studies that were summarised and evaluated by international bodies such as the Food and Agricultural Organization/World Health Organization (FAO/WHO: Joint Meeting of the FAO Working Party of Experts and the WHO Expert Committee on Pesticide Residues (JMPR) (FAO69).

In October 2002, the President of the Health Council released a draft of the document for public review. Comments were received from the following individuals and organisations: J Soave (Health and Safety Executive, London, England).

An additional search in Toxline and Medline in May 2003 did not result in information changing the committee's conclusions.

2 Identity

name	:	dioxathion
synonyms	:	phosphorodithioic acid *S*,*S*'-1,4-dioxan-2,3-diyl *O*,*O*,*O*',*O*'-tetraethyl ester; 2,3-*p*-dioxanedithiol *S*,*S*-bis(*O*,*O*-diethyl phosphorodithioate); 1,4-dioxane-2,3-diyl *O*,*O*,*O*',*O*'-tetraethyl di(phosphorodithioate); Delnav®; Hercules AC-528
molecular formula	:	$C_{12}H_{26}O_6P_2S_4$

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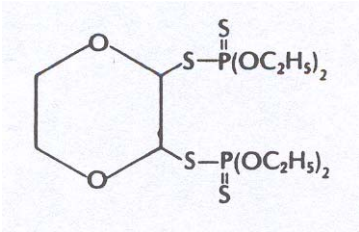
structural formula :



CAS number : 78-34-2

3 Physical and chemical properties

molecular weight	:	456.54
boiling point	:	decomposes above 135ºC
melting point	:	-20ºC
vapour pressure	:	at 25ºC: non-volatile
solubility in water	:	at 25ºC: insoluble
Log $P_{octanol/water}$	:	3.0
conversion factors	:	not applicable

Data from ACG99, Gal91.

Dioxathion is a non-volatile, very stable, dark amber liquid. Dioxathion in its most common commercial technical grade form contains 68% *cis*- and *trans*-isomers (1:2 ratio) of 2,3-*p*-dioxanedithiol *S*,*S*-bis(*O*,*O*-diethyl phosphorodithioate) as the principal ingredient. The remaining 32% consists of insecticidally active related compounds (Cas59, Fra63). It is unstable on iron or tin surfaces, and decomposes on heating above 135ºC.

4 Uses

Dioxathion is an acaricide, insecticide, and miticide used on citrus, grapes, walnuts, and stone fruits. It is also used to control ticks, lice, and horn flies on cattle, goats, dogs, horses, and sheep. Dioxathion is available as a 25% wettable powder and a 48% emulsifiable concentrate (Gal91).

According to the database of the Dutch Pesticide Authorisation Board (CTB)*, dioxathion is at present not registered for its use as an active ingredient

in pesticides in the Netherlands. In the USA, dioxathion as an active ingredient is no longer contained in any registered product, and, thus, the Office of Pesticide Programs of the US Environmental Protection Agency has characterised dioxathion as 'cancelled' in its Pesticide Registration Status (EPA98) implying that no toxicological review for a reregistration eligibility decision will be prepared.

5 Biotransformation and kinetics

^{32}P-labelled dioxathion, applied dermally to cattle, was absorbed into the blood rapidly and a peak level of radioactivity was reached within 3 hours. About 20% of the administered dose (20.4%) was recovered from the urine and traces from the faeces within 7 days after the application. Diethyl phosphate (DEP), diethylphosphorothioate (DEPT) and diethylphosphorodithioate (DEPDT) were detected in the urine. Traces of radioactivity, mainly non-metabolised dioxathion, were found in the fat of the cattle 7 days following dermal application (Cha60). Rats were treated orally with ^{32}P-labelled dioxathion (*trans*/*cis* ratio 2:1) at levels of 1, 5, and 15 mg/kg bw/day for 10 days. Metabolites were primarily excreted in the urine and to a lesser extent in the faeces. Metabolic products excreted in the first 12 hours after treatment with 15 mg/kg were identified as DEP, DEPT, and DEPDT (Art59). In a later study, male albino Sprague-Dawley rats were given single oral doses of 1.6 or 2.05 mg/kg bw of *trans*-dioxathion and 3.0 or 3.2 mg/kg bw of *cis*-dioxathion. Both isomers were ^{14}C-labelled either in the ethoxy moiety or in the dioxane ring. Both *cis*- and *trans*-dioxathion were rapidly excreted: between 75 and 98% of the administered dose within 96 hours, of which 80-87% of both isomers was present in the urine. Most of the radiocarbon recovered within 96 hours was excreted during the first 24-hour period following administration, i.e., 92-96% for urine, 72-91% for faeces, and 88-95% for $^{14}CO_2$. The principal metabolic pathway for both the *trans*- and *cis*-isomer was hydrolytic cleavage of the phosphorodithioate grouping at the phosphorus-sulphur as well as the carbon-sulphur bonds, forming DEPT (46 and 47% of administered *trans*- and *cis*-isomers, respectively) and DEPDT (15 and 3% of administered *trans*- and *cis*-isomers, respectively). A secondary pathway involves oxidation of P=S to P=O, forming the corresponding oxons and dioxons, with subsequent degradation by hydrolysis to DEP (13 and 17% of administered *trans*- and *cis*-isomers, respectively). The compound also undergoes cleavage of the dioxane ring as demonstrated by

* at: http://www.ctb-wageningen.nl/geel.html.

formation of $^{14}CO_2$ (approximately 6% of dose) from both isomers. Parent dioxathion appeared in the faeces, more with the *cis*- (4.7% of dose) than with the *trans*-isomer (2.1% of dose) (Har76).

6 Effects and mechanism of action

Human data

Acute toxicity

One case of acute poisoning has been described in a 5-year-old boy. Within 30 seconds after he had received 3/4 teaspoonful of a dioxathion formulation mistaken for cough medicine, he started vomiting. Within 2 hours after ingestion, the child was mentally dull and unable to stand; he had shallow rapid respirations, muscle fasciculation, tearing, and miosis. Serum cholinesterase (ChE) activity was less than 10% of normal. After 12 hours of appropriate treatment, most of the signs and symptoms cleared. The dose ingested was estimated to be 1100 mg of technical dioxathion, equivalent to 75 mg/kg bw. The absorbed dose was somewhat less; both the colour and odour of the formulation were detected in the vomitus (Gal91).

Short-term toxicity

In a study with human volunteers, 5 males and 5 females were given 0.075 mg/kg bw/day of dioxathion (as Delnav), for 28 days. No changes were observed in plasma ChE or red blood cell AChE activity compared to pre-treatment levels. Treatment was continued for another 28 days at levels of 0.075 and 0.150 mg/kg bw/day in one male and one female per dose group. No inhibition of red blood cell AChE was observed at any of these levels, but plasma ChE was inhibited by 10 to 20% in the 2 subjects who received 0.150 mg/kg/day. Two weeks after cessation of exposure, plasma ChE activity returned to pre-treatment level. Transient clinical symptoms, like nausea, vomiting, diarrhoea, headache, prolonged menstrual cycle, and hay fever were reported throughout the 3-4 months observation period. In 4 control subjects, receiving placebos, identical symptoms were reported during the same period. The symptoms, therefore, were considered not related to Delnav administration (Fra63).

Animal data

Irritation and sensitisation

Dioxathion produced mild, transient conjunctivitis but no transient or permanent corneal damage when 0.1 mL was instilled into the eyes of rabbits (Fra63).

The committee did not find data from studies on the possible sensitising properties of dioxathion.

Acute toxicity

Acute lethal toxicity values in test animals are summarised in Table 1.

Table 1 Summary of acute lethal toxicity studies for dioxathion in experimental animals.

exposure route	vehiculum	species (strain)	sex	LC_{50}/LD_{50}	reference
inhalation		rat (Wistar)	male, female	1398 mg/m^3 (1 h)	Fra63
		mouse	male, female	340 mg/m^3 (1 h)	Fra63
dermal	xylene	rat (Sherman)	male	235 mg/kg bw	Gai60
	xylene	rat (Sherman)	female	63 mg/kg bw	Gai60
	xylene	rabbit	male, female	100 mg/kg bw	Fra63
	none	rabbit	male, female	106 mg/kg bw	Fra63
		rabbit	not specified	85 mg/kg bw	NIO02
oral	corn oil	rat (Osborne-Mendel)	male	118 mg/kg bw	Hag61
	peanut oil	rat (Sherman)	male	43 mg/kg bw	Gai60
	peanut oil	rat (Sherman)	female	23 mg/kg bw	Gai60
	corn oil	rat (Holtzman)	male	50 mg/kg bw	Fra63
	ethanol-propylene glycol	rat (Sprague-Dawley)	male	45 mg/kg bw	Fra63
	corn oil	rat (Sprague-Dawley)	male	64 mg/kg bw	Fra63
		rat	not specified	20 mg/kg bw	NIO02
	corn oil	mouse	male	176 mg/kg bw	Fra63
	none	dog (mongrel)	male, female	10-40 mg/kg bw	Fra63
		chicken (Rhode Island Red)	female	316 mg/kg bw	Fra63
intraperitoneal	ethanol-propylene glycol	rat (Sprague-Dawley)	female	30 mg/kg bw	Fra63
		mouse	not specified	33 mg/kg bw	NIO02

The *cis*-isomer is more toxic than the *trans*-isomer (subcutaneous rat LD_{50}: *cis*: 66-86 mg/kg bw; *trans*: 230-290 mg/kg bw). Hypersalivation, diarrhoea, lachrymation, rapid breathing, and tremors were typical symptoms of toxicity. Death was usually preceded by clonic seizures. Following intraperitoneal administration of 13 mg/kg bw of Delnav to rats, red blood cell and brain AChE activities were inhibited by 60-80% and plasma ChE by 100%. Recovery to normal activities required 3 weeks for plasma ChE and over 3 weeks for red blood cell and brain AChE (Fra63).

Delnav did not produce acute delayed neurotoxicity in hens following single oral doses of 10-1000 mg/kg bw or subcutaneous doses of 25-200 mg/kg bw (Fra63).

Short-term toxicity

Weanling albino Charles River rats (n=25/sex/group) were given dietary levels equivalent to 0, 0.077, 0.22, 0.78, 7.5, and 37 mg/kg bw of Delnav, for 90 days. Five animals per sex per group were sacrificed after 3, 6, 9, and 13 weeks of treatment while the remaining 5 animals per sex were placed on a control diet for 3 weeks before being sacrificed. Animals fed 37 mg/kg bw/day were sacrificed after one week because of marked food refusal and body weight loss. Clinical signs observed were limited to hyperexcitability and slight tremors in female rats fed 7.5 mg/kg bw/day. Neither increase in mortality, nor any gross or microscopic pathology related to the compound were observed in any of the groups. Throughout the treatment period, plasma ChE and red blood cell AChE were inhibited by about 95% and brain AChE by about 80% in rats fed 7.5 mg/kg bw/day. After cessation of administration of Delnav, plasma ChE returned to almost normal activity while brain and red blood cell AChE recovered more slowly remaining statistically significant below control levels. At 0.78 mg/kg bw, treatment did not affect brain AChE activity. Plasma ChE and red blood cell AChE activities were statistically significantly lower than those in control animals throughout treatment but returned to normal values during the recovery period. At 0.22 and 0.077 mg/kg bw, no statistically significant alterations in brain or red blood cell AChE or plasma ChE were observed (Fra63). According to the committee, the NOAELs in this study are 0.22 mg/kg bw for plasma ChE and red blood cell AChE activities and 0.78 mg/kg bw for brain AChE activity.

In another 13-week study, 30 male and 30 female rats (strain: Holzman) were given levels equivalent to 0.01, 0.05, 0.25, and 1.25 mg/kg bw/day of dioxathion in the diet. Fifteen animals of each sex were used for determination of

cholinesterase activities in brain, liver, and serum and 15 of each sex for determination of carboxylesterase (aliesterase) activity. The latter enzyme was measured to investigate possible potentiation by Delnav of the toxicity of organophosporus pesticides containing carboxyester linkages, e.g., malathion. At 1.25 mg/kg bw/day, the chemical produced inhibition of brain AChE (by 2-30%), serum ChE (by 45-71%), and liver ChE (by 47-58%) activities. Feeding of 0.25 mg/kg bw did not inhibit brain AChE activity, but serum and liver ChE activities were depressed by 0-27% and 10-34%, respectively. At 0.05 mg/kg bw/ day and below, no significant inhibition of the enzyme activity was found in any of the tissues. The NOAEL for inhibition of brain AChE activity was 0.25 mg/kg bw and for inhibition of serum or liver ChE activity 0.05 mg/kg bw. Carboxylesterase was found to be more susceptible to inhibition by Delnav than cholinesterase activities. The NOEL for inhibition of carboxylesterase activity in liver was 0.01 mg/kg bw and in serum 0.05 mg/kg bw (Dub68).

In a range-finding dog study (mongrel; n=2/sex/group), Delnav was administered at doses equivalent to 0.25 and 0.80 mg/kg bw, for 12 days (5 days/week), 2.5 mg/kg bw, for 10 days, and 8.0 mg/kg bw, for 5 days. At the top dose only, dogs developed symptoms of intoxication (diarrhoea, hypersalivation, tremors). Concomitant red blood cell AChE and plasma ChE activities were inhibited by 79% and 75%, respectively. Administration of 2.5 mg/kg bw for 10 days produced inhibitions of 63% for red blood cell AChE and of 87% for plasma ChE activity. No significant inhibition of red blood cell AChE activity was observed at the lowest dose. However, plasma ChE activity was inhibited by 25%. The NOAEL for inhibition of red blood cell AChE activity was 0.25 mg/kg bw (Fra63). In the subsequent study, groups of dogs (mongrel; n=2/sex/group) fed levels equivalent to 0.013, 0.025, or 0.075 mg/kg bw, 5 days/week, for 90 days, did not show statistically significant inhibition of either red blood cell AChE or plasma ChE, measured throughout the study and during a 4-week exposure-free period, when compared to 3 pre-treatment cholinesterase values (Fra63). The NOAEL in dogs for plasma ChE and red blood cell AChE in this study was 0.075 mg/kg bw/d, the highest dose tested.

A summary of the above studies is presented in Table 2.

Table 2 Summary of short-term oral toxicity studies for dioxathion.

species (strain; number; sex)	dose levels (mg/kg bw/d)	exposure duration	critical effect[a]	NOAEL (mg/kg bw/d)	reference
rat (Charles River ; n=25/sex/group)	0.077, 0.22, 0.78, 7.5, 37	13 weeks	BAChE RAChE	0.78 0.22	Fra63
rat (Holzman; n=30/sex/group)	0.01, 0.05, 0.25, 1.25	13 weeks	BAChE	0.25	Dub68
dog (mongrel; n=2/sex/group))	0.25, 0.80 (12 d); 2.5 (10 d); 8.0 (5 d)	5, 10, 12 days	RAChE	0.25	Fra63
dog (mongrel; n=2/sex/group))	0.013, 0.025, 0.075	13 weeks	RAChE	0.075	Fra63

[a] BAChE = brain AChE; RAChE = red blood cell AChE.

Long-term toxicity and carcinogenicity

Osborne-Mendel rats (n=50/sex/group) were given technical-grade dioxathion (purity: 68-75%) in the feed for 33 weeks, at concentrations equivalent to 0, 2.6, or 5.2 mg/kg bw/day for males and 0, 1.3, or 2.6 mg/kg bw/day for females. Then, dioxathion concentrations were increased to 3.5 or 7.0 mg/kg bw/day for males, and to 1.75 or 3.5 mg/kg bw/day for females, during the following 45 weeks. After the 78-week dosing period, observation of the rats continued for an additional 33 weeks. Clinical signs of toxicity in all treated groups included tremors, hyperactivity, and apparent hind-limb paralysis. No dose-related changes in mortality or in mean body weights were seen. A variety of neoplasms was observed in treated and control animals of both sexes. However, the incidence of neoplasms in treated groups was not statistically significantly different from controls. Gross and microscopic examination did not reveal any dose-related non-carcinogenic effects. Cholinesterase activities were not determined (NCI78).

Dioxathion was also administered in the feed of B6C3F1 mice (n=50/sex/group) at initial concentrations equivalent to 0, 23, or 47 mg/kg bw/day for males and 0, 37, or 74 mg/kg bw/day for females. Twenty animals of each sex were used as controls. In week 18, concentrations were increased to 31 or 62 mg/kg bw/day for males, and to 52 or 105 mg/kg bw/day for females. At the end of the 78-week dosing period, the mice were observed for an additional 12 to 13 weeks. No clinical signs of intoxication were reported. Survival and mean body weight gain were not affected. There was no evidence of carcinogenicity in either male

or female mice. However, a dose-related increase in the incidence of nodular hyperplasia of the liver was observed in male mice. Cholinesterase activities were not determined (NCI78).

Mutagenicity and genotoxicity

Dioxanthion was tested for reverse mutations in several strains of *S. typhimurium* (TA97, TA98, TA100, TA1535, TA1537) at concentrations of 0.10, 0.33, 1.0, 3.3, 6.6, and 10 mg/plate in the presence and absence of rat or hamster liver S9. The compound was positive in all strains at 1.0 mg/plate and above (Mor86).

The committee did not find results from other mutagenicity/genotoxicity studies on dioxathion.

Reproduction toxicity

A 3-generation reproduction study was conducted in groups of weanling Sprague-Dawley albino rats, each consisting of 8 males and 16 females. The animals were fed dietary levels equivalent to 0, 0.15, and 0.5 mg/kg bw of Delnav, for 39-42 weeks, starting at 28 days of age. No treatment-related increased mortality and no changes in body weight gain, behaviour, haematological and biochemical data, and gross and microscopic histology were found in any of the parental generations after 39-42 weeks of treatment. The incidence of tumours in the treated groups was not different from control animals. No effect on mating, fertility, and pregnancy indices, and on gestation time was observed in test animals compared to the control group. No effect on parturition, number of litters and live births, pup viability at birth and at various intervals in the lactation period, and on weanling body weight gain was noted at either level. Brain AChE, red blood cell AchE, and plasma ChE activities were not different between test and control groups of F2 parental animals. In summary, findings among all test animals, 3 parental generations and 6 litters of progeny were comparable to control animals for all parameters. The NOAEL for parental and reproductive effects in this study was 0.5 mg/kg bw, the highest dose tested (Ken73).

7 Existing occupational exposure limits

The current administrative occupational exposure limit (MAC) for dioxathion in the Netherlands is 0.2 mg/m^3, 8-hour TWA, with a skin notation.

Existing occupational exposure limits in some European countries and the USA are summarised in the annex.

8 Health hazard assessment

Workers can be exposed to dioxathion through inhalation of aerosols or by direct skin contact. No quantitative data is available of the percentage absorption of dioxathion through the lungs. The dermal absorption is about 20% of the applied dose in cattle, but no data is available of skin absorption in humans. The extent of absorption following oral intake is between 75% and 98% of the dose in rats. Following absorption, dioxathion is rapidly metabolised into breakdown products, e.g., DEPT, DEP and DEPDT, which are mainly excreted in the urine.

No cases of intoxication have been reported in humans involved in manufacture or use of the compound. One case of intoxication following ingestion of dioxathion by a child showed that it takes 2-3 hours for symptoms and signs to become manifest, such as, inhibition of plasma ChE, respiratory difficulties, and muscle fasciculations. In a human volunteer study, oral intake of 0.075 for 28 days, did not produce inhibition of plasma ChE or red blood cell AChE activity in 5 males and 5 females while treatment for another 28 days at levels of 0.075 and 0.15 mg/kg bw (n=1/sex/group) caused a decrease of plasma ChE activity by 10 to 20% in the high-dose group. Red blood cell AChE activity was not affected. A LOAEL for red blood cell AChE inhibition could not be established. The NOAEL was, therefore, equal to or greater than 0.150 mg/kg bw/day.

Dioxathion is slightly irritating to eyes of rabbits. The committee did not find data on skin irritation or sensitisation of the compound. Based on results of acute lethal toxicity studies in test animals, the committee considers the compound as toxic after respiratory, dermal, and oral exposure. The compound did not cause acute delayed neurotoxicity in hens when tested at single oral or subcutaneous doses up to 1000 and 200 mg/kg bw, respectively. No significant systemic effects have been reported in short-term studies in rats and dogs, apart from inhibition of plasma ChE, red blood cell AChE, or brain AChE. Brain and red blood cell AChE were found to be less sensitive to inhibition by dioxanthion compared to plasma ChE. In two 13-week studies in rats, the NOAELs for brain AChE inhibition were 0.78 and 0.25 mg/kg bw, respectively, and for red blood cell AChE inhibition were 0.22 or 0.25 mg/kg bw; in a 13-week dog study, the NOAEL for red blood cell AChE inhibition was equal to or greater than 0.075 mg/kg bw (higher doses not tested).

Dioxathion was positive in one bacterial mutagenicity test. The committee did not find data from other *in vitro* or *in vivo* mutagenicity/genotoxicity tests. Carcinogenicity studies in rats and mice did not show a treatment-related increase in tumour incidence. The committee concludes that the positive result of the bacterial mutagenicity test was not reflected in carcinogenicity. The compound did not induce maternal or reproduction toxicity in rats at a dietary concentrations up to 0.5 mg/kg bw. No teratology studies have been reported.

Based on the above data, the committee concludes that the mechanism of toxicity of dioxathion in mammals is through inhibition of AChE activity in nerve tissue. The committee identifies inhibition of AChE in brain tissue as the most sensitive adverse toxic effect of dioxathion in animal studies, occurring at dose levels that are lower than those causing other toxic effects. In human beings, for obvious reasons, brain AChE cannot be measured. Instead, red blood cell AChE, being the same molecular target for inhibition by organophosporus pesticide as brain AChE, is used as a surrogate for brain AChE in assessing the health risk of exposure to dioxathion (Jey94).

The committee takes the dose of 0.075 mg/kg bw that did not affect plasma ChE and red blood cell AChE activity in 10 volunteers exposed for 28 days and in 2 exposed for an additional, subsequent 28 days as a starting point in deriving a health- based- recommended occupational exposure limit (HBROEL). Since workers are exposed for 5 days a week, this NOAEL from a continuous study (i.e., 7 days a week) is adjusted by multiplying with a factor of 7/5 resulting in a no-adverse-effect level (NAEL) of 0.105 mg/kg bw. For extrapolation to a HBROEL, an overall assessment factor of 3, covering intraindividual variation, is applied, resulting in a NAEL for humans of 0.035 mg/kg bw/day. Assuming a 70-kg worker inhales 10 m^3 of air during an 8-hour working day and a retention of 100%, and applying the preferred value approach, a health-based occupational exposure limit of 0.2 mg/m^3 is recommended for dioxathion.

The committee recommends a health-based occupational exposure limit for dioxathion of 0.2 mg/m^3, as an 8-hour time-weighted average (TWA).

A ratio of the dermal LD_{50} and the calculated inhalation LD_{50} of less than 10 is proposed as one of the criteria for assigning a skin notation (ECE98). Since this criterion is met for dioxathion*, the committee recommends a skin notation.

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* The dermal LD_{50} in rats is 235 or 63 mg/kg bw, for males or females, respectively; the inhalation LD_{50} calculated from the 1-hour LC_{50} of 1398 mg/m^3 in rats (assuming a retention of 1.0 and a minute volume of 125 mL/min for a 200-g weighing rat) is ca. 50 mg/kg bw.

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NIO02 National Institute for Occupational Safety and Health (NIOSH). Phosphorodithioic acid, S,S'-p-dioxane-2,3-diyl O,O,O',O'- tetraethyl ester. In: Registry of Toxic Effects of Chemical Substances (RTECS) (last update: July 2000); http://www.cdc.gov/niosh/rtecs/te331dfo.html.

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Swe00 Swedish National Board of Occupational Safety and Health. Occupational exposure limit values and measures against air contaminants. Solna, Sweden: National Board of Occupational Safety and Health, 2000; Ordinance AFS 2000:3.

SZW03 Ministerie van Sociale Zaken en Werkgelegenheid (SZW). Nationale MAC-lijst 2003. The Hague, the Netherlands: Sdu, Servicecentrum Uitgevers, 2003: 25.

TRG00 TRGS900. Grenzwerte in der Luft am Arbeitsplatz; Technische Regeln für Gefahrstoffe. BArbBl 2000; 2.

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Annex

Occupational exposure limits for dioxathion in various countries.

country - organisation	occupational exposure limit		time-weighted average	type of exposure limit	note[a]	reference[b]
	ppm	mg/m^3				
the Netherlands						
- Ministry of Social Affairs and Employment	-	0.2	8 h	administrative	S	SZW03
Germany						
- AGS	-	0.2			S	TRG00
- DFG MAK-Kommission	-	-				DFG02
Great Britain						
- HSE	-	0.2	8 h	OES	S	HSE02
Sweden	-	-				Arb02
Denmark	-	0.2	8 h		S	Swe00
USA						
- ACGIH	-	0.1[c]	8 h	TLV	S, A4[d]	ACG03b
- OSHA	-	-				ACG03a
- NIOSH	-	0.2	10 h	REL	S	ACG03a
European Union						
- SCOEL	-	-				EC03

[a] S = skin notation, which means that skin absorption may contribute considerably to body burden; sens = substance can cause sensitisation.

[b] Reference to the most recent official publication of occupational exposure limits.

[c] Measured as inhalable fraction of vapour and aerosol.

[d] Classified in carcinogen category A4, i.e., not classifiable as a human carcinogen: agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories.