# Oxalic acid

(CAS No: 144-62-7)

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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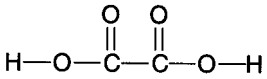
## 1 Introduction

The present document contains the assessment of the health hazard of oxalic acid 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 AAE Wibowo, Ph.D. (Coronel Institute, Academic Medical Centre, Amsterdam, the Netherlands).

In November 1998, literature was searched in the databases Medline, Embase, and Chemical Abstracts, starting from 1966, 1988, and 1970, respectively. CD-ROM databases HSELINE, CISDOC, MHIDAS, and NIOSHTIC, covering the period from 1985/1987 up to and including 1998, and POLTOX (Toxline, Cambridge Scient. Abstr., FSTA), covering the period 1990 up to and including 1994, were consulted as well. The following key words were used: oxalic acid and 144-62-7. Review papers from Baselt and Cravey (Bas89), Von Burg (Bur94), Hodgkinson and Zarembski (Hod68), Katz and Guest (Kat94), and Lundberg (Lun88) have been used. Where relevant, the original publications were reviewed and evaluated as will be indicated in the text. The final literature search was carried out in Toxline and Medline in September 2003.

In October 2003, the President of the Health Council released a draft of the document for public review. No comments were received.

## 2 Identity

| | | |
|---|---|---|
| name | : | oxalic acid |
| synonyms | : | ethanedioic acid; dicarboxilic acid |
| molecular formula | : | $C_2H_2O_4$ |
| structural formula | : |  |
| CAS number | : | 144-62 –7 |

Data from ACG99.

## 3 Physical and chemical properties

| | | |
|---|---|---|
| molecular weight | : | 90.04 |
| boiling point | : | not available |
| melting point | : | 189.5°C; decomposes |
| flash point | : | not available |
| vapour pressure | : | <0.1Pa |
| solubility in water | : | soluble (at 20°C: 14 g/100mL ) |
| log $P_{octanol/water}$ | : | -1.74 (estimated) |
| conversion factors | : | not applicable |

Data from ACG99, NLM01, http://esc.syrres.com.

Anhydrous oxalic acid is an odourless, white powder. Upon heating, it decomposes into carbon dioxide, carbon monoxide, formic acid, and water. The dihydrate is an odourless, colourless crystalline substance (ACG99, NLM01).

## 4 Uses

The major uses of oxalic acid are in textile finishing, stripping and cleaning, calico printing and dyeing, paint, varnish, and rust removal, metal and equipment cleaning, wood cleaning, dye manufacture, chemical synthesis, and in paper, ceramics, photographic, and rubber industries (Kat94). In the US, EPA has published a Reregistration Eligibility Document for the use of oxalic acid as a disinfectant to control bacteria and germs, and as a sanitiser in toilet bowls, urinals, and bathroom premises (EPA92). According to the database of the Dutch Pesticide Authorisation Board (CTB), oxalic acid is not permitted for such uses in the Netherlands*.

Oxalate is present in certain dietary plants, such as spinach, rhubarb, and tea (Bur94).

## 5 Biotransformation and kinetics

The committee did not find information on the kinetics of oxalic acid following inhalation or dermal exposure.

Following oral exposure, absorption through the gastrointestinal tract of normal healthy human is estimated to be 2.4% of the total oxalate load in food.

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

Most of the absorption occurs within 1 to 8 hours after ingestion (Pre84). Berg (Ber90) and Williams (Wil79) reported an absorption by the gastrointestinal tract of 5 to 10%. In rats orally (gavage) dosed with $^{14}C$-labelled oxalate, ca. 25 and 73% of the radiolabel were recovered in the urine and faeces, respectively, within 7 days (Ban79). In a normally fed dog, 80% of a single oral dose of 1000 mg of oxalate was excreted in the urine within 9 days, while in a fasting dog, a dose of 1338 mg caused anuria for several days followed by urinary excretion of 75% of the dose over the next 9 days. In pigs, 45-50% of an oral dose was urinary excreted (Bur94).

There is little or no binding of oxalic acid by plasma proteins at physiological pH, and whole blood oxalate concentrations are only slightly higher (average 1.7 mg/L) than plasma concentrations (Bas89). An average serum oxalate concentration of 1.4 mg/L with an upper limit of 2.4 mg/L was found in 20 normal subjects (Bas89, Hod68).

There is no evidence that oxalate is utilised or further metabolised by human tissues (Hod68). Following intravenous injection of radiolabelled oxalic acid, volunteers excreted 88-99% of the radiolabel in the urine within 36 hours (Bas89). The elimination half-life of oxalate was estimated to be about 90 minutes (Ber90). Wahl and Kallee reported levels of 0.10 and 0.18 mmol/L oxalic acid in the saliva of healthy male and female subjects, respectively (Wah94). Urinary oxalic acid, which usually ranges from 8 to 40 mg/day, is derived largely from dietary ascorbic acid (35-44%), from the metabolism of glycine (40%), and the remainder from minor metabolic sources and from dietary oxalic acid. Calcium oxalate is a major constituent of urinary calculi and also often occurs as crystals in freshly voided urine. Normal tissue concentrations of oxalate, determined on single specimens, are 0.6, 2.3, and 4.0 mg/kg in the brain, the liver, and the kidney, respectively (Bas89).

## 6 Effects and mechanism of action

The primary target organs for systemic oxalate toxicity appear to be the kidneys and the nervous system (Bur94). Systemic effects of oxalic acid toxicity are attributed largely to the calcium-complexing action of the acid, which depresses the level of calcium ions in body fluids. The resulting condition of hypocalcaemia produces severe disturbances in the activity of the heart and neural system (Kat94). The formation of calcium oxalate crystals, which is one of the factors in the pathogenesis of urinary stone disease, may also be attributed to exposure to oxalic acid.

## Human data

Exposure to airborne levels of oxalates is irritating to the eyes, nose, and throat; inhalation causes breathing difficulties and loss of consciousness (Bur94). Systemic oxalate poisoning in humans is characterised by local corrosive effects, renal damage, and a marked fall in plasma calcium levels, resulting in shock, collapse, and convulsions (Bas89).

Oxalic acid may cause corrosion of the skin (Fit85). Skin lesions may be manifested by dermal cracking and slowly healing ulcers (Bur94). Gehring et al. reported that oxalic acid is a potent sensitising agent. Skin testing of oxalic acid in 26 patients with eczema on the dorsum of the foot from leather caused a positive reaction in 53.8% of these patients (Geh88).

Laerum and Aarseth studied the cumulative prevalence of urolithiasis-induced colic episodes in 393 male workers of a Norwegian railroad depot using a questionnaire. A saturated oxalic acid solution had been used in repainting and cleaning of railroad cars for 28 years. Occupational exposure may have occurred by inhalation of oxalic-acid-containing steam or dust, and by skin contact with the solution. The levels of oxalic acid in workroom air were not measured. They workers were divided into 3 groups according to the magnitude of exposure: workers involved in the paint shop work with ‘high’ exposure, 3-4 hours/day (n=15); workers not involved in the paint shop work but occasionally using oxalic acid with ‘low-moderate’ exposure, 1-8 hours/week (n=25); and a group with no exposure to oxalic acid (n=353). A significant difference in the prevalence rate of urinary stone colic episodes was found between the groups with prevalence rates of 53.3, 32.0, and 11.9% for the ‘high’, ‘low-moderate’, and not exposed group, respectively, compared with a regional prevalence rate of 2 cases per 1000 inhabitants per year. A selected group of 7 persons from the paint shop, who had had the most severe and long-lasting exposure to oxalic acid, reported a constant pharyngeal irritation and coughing when inhaling the steam containing oxalic acid, pollakiuria (an abnormal condition characterised by unduly frequent passage of urine), and slight dysuria, which regularly occurred during the first 20-30 minutes of exposure (Lae85)

A comparative epidemiological study on renal lithiasis in gypsies in Spain showed that there was a relationship between family history of lithiasis and consumption of meat products, dairy products, and food rich in oxalic acid. The study included 11,871 gypsies and 4621 non-gypsies from the provinces of Granada and Almeria, and was based on personal interviews of a cultural, anthropological, and social nature (Tor84).

Ingestion of sorrel (*Rumex crispus*) with an estimated amount of 6 to 8 g of oxalic acid caused vomiting, diarrhoea, and impaired consciousness followed by hypocalcaemia, severe metabolic acidosis, kidney and liver failure, deep coma with respiratory depression, and death (from ventricular fibrillation) of a 53-year old man. Necropsy revealed hepatic centrilobular necrosis, swelling and retraction of glomeruli, and crystals of calcium oxalate in the renal cortex and vessels and capillaries of the liver, lung, and heart (Far89). In another case, accidental ingestion of about 15 g of oxalic acid had caused acute renal insufficiency. Renal biopsy showed acute tubular necrosis (Cec73).

## Animal data

*Irritation and sensitisation*

Like other strong acids, oxalic acid produces severe local burns of eyes, mucous membranes, and skin in animals. However, because its alkali salts are also corrosive, the acidity of oxalic acid is probably not primarily responsible for its effects on mucous membranes (Kat94).

Oxalic acid, applied at an amount of 500 mg for 24 hours, was stated to be mildly irritating to the skin of rabbits (Kat94). When an ear of a rabbit was partly immersed in a saturated solution (stated to be 9.1% at 22ºC) of anhydrous oxalic acid for 1 minute, no cutaneous reaction occurred while immersion for 5 minutes resulted in soon appearing redness that was still present with scaliness after 24 hours. When a lintine disc saturated with a similar oxalic acid solution was applied to the shaved back skin of a rabbit for 24 hours, no skin reaction was seen (Kla55).

Referring to separate reports, it was stated that instillation of 250 µg for 24 hours or 100 mg for 4 seconds into the eyes of rabbits had caused severe irritation (Kat94).

*Acute toxicity*

The committee did not find data on the effects of oxalic acid following single exposure by inhalation.

Dermal application of a dose of oxalic acid (as a 5% aqueous solution) of 20,000 mg/kg bw did not induce mortality in rabbits. Following oral administration, $LD_{50}$ values of 474 and 375 mg/kg bw were listed for male and female rats, respectively. When injected intraperitoneally, an $LD_{50}$ of 270 mg/kg bw in mice was mentioned (Kat94).

Kluwe et al. studied the effects of oxalic acid on the urogenital system of male F344 rats by giving the animals a single subcutaneous injection of 75 mg/kg bw and subsequent evaluation after 24 hours and 3, 8, 25, and 75 days. Many of the dosed rats developed local lesions, like loss of hair and hard subcutaneous lumps. No behavioural changes or mortality were seen. The treatment produced glucosuria that persisted for at least 3 days. The serum calcium ion concentrations were unaffected, but serum sodium and potassium ion concentrations were transiently increased 24 hours and 3 days post-treatment. The serum creatinine concentrations were increased progressively 24 hours and 3 days after treatment, but returned to normal by the eighth day. Similar effects occurred with blood urea nitrogen (BUN). Histological examinations showed birefringent crystals of calcium oxalate at the cortico-medullary junction and in the papilla of the kidneys, and were often associated with focal necrosis and mineralisation. There were no changes in weight and histology of the epididymides and testes. Other organ weights, including that of the brain, were unaffected by the treatment (Klu83).

*Repeated-dose toxicity*

The committee did not find studies on the toxicity of oxalic acid following repeated exposure by inhalation. In the available oral studies, no complete toxicological evaluation was made.

Daily dietary administration of 0, 2.5% (females: 1980 mg/kg bw/day; males: 1780 mg/kg bw/day), and 5% (females: 5300 mg/kg bw/day; males: 5200 mg/kg bw/day), continuously for 70 days, to rats (Long-Evans; n=9-12/sex/group) caused mortality rates of 25% and less than 10% in the high- and low-dose group, respectively. In the high-dose group, clinical signs of toxicity (emaciation, stunted, gaunt with arched backs), increased food and water consumption, decreased body weights and growth rates, decreased absolute and increased relative organ weights (liver, kidney, spleen, adrenals, thyroid, reproductive organs), absence of body fat, minimal presence of adipose tissue normally adherent to visceral and endocrine tissues, and histological lesions in the kidneys and male and female reproductive tissues were observed. In the low-dose group, there were no overt signs of toxicity, and food and water consumption were comparable to that of controls. Body weight, growth rate, organ weight, and histological changes were similar but less consistent and pronounced than those found in the high-dose group (see also under ‘Reproduction toxicity’) (Gol77). In a subsequent study using the same protocol as described above, the effects of oxalic acid on the thyroid function were

investigated. Based on food intake, Goldman and Doering calculated that the daily intakes were 2100 and 1900 mg/kg bw for low-dose females and males, respectively, and 5300 mg/kg bw for both high-dose females and males. No data on mortality were presented, but otherwise results concerning overt signs of toxicity, body weight (gain), and liver, kidney, spleen, and endocrine tissue weights confirmed those of the previous study. Absolute thyroid weights were decreased in the high-dose, but not in the low-dose animals while relative thyroid weights were decreased in both dose groups. A marked reduction in the 24-hour radiolabelled iodine uptake was found in the high-dose, but not in the low-dose group. Furthermore, there were reductions in plasma $^{125}I$ in both dose groups, dose-related increases - being statistically significant in the high-dose group - in plasma thyroid-stimulating hormone (TSH) levels, and increases in the thyroidal labelling of triiodothyronine ($T_3$) content in the high-dose group, while labelling of tetraiodothyronine ($T_4$) was unaffected. The authors concluded that dietary ingestion of doses of 5300 mg/kg bw oxalic acid can induce hypothyroidism or exacerbate conditions of latent hypothyroidism (Gol79).

In the first, dose range-finding part of a reproduction toxicity according to the NTP Reproductive Assessment by Continuous Breeding (RACB) protocol (see below under 'reproduction toxicity'), CD-1 mice (n=8/sex/group) were given daily oral (drinking water) doses of oxalic acid dihydrate of 0.25 to 5.0% (estimated to be ca. 350 to 3500 mg/kg bw/day), for 14 consecutive days. Clinical signs of toxicity (rough hair coat; hunched back) were observed in almost all animals of the 2 highest dose groups (i.e., 2.5 and 5%, ca. 1600 and 3500 mg/kg bw/day) starting at day 6 while one male animal of the 1%-dose group (ca. 1000 mg/kg bw/day) had rough hair coat. Body weight losses (by about 35-45%) and very high mortality (75-88%) were seen in the 2 highest dose groups. There were no deaths (apart from one male of the 0.25%-dose group) or effects on body weight gain (apart from a 3% increase in males of the 1%-dose group vs. 11% in male controls) in any of the other groups.

In the second part, parental animals (n=20/sex/group; controls: n=40/sex) were given daily oral (drinking water) doses of 0, 0.05, 0.10, and 0.2% (estimated to be 0, 89, 162, and 275 mg/kg bw/day, respectively), for 18 weeks. All but 10 animals per sex representative of the control and high-dose group were sacrificed during week 19-21. Of the selected animals necropsied at week 23, body, liver, kidney (including adrenal glands), prostate, testis, cauda, epididymis, and seminal vesicle (with coagulating glands) weights and blood serum calcium levels were determined and sperm morphology and vaginal cytology evaluated (see below under 'reproduction toxicity'). It was, however, not clear to the committee whether these high-dose animals were treated during

week 18-23. No symptoms of toxicity or compound-related mortality were observed during treatment. In the 2 highest dose groups, there was a dose-related decrease in water consumption. No effect on body weight (gain) was noticed in any of the treated groups at any of the measurement points. Apart from a statistically significant increase in kidney weights adjusted for body weight at necropsy* in females, no effect was seen on body weight, absolute and adjusted liver and kidney weight, and blood serum calcium levels in the high-dose mice selected for necropsy. In males, there was a decrease in absolute and adjusted prostate weight while the other reproductive organ weights did not differ from those of controls (Gul85).

When solutions of oxalic acid of 0, 30, 50, or 60 mg/animal (i.e., 0, 136, 227, 272 mg/kg bw) were orally (gavage) administered to female rats (Wistar; n=5/group) mated 10 days previously, all animals of the 2 higher dose groups died within 7 days showing anorexia, depression, rapid breathing, and body weight loss before death. At necropsy, macro- and microscopic findings included severe haemorrhagic gastritis, ballooned, most empty small intestine, small amounts of blood in the small intestine, and oxalate crystals in the gastric mucosa and the renal tubules, accompanied by tubulonephrosis. In the animals of the low-dose group, no compound-related effects were seen during exposure and upon post-mortem evaluation. In the subsequent study in which mated female animals (n=10/group) were given 0, 35, or 45 mg/animal (i.e., 0, 175, 225 mg/kg bw), mortality (low dose: 1/10, high dose: 1/10), haemorraghic gastritis with oxalate crystals in gastric mucosa (in 1/10 and 3/10, respectively), and marked renal oxalosis (in 5/10 and 7/10, respectively) were observed (She80).

*Mutagenicity and genotoxicity*

*In vitro*, (anhydrous) oxalic acid was negative when tested in the absence and the presence of metabolic activation systems obtained from induced rat and hamster livers in *S. typhimurium strains* TA98, TA100, TA1535, and TA1537 (Haw83). In separate studies, oxalic acid was reported to be negative in *S. typhimurium* strains TA92, TA94, TA98, TA100, TA1535, TA1537 (tested with and without induced rat liver S9) (Ish84) or TA97, TA98, TA100, TA102, TA104 (tested with and without induced rat liver S9) (Say87). Oxalic acid was found positive when tested without metabolic activation in the Microscreen assay using *E. coli*

* It was not clear how these adjusted organ weights were determined or calculated. They were not relative weights expressed as g organ weight/100 g bw.

strain WP2s(λ) with lambda prophage induction (indicative of DNA damage) as an endpoint (not tested with S9) (Ros91).

Tested in mammalian cell systems, oxalic acid was found negative in a test for polyploidy and chromosomal aberrations in Chinese hamster lung fibroblasts (tested without metabolic activation only) (Ish84).

The committee did not find data on the (potential) *in vivo* genotoxicity of oxalic acid.

*Reproduction toxicity*

Daily dietary administration of oxalic acid of 5300 mg/kg bw, for 70 days, to female rats (Long-Evans; n=10) caused decreased absolute and relative ovary and uterus weights and prolonged dioestrus. Upon histological examination, the ovarian tissue was dense and compact, with small cells, absence of adipose tissue, depressed follicular development, and dense, compact interstitial tissue. Luteal cells contained dark, condensed, and shrunken nuclei. In male rats (n=9) given 5200 mg/kg bw, absolute weights of the testes and absolute and relative weights of prostate and seminal vesicles were decreased while relative testes weights were increased. Histological examination showed compact testis tissue with seminiferous tubules of small diameter containing immature Sertoli cells and spermatogonia with absence of mitosis, as well as decreased interstitial tissue. Similar but less intense effects were seen in male and female rats given daily doses of 1780 and 1980 mg/kg bw, respectively. It should be noted that these doses caused rather severe systemic toxicity (see also under ‘Repeated dose toxicity’) (Gol77).

The (potential) effects of oxalic acid (dihydrate) on fertility and reproduction were assessed according to the NTP RACB protocol. CD-1 mice (n=20/sex/group; controls: n=40/sex) were given daily oral (drinking water) doses of 0, 0.05, 0.10, and 0.2% (estimated to be 0, 89, 162, and 275 mg/kg bw/day, respectively), for a 1-week pre-mating period, a 14-week cohabitation period (during which animals were pairwisely housed), and an additional 6-week period during which the dams were allowed to deliver and wean a final litter. Thereafter, animals of the last litter of the high-dose group (n=10/sex; F1 generation) were treated with the same dose and allowed to mate and deliver one F2 litter. Of the high-dose F0 and F1 generation, 10 animals per sex per group were selected for sperm morphology (motility, density, abnormality) and vaginal cytology (relative frequency of oestrus stages, oestrus cycle length) evaluation. At the 2 lower doses, there were no effects on maternal, fertility, and reproduction toxicity parameters, apart from a decrease in water consumption in

the mid-dose group. In the high-dose group, the only effects seen in the parental F0 mice were decreased water consumption in both sexes and increased adjusted* kidney weights in females. With respect to fertility and reproductive organs, decreases in absolute and adjusted prostate weights ($p<0.05$) and increases in the incidence of abnormal sperm (7.20 vs. 5.33; not stat. sign.), in the average oestrus cycle length (5.3 days vs. 4.8 days), and in the relative frequency of the oestrus stage (21% vs. 11%) were observed. Further, there were decreases in the number of litters per fertile pairs (4.7 vs. 4.92 in controls; $p<0.05$) and in average pup weight (adjusted for litter size; 1.53 vs. 1.56 in controls; $p<0.01$). Evaluation of the final litter produced by the F0 animals showed that treatment did not affect pup survival or pup body weight gain for up to 14 days after delivery. With respect to the F1 animals, there was no effect on water consumption. At necropsy, statistically significant increases in absolute (males) or adjusted (females) kidney weights were found. As to fertility and reproductive organs, prostate weights were not affected, the incidence of abnormal sperm was increased (4.01 vs. 2.22 in controls; $p<0.05$), the average oestrus cycle length was similar among groups (4.9 days vs. 4.8 days) while the relative frequency of oestrus was increased (37% vs. 31%). Further, statistically significant decreases in the total number of live fetuses and in the number of live female pups were observed (Gul85).

When pregnant female rats (Wistar; n=5/group) were orally (gavage) given daily doses of 30 mg/animal (i.e., 136 mg/kg bw/day, starting day 10 after mating until parturition, tubulonephrosis (marked vacuolation of proximal tubular cells, pycnotic and karyorrhectic nuclei) but no oxalosis was observed in the kidneys of all newborn. In the maternal animals, no compound-related effects were seen during exposure and upon post-mortem evaluation. In the follow-up study at doses of 35 and 45 mg/animal (i.e., 175, 225 mg/kg bw), inducing mortality and gastric and renal effects in the maternal animals, no abortions, gross malformations, or renal effects were seen in the offspring. However, there was a dose-related reduction in litter sizes (8.8 and 7.2, respectively, vs. 12.2 in controls) (see also under ‘repeated dose toxicity’) (She80).

*In vitro experiments*

Using blood samples from human volunteers, oxalic acid significantly inhibited human thrombocyte aggregation. Oxalic acid was suggested to bind platelet

* It was not clear how these adjusted organ weights were determined or calculated. They were not relative weights expressed as g organ weight/100 g bw.

cytosolic calcium and to inhibit cAMP function after transmembrane diffusion (Cam86).

Using LLC-PK1 cell cultures, exposure to high levels of oxalate produced damage of renal epithelial cells as evidenced by morphological alterations, increased uptake of vital dyes, and decline in cell numbers (Sch95).

## 7 Existing guidelines

The current administrative occupational exposure limit (MAC) for oxalic acid in the Netherlands is 1 mg/m$^3$, 8-hour TWA.

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

## 8 Assessment of health hazard

Occupational exposure to oxalic acid may occur by inhalation of its aerosols (from steam of hot water solution) or dusts, and possibly also from direct skin contact with an oxalic-acid-containing solution. Being a strong acid, the compound may cause severe local effects. Systemic effects of oxalic acid toxicity are attributed largely to the calcium-complexing action of the acid, which depresses the level of calcium ions in body fluids. The resulting condition of hypocalcaemia produces severe disturbances in the activity of the heart and neural system. The formation of calcium oxalate crystals, which is one of the factors in the pathogenesis of urinary stone disease, may also be attributed to exposure to oxalic acid.

The committee did not find data on the kinetics of oxalic acid following inhalation or dermal exposure. Following oral ingestion, humans absorb about 2 to 10% of oxalate in the food through the gastrointestinal tract while in rats, ca. 25 and 73% of radiolabelled oxalate were excreted in the urine and faeces, respectively. There is no evidence that oxalate is utilised or metabolised by human tissues. Human serum, urine, and tissues can contain oxalate originating from dietary and metabolic (glycine) sources.

Skin testing of oxalic acid in patients with eczema on the dorsum of the foot from leather caused a positive sensitising reaction in half of these patients. Respiratory tract irritation as well as urination problems were reported by railroad shopmen occupationally exposed to steam containing unknown levels of oxalic acid. In these workers, a causal relationship between occupational exposure to oxalic acid and increased prevalence of urolithiasis-induced colic episodes was found.

In rabbits, oxalic acid was mildly and severely irritating to the skin and eyes, respectively. The committee did not find experimental animal data on local and systemic effects following single or repeated exposure by inhalation. No mortality was observed in rabbits dermally exposed to single doses of 20,000 mg/kg bw. In rats, oral $LD_{50}$ values of 375 and 474 mg/kg bw were found for females and males, respectively.

In a 70-day repeated oral (diet) rat study (Gol79), doses of 1780 (males) or 1980 (females) mg/kg bw induced mortality, changes in body weight (gain), in weights of several organs including male and female reproductive organs, and in oestrus cycle, and histological lesions in kidneys and in male and female reproductive organs. Lower doses were not tested in this study. In a fertility and reproduction toxicity study (Gul85) in which parental mice were orally (drinking water) given daily doses up to 275 mg/kg bw, for 18 weeks, no toxic symptoms, treatment-related mortality, or effects on body weight were observed. Apart from a statistically significant increase in kidney weights adjusted for body weight at necropsy in females and a decrease in absolute and adjusted prostate weight in males, no effects were seen on absolute and adjusted liver, kidney, and reproductive organ weights, and blood serum calcium levels. The committee did not find data from lifetime toxicity studies.

Oxalic acid was not mutagenic in *S. typhimurium* but caused DNA damage in *E. coli* (tested without metabolic activation). It was not clastogenic in Chinese hamster fibroblasts. The committee did not find data from other *in vitro* or *in vivo* mutagenicity and genotoxicity studies.

In a 2-generation reproduction toxicity study using mice (Gul85), no effects were seen on parental toxicity and reproductive (including fertility) toxicity at doses up to 162 mg/kg bw. At 275 mg/kg bw, the highest dose tested, parental effects as described above and reproductive effects including increases in the percentage of abnormal sperm, in the average oestrus cycle length, and in the relative frequency of the oestrus stage, as well as modest decreases (4-5%) in the number of litters per pair and in pup weights, adjusted for litter size, were found in the F0 generation while in the F1 generation, increased female kidney weights (adjusted for body weight at necropsy), increased abnormal sperm, increased relative frequency of oestrus length, and decreased number of live pups per litter were seen.

The committee considers irritation of the upper respiratory tract, eyes, and skin to be the critical effects in occupational exposure to oxalic acid. However, the committee did not find data on thresholds of these effects.

The committee considers the toxicological database on oxalic acid too poor to justify recommendation of a health-based occupational exposure limit.

From the NOAEL of 162 mg/kg bw/day found in a 2-generation reproduction toxicity study in mice, the committee concludes that the current MAC value of 1 $mg/m^3$ offers sufficient protection from systemic effects from inhalation exposure to oxalic acid. However, because of lack of information, the committee cannot conclude whether the current MAC value offers sufficient protection from irritation.

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## Annex

Occupational exposure limits for oxalic acid 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 | - | 1 | 8 h | administrative | | SZW03 |
| Germany | | | | | | |
| - AGS | - | 1[c] | 8 h | | | TRG00 |
| - DFG MAK-Kommission | - | - | | | | DFG03 |
| Great Britain | | | | | | |
| - HSE | - | 1 | 8 h | OES | | HSE02 |
| | - | 2 | 15 min | | | |
| Sweden | - | 1 | 8 h | | | Swe00 |
| | - | 2 | 15 min | | | |
| Denmark | - | 1 | 8 h | | | Arb02 |
| USA | | | | | | |
| - ACGIH | - | 1 | 8 h | TLV | | ACG03b |
| | - | 2 | 15 min | STEL | | |
| - OSHA | - | 1 | 8 h | PEL | | ACG03a |
| - NIOSH | - | 1 | 10 h | REL | | ACG03a |
| | - | 2 | 15 min | STEL | | |
| European Union | | | | | | |
| - SCOEL | - | 1 | 8 h | ILV[d] | | EC04 |

[a] S = skin notation; which mean 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 the inhalable fraction of the aerosol.

[d] Listed among compounds for which OELs are already included in Commission Directives.