POTASSIUM BROMATE

This substance was considered by previous working groups, in 1985 (IARC, 1986) and 1987 (IARC, 1987). Since that time, new data have become available and these have been incorporated into the monograph and taken into consideration in the present evaluation.

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 7758-01-2
Chem. Abstr. Name: Bromic acid, potassium salt
IUPAC Systematic Name: Potassium bromate

1.1.2 *Structural and molecular formulae and relative molecular mass*

$KBrO_3$ Relative molecular mass: 167.01

1.1.3 *Chemical and physical properties of the pure substance*

From Budavari (1996)

(*a*) *Description*: White crystals or granules
(*b*) *Melting-point*: About 350°C; decomposes at about 370°C with evolution of oxygen
(*c*) *Density*: 3.27 g/cm^3
(*d*) *Solubility*: Soluble in water; slightly soluble in acetone, dimethyl sulfoxide, ethanol, methanol and toluene (National Toxicology Program, 1991)

1.2 Production and use

Information available in 1995 indicated that potassium bromate was produced in Argentina, Brazil, China, Germany, India, Israel, Italy, Japan and Spain (Chemical Information Services, 1995).

Potassium bromate is used primarily as a maturing agent for flour and as a dough conditioner. It is also used as a laboratory reagent and oxidizing agent, in permanent-wave compounds, as a food additive and in explosives (National Toxicology Program, 1991; Budavari, 1996).

1.3 Occurrence

1.3.1 *Natural occurrence*

Potassium bromate is not known to occur naturally.

1.3.2 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (National Institute for Occupational Safety and Health, 1998), approximately 27 000 workers in the United States were potentially exposed to potassium bromate. Occupational exposure to potassium bromate may occur during its production and during its use as a dough conditioner and food additive.

1.3.3 *Dietary exposure*

In a survey of retail bread samples in the United Kingdom in 1989, potassium bromate was found in all six unwrapped breads analysed, with a median concentration of 35 μg/kg (range, 17–317 μg/kg), and in seven of 22 wrapped breads, with a median concentration of < 12 μg/kg (range, < 12–238 μg/kg). In a second survey of the same brands in 1992, all samples contained less than the detection limit of 12 μg/kg flour (Dennis *et al*., 1994).

1.3.4 *Water*

Ozonization of surface waters containing bromide ion can result in the formation of bromate (Glaze, 1986).

1.4 Regulations and guidelines

No international guidelines for potassium bromate in drinking-water have been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

Previous evaluation

Potassium bromate was tested for carcinogenicity in one experiment in rats by oral administration. It produced a high incidence of renal tubular tumours (adenomas and/or carcinomas) in animals of each sex, an increased incidence of mesotheliomas of the peritoneum of males and tumours of the thyroid in female rats. Experiments in mice and rats fed diets containing bread baked from flour containing potassium bromate were inadequate for evaluation. In two experiments with rats, potassium bromate exerted an

enhancing effect on the induction by *N*-nitrosoethylhydroxyethylamine of kidney tumours and dysplastic foci (IARC, 1986).

New studies

3.1 Oral administration

Mouse: Groups of 50 male B6C3F$_1$ mice, 28–30 days of age, were given potassium bromate (purity, > 99%) in their drinking-water at target concentrations of 0, 0.08, 0.4 or 0.8 g/L (ppm) for up to 100 weeks, when all surving mice were killed. The mean daily dose was calculated to be 0, 9.1, 42 and 98 mg/kg bw per day for the four groups, respectively. The survival rate ranged from 82% in the group at the high dose to approximately 69% in that at the low dose, with controls intermediate at 75%. There were also no significant differences between groups in body-weight gain. A statistically significant ($p < 0.05$) increased incidence of renal-cell tumours (adenomas and carcinomas) occurred at the low dose, but the incidences at the higher doses were not statistically significant. The incidences were 0/40 (controls), 5/38 (low dose), 3/41 (intermediate dose) and 1/44 (high dose) (De Angelo *et al*., 1998).

Rat: Groups of 20 or 24 male Fischer 344 rats, seven weeks of age, were given potassium bromate (food-additive grade) in their drinking-water at concentrations of 0, 15, 30, 60, 125, 250 or 500 mg/L (ppm) for 104 weeks. When water intake and body weight were accounted for, the intakes represented doses of 0, 0.9, 1.7, 3.3, 7.3, 16 and 43 mg/kg bw per day. Because the group receiving 500 mg/L had lower body weights and higher water consumption than other groups, their total intake of potassium bromate was approximately three times greater than that of the group given 250 ppm. The survival of rats receiving 500 ppm was significantly shorter ($p < 0.01$) at 83 ± 12 weeks than that of controls at 100 ± 3.3 weeks, but the lengths of survival of controls and other treated groups were comparable. As shown in Table 1, the incidences of renal tubular tumours (adenomas and adenocarcinomas) were significantly increased at doses of 125, 250 and 500 ppm, and the incidences of tubules with atypical hyperplasia were significantly increased at 30 ppm and higher. The incidences of thyroid follicular tumours and mesotheliomas of the peritoneum were also increased at the high dose of 500 ppm (Kurokawa *et al*., 1986).

Groups of 50 male Fischer rats, 28–30 days of age, were given potassium bromate (purity, > 99%) in the drinking-water at target concentrations of 0, 0.02 0.08, 0.4 or 0.8 g/L (ppm) for up to 100 weeks, when all surving rats were killed. The mean daily doses were calculated to be 0, 1.5, 7.9, 17 and 38 mg/kg bw per day for the five groups, respectively. The survival rates ranged from 44% at the high dose to approximately 72% at the low dose, with 65% in the controls. Animals at the high dose also had a significant decrease in body-weight gain. There were statistically significant increases in the incidences of mesotheliomas of the testicular tunica vaginalis, renal-cell tumours and thyroid follicular adenomas and carcinomas. The incidences of mesotheliomas were 0/47, 4/49, 5/49 ($p < 0.05$), 10/47 ($p < 0.002$) and 27/43 ($p < 0.002$); those of renal tumours were 1, 1, 6, 3 and 12 ($p < 0.002$); and those of thyroid tumours (adenomas and carcinomas

Table 1. Incidences of primary tumours in male Fischer 344 rats exposed to potassium bromate

Treatment (ppm)	Animals with tumours		
	Renal tubular adenoma or carcinoma	Peritoneal mesothelioma	Follicular cell adenoma or carcinoma of the thyroid
Control	0/19	0/19	0/16
15	0/19	0/20	0/19
30	0/20	3/20	0/20
60	1/24	4/24	1/24
125	5/24*	2/24	0/24
250	5/20**	3/20	3/20
500	9/20*	15/20**	7/19*

From Kurokawa *et al.* (1986)
*Significantly different from controls at $p < 0.05$; **at $p < 0.001$

combined) were 0, 4, 1, 4 and 14 ($p < 0.002$) at the five doses, respectively (De Angelo *et al*., 1998).

Hamster: Groups of 20 male Syrian golden hamsters, six weeks of age, were given potassium bromate (purity, 99.5%) in the drinking-water at concentrations of 0, 125, 250, 500 or 2000 mg/L (ppm) for 89 weeks. These concentrations represented total intakes of potassium bromate of 0, 5.6, 12, 20 and 84 g/kg bw, respectively. There was no difference in survival rate between groups. The incidence of renal tubular tumours was increased but not in a statistically significant or dose-related manner (0 in controls compared with 0, 1, 4 and 2 in the respective dose groups) (Takamura *et al*., 1985).

3.2 Subcutaneous injection

Mouse: Groups of newborn male and female ICR mice [initial numbers not specified] were injected subcutaneously at one day of age or once a week for four weeks until weaning, with potassium bromate (food-additive grade) in olive oil at doses of 0, 12.5, 25, 50, 100 or 200 mg/kg bw. The high dose of 200 mg/kg bw had been determined to be the maximally tolerated dose. Animals that survived beyond 52 weeks were included as effective numbers, which ranged from 7 to 20. The combined incidence of lymphomas and leukaemias was increased ($p < 0.05$) in male mice receiving cumulative total doses of 400–800 mg/kg bw (8/20) when compared with controls (1/15) (Matsushima *et al*., 1986).

Rat: Groups of newborn male and female Fischer 344 rats [initial number not specified] were injected subcutaneously at one day of age or once a week for four weeks until weaning, with potassium bromate (food-additive grade) in olive oil at doses of 0, 12.5, 25,

50 or 100 mg/kg bw. The high dose of 100 mg/kg bw had been determined to be the maximally tolerated dose. Animals that survived beyond 52 weeks were included as effective numbers, which ranged from 6 to 21. There were no significant differences in tumour incidence between treated and control rats of either sex (Matsushima *et al*., 1986).

3.3 Administration with known carcinogens or modifying factors

Rat: Potassium bromate was tested for promoting activity in a model of renal tubular carcinogenesis. Groups of 15 male Wistar rats, six weeks old, were fed a diet containing *N*-nitrosoethylhydroxyethylamine (NEHEA) for two weeks and were then unilaterally nephrectomized by removal of the left kidney at week 3; subsequently, potassium bromate [purity unspecified] was administered in the diet at a concentration of 500 mg/kg (ppm), or the rats received basal diet alone. Five rats per group were killed at weeks 8, 12 and 20. The incidence of preneoplastic renal tubular lesions, diagnosed as adenomatous hyperplasia, was increased at weeks 12 and 20 (2/5 and 2/5 and 3/5) over that in the group given NEHEA plus basal diet (0/5 and 0/5) (Hiasa *et al*., 1991).

Potassium bromate was tested for initiating activity in a model of renal tubular carcinogenesis. Groups of 39 male Fischer 344/NCr rats, six weeks of age, were given a single intragastric dose of 300 mg/kg bw potassium bromate in distilled water, followed two weeks later by either a basal diet or a diet containing 4000 mg/kg diet (ppm) sodium barbital as a promoting agent until termination of the study at week 104. Other groups of 29 rats received basal diet alone or sodium barbital in the diet from week 2. There was no difference in the incidence of renal tubular tumours or atypical tubular hyperplasia between the group exposed to both potassium bromate and sodium barbital and the group exposed only to sodium barbital, indicating no renal tumour initiating activity (Kurata *et al*., 1992).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

The Working Group noted that in experiments in which animals were fed bread made from flour treated with potassium bromate, bromate at the concentrations tested would have been converted to bromide during bread-making.

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

After mice (Theiller's original strain) received diets containing 79% bread crumbs made from flour treated with 50 or 75 mg/kg (ppm) potassium bromate, concentrations of

1 and 2 mg/kg bromine, respectively, were detected in adipose tissue (Ginocchio *et al*., 1979).

Bromine did not accumulate in the adipose tissue of Wistar-derived Porton rats fed for 104 weeks on diets composed of 79% bread crumbs made from flour treated with 75 mg/kg potassium bromide (Fisher *et al*., 1979). In a further study, male Wistar rats, six to eight weeks of age, were given 100 mg/kg bw potassium bromate by gavage in an aqueous solution as bromate. Animals were killed at various times after treatment, and bromate was assayed in the stomach, small intestinal contents, plasma and bladder urine. Bromate was found to be rapidly absorbed and eliminated (or degraded): 2 h after administration, bromate was no longer detected in plasma, and 4 h after treatment, bromate was no longer detected in bladder urine or small intestine. Twenty-four hours after administration of potassium bromate at a dose ≤ 2.5 mg/kg bw, bromate was not detected in urine. At doses of 5–100 mg/kg bw, the concentrations of bromate in urine after 24 h increased proportionally with dose (Fujii *et al*., 1984).

4.2 Toxic effects

4.2.1 *Humans*

A number of case reports of acute poisoning by potassium bromate solutions have been reviewed (Norris, 1965). In children 1.5–3 years of age, ingestion of 2–4 oz (57–133 g) of a 2% solution of potassium bromate caused nausea and vomiting, usually with epigastric and/or abdominal pain; diarrhoea and haematemesis occurred in some cases (Parker & Barr, 1951; Gosselin *et al*., 1976). In both children and adults, oliguria and death from renal failure have been observed (Dunsky, 1947; Ohashi *et al*., 1971; Gradus *et al*., 1984). Partial hearing loss and complete deafness have also been reported (Matsumoto, 1973; Quick *et al*., 1975; Gradus *et al*., 1984). The toxic or lethal dose of potassium bromate in humans has not been accurately established (Kurokawa *et al*., 1990), but a dose of 500 mg caused serious symptoms in a 15-month-old child (Quick *et al*., 1975).

De Vriese *et al*. (1997) described the clinical symptoms of a patient who ingested 300 mL of a cold-wave neutralizer consisting of 10% potassium bromate. They also reviewed 49 other cases of human exposure published since 1947. The characteristic symptoms after ingestion of various solutions containing bromate include nausea, vomiting, abdominal pain and diarrhoea shortly after ingestion. Acute renal failure varying from mild to severe anuric forms have been reported in both children and adults. Nine cases of adult poisoning (33%) resulted in death. Severe irreversible sensorineural hearing loss within 4–16 h of ingestion was recorded in almost all of the adults but in only a few children.

4.2.2 *Experimental systems*

The oral LD_{50} of potassium bromate in Fischer 344 rats was 400–500 mg/kg bw. A dose of ≥ 700 mg/kg bw potassium bromate given as a single intragastric administration was lethal to rats, mice and hamsters (Kurokawa *et al*., 1990).

The acute hypotensive effects of potassium bromate in rabbits are due to both the potassium and the bromate ions. Rabbits did not survive single intravenous injections of

0.2 g potassium bromate solution for longer than 4 min, and did not survive six intravenous injections (total dose, 1 g) longer than 43 min. The resulting gastric damage was ascribed to the bromate ion. Renal and gastric damage were seen in guinea-pigs and dogs treated with sodium bromate (Santesson & Wickberg, 1913).

In guinea-pigs, subcutaneous injections of 100 mg/kg bw sodium bromate produced cochlear damage—i.e. degenerative changes of the outer hair cells—by 24 h. Animals killed at that time revealed hyaline degeneration, cloudy swelling and necrosis of the epithelial cells in renal tubules, which were most severe in the proximal convoluted tubules. After injection of 200 mg/kg bw, there was more rapid onset of similar effects (Matsumoto, 1973).

Mice (Theiller's original strain) fed for 80 weeks on diets containing 79% bread crumbs prepared from flour treated with 50 or 75 mg/kg potassium bromate showed no significant alteration in blood chemistry, renal function or histopathological parameters, except for a transient reduction in red blood cell counts at three months (Ginocchio *et al*., 1979). No adverse effect was detected in Wistar rats fed similar diets for 104 weeks (Fisher *et al*., 1979).

Dogs (greyhounds, red Irish setters and spaniels) of each sex fed diets containing flour treated with 200 mg/kg potassium bromate for 17 months showed no adverse effect (Impey *et al*., 1961).

Potassium bromate administered intragastrically at a dose of 400 mg/kg bw increased the concentration of 8-hydroxydeoxyguanosine, a DNA lesion formed by oxygen radicals, in kidneys but not the liver of male Fischer 344 rats (Kasai *et al*., 1987). An active oxygen species—probably singlet oxygen—was formed *in vitro* from the interaction of potassium bromate with cells or homogenates prepared from male Fischer 344 rat kidney, but not liver. 8-Hydroxydeoxyguanosine concentrations were also elevated when potassium bromate was incubated with renal proximal tubules or renal nuclei (Sai *et al*., 1992).

Potassium bromate given as a single intravenous dose of 77–150 mg/kg bw increased lipid peroxidation in the kidneys of male Fischer 344 rats, but no significant increases were detected in the kidneys of male BDF_1, CDF_1 or $B6C3F_1$ mice or male Syrian golden hamsters. Dose- and time-dependent increases in serum non-protein nitrogen, blood urea nitrogen and creatinine concentrations and in the absolute and relative weights of the kidneys of male rats were seen. Eosinophilic droplets were observed in the cytoplasm of the proximal tubular epithelium of potassium bromate-treated rats. Treatment of rats given potassium bromate with cysteine and glutathione had a protective effect against the lethality and the other changes reported (Kurokawa *et al*., 1987).

Male Fischer 344 rats were given a single intragastric dose of potassium bromate at 0, 50, 300, 600 or 1200 mg/kg bw and were observed for four weeks for deaths, kidney:body weight ratios and histological appearance of the kidneys. The maximal tolerated dose was 300 mg/kg bw, since most of the animals died after administration of higher doses. Basophilic regenerative tubules and focal accumulation of eosinophilic droplets in the proximal tubules were observed in rats that survived the 300 mg/kg bw dose (Kurata *et al*., 1992).

Male and female Fischer 344 rats, six weeks of age, were exposed to potassium bromate, potassium bromide (males only) or sodium bromate (males only) at concentrations of 500, 1750 or 500 mg/L (ppm), respectively, in their drinking-water for two weeks to assess protein droplet accumulation and immunohistochemical staining for α_{2u}-globulin in their kidneys. [As the consumption of drinking-water was not given, the Working Group could not convert the doses to milligrams per kilogram of body weight.] A separate group of rats was exposed to the same concentrations of chemicals for two, four and eight weeks to assess renal cell proliferation. Protein droplets were observed in male rat kidneys after administration of potassium bromate or sodium bromate, and these droplets stained for α_{2u}-globulin. Cell proliferation in the proximal tubules was increased only in male rats exposed to potassium bromate or sodium bromate, but not potassium bromide, at two, four and eight weeks of treatment (Umemura *et al*., 1993).

No treatment-related increase in the frequency of non-neoplastic lesions in liver, kidney or thyroid and no alterations in serum chemical measurements were seen in male $B6C3F_1$ mice and Fischer 344 rats given drinking-water containing 0, 0.08, 0.4 or 0.8 g/L potassium bromate [0, 9.1, 42 or 78 mg/kg per day] or 0, 0.02, 0.1, 0.2 or 0.4 g/L potassium bromate [0, 1.5, 7.9, 17 or 38 mg/kg bw per day], respectively, for up to 100 weeks (De Angelo *et al*., 1998).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

The reproductive toxicity of sodium bromate in Sprague-Dawley rats was evaluated in a short-term test for reproductive and developmental toxicity (Kaiser *et al*., 1996; National Toxicology Program, 1996). The compound was administered in drinking-water at concentrations of 0, 25, 80 or 250 mg/L (ppm) over 35 days to one group of 10 male rats and two groups of 10 and 13 female rats. The overall average daily consumption was 2.6, 9.1 and 26 mg/kg bw sodium bromate, respectively. The first group of females was exposed during conception and early gestation, while the second group was exposed from gestation day 6 until parturition. The reproductive outcomes measured included the numbers of ovulations, implantations and viable fetuses, growth and clinical and histological assessment and sperm analysis in the adults. No changes were observed in the reproductive function of the females. There were no changes in body weights, feed consumption, clinical observations, gross findings or relative organ weights (males only). Males showed no treatment-related histological changes in the kidneys, liver, spleen, testis or epididymis, but the activity of serum alanine aminotransferase was decreased by 14% at the two higher doses. There was a significant (18%) decrease in epididymal sperm density in males at the high dose.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 2 for references)

Potassium bromate did not induce DNA repair in *Bacillus subtilis*. It induced gene mutation in *Salmonella typhimurium* TA100 in the presence of exogenous metabolic activation but not in TA98. It induced 8-hydroxydeoxyguanosine in isolated Fischer 344 rat renal proximal tubules *in vitro*. In several studies, potassium bromate was clastogenic in Chinese hamster and rat cells *in vitro*. It inhibited gap-junctional intercellular communication in Madin-Darby canine kidney epithelial cells. It induced 8-hydroxydeoxyguanosine in the DNA of rat kidney cells *in vivo* in several studies; only a weak or no response was observed in two studies in rat liver cells *in vivo*. Potassium bromate induced micronucleus formation in mice in five studies and in rats in one study. It also induced chromosomal aberrations in the bone-marrow cells of rats treated *in vivo* by intraperitoneal or oral administration.

4.5 Mechanistic considerations

Potassium bromate is highly toxic. It produces lipid peroxidation and oxidative DNA damage in rat kidney; there is also evidence that it increases the concentration of α_{2u}-globulin in male rat kidneys. The available data, including evidence of genetic toxicity, suggest, however, that potassium bromate causes renal tumours through a mechanism that involves oxidative damage to DNA.

Potassium bromate induced 8-hydroxydeoxyguanosine in rat kidney, which is the target organ of carcinogenesis in that species, but the response in liver was questionable. In contrast, the activity of 8-hydroxyguanine glycosylase, which removes 8-hydroxyguanine residues from DNA strands as a free base, was increased in the kidney but not in the liver of potassium bromate-treated rats (Lee *et al*., 1996). Therefore, the contribution of 8-hydroxydeoxyguanosine to gene mutation is not clear.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Exposure to potassium bromate may occur during its production and use as a dough conditioner and food additive. Bromate may also be found in some drinking-water samples as a by-product of ozone disinfection.

5.2 Human carcinogenicity data

No data were available to the Working Group.

Table 2. Genetic and related effects of potassium bromate

Test system	Results[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Bacillus subtilis rec strains, differential toxicity	–	–	NR	Kawachi *et al*. (1980)
Salmonella typhimurium TA100, reverse mutation	–	+	NR	Kawachi *et al*. (1980)
Salmonella typhimurium TA100, reverse mutation	NT	+	3000 µg/plate	Ishidate *et al*. (1984)
Salmonella typhimurium TA98, reverse mutation	–	–	NR	Kawachi *et al*. (1980)
Salmonella typhimurium TA98, reverse mutation	NT	–	3000 µg/plate	Ishidate *et al*. (1984)
DNA damage (8-OH-dGua formation), rat kidney cells *in vitro*	+	NT	334	Sai *et al*. (1994)
Chromosomal aberrations, Chinese hamster Don-6 cells *in vitro*	+	NT	84	Sasaki *et al*. (1980)
Chromosomal aberrations, Chinese hamster lung cells *in vitro*	+	+	63	Ishidate *et al*. (1984)
Chromosomal aberrations, Chinese hamster lung fibroblasts *in vitro*	+	NT	NR	Kawachi *et al*. (1980)
Inhibition of gap-junctional intercellular communication, canine kidney cells *in vitro*	+	NT	84	Noguchi *et al.* (1998)
DNA damage (8-OH-dGua formation), Fischer 344 rat kidney *in vivo*	+		400 po × 1	Kasai *et al*. (1987)
DNA damage (8-OH-dGua formation), Fischer 344 rat liver *in vivo*	–		400 po × 1	Kasai *et al*. (1987)
DNA damage (8-OH-dGua formation), Fischer 344 rat kidney *in vivo*	+		80 ip × 1	Sai *et al*. (1992a)
DNA damage (8-OH-dGua formation), Sprague-Dawley rat kidney *in vivo*	+		500 ip × 1	Cho *et al*. (1993)
DNA damage (8-OH-dGua formation), Sprague-Dawley rat liver *in vivo*	(+)		500 ip × 1	Cho *et al*. (1993)
DNA damage (8-OH-dGua formation), Sprague-Dawley rat kidney *in vivo*	+		100 ip × 1	Chipman *et al.* (1998)
DNA damage (8-OH-dGua formation), Fischer 344 rat kidney *in vivo*	+		500 ppm (drinking-water; 1 w)	Umemura *et al.* (1998)
Micronucleus formation, MS and ddY mouse bone-marrow cells *in vivo*	+		25 ip × 1	Hayashi *et al*. (1982)
Micronucleus formation, ddY mouse bone-marrow cells *in vivo*	+		100 po × 2	Hayashi *et al*. (1988)
Micronucleus formation, MS/Ae and CD-1 mouse bone-marrow cells *vivo*	+		37.5 ip or po × 1	Nakajima *et al*. (1989)
Micronucleus formation, CD-1 mouse peripheral blood reticulocytes *in vivo*	+		37.5 ip × 1	Awogi *et al*. (1992)

Table 2 (contd)

Test system	Results[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
Micronucleus formation, ddY mouse peripheral blood reticulocytes *in vivo*	+		50 ip × 1	Suzuki *et al*. (1995)
Micronucleus formation, Fischer 344 rat peripheral blood reticulocytes *in vivo*	+		40 ip × 1	Sai *et al*. (1992b)
Chromosomal aberrations, rat bone-marrow cells *in vivo*	+		NR	Kawachi *et al*. (1980)
Chromosomal aberrations, male Long-Evans rat bone-marrow cells *in vivo*	+		167 ip × 1	Fujie *et al*. (1988)
Chromosomal aberrations, male Long-Evans rat bone-marrow cells *in vivo*	+		344 po × 1	Fujie *et al*. (1988)

8-OH-dGua, 8-hydroxydeoxyguanosine

[a] +, positive; (+), weakly positive; –, negative; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; unless otherwise stated, in-vitro test, µg/mL; in-vivo test, mg/kg bw per day; NR, not reported; po, oral; ip, intraperitoneal; w, week

5.3 Animal carcinogenicity data

Potassium bromate has been tested by oral administration in several studies in rats and in one study each in mice and hamsters. In rats, it produced renal tubular tumours (adenomas and carcinomas) and thyroid follicular tumours in animals of each sex and peritoneal mesotheliomas in males. In mice, it produced a low incidence of renal tubular tumours in males. In hamsters, the incidence of renal tubular tumours was marginally increased. Potassium bromate did not increase tumour incidence in bioassays in newborn rats and mice, but it enhanced the induction of kidney tumours by *N*-nitrosoethylhydroxyethylamine in several experiments.

5.4 Other relevant data

No data were available on the absorption, distribution, metabolism or excretion of potassium bromate in humans, and limited information was available on rats. Bromate was found to be rapidly absorbed in rats and eliminated (or degraded).

A number of case reports of acute poisoning by potassium bromate have been reported. Potassium bromate is highly toxic. It produces lipid peroxidation and oxidative DNA damage in rat kidney. There is also evidence that it increases the amount of α_{2u}-globulin in male rat kidney. The available data, including evidence of genetic toxicity, indicate, however, that potassium bromate causes renal tumours through a mechanism involving oxidative damage.

No data were available on the developmental and reproductive effects of potassium bromate. However, in a single, short-term assay to screen for reproductive toxicity, involving exposure of male and female rats to sodium bromate before and during gestation, no developmental toxicity was observed. A decrease in epididymal sperm concentration was found in males.

No data were available on the genetic and related effects of potassium bromate in humans. It is genotoxic in experimental systems *in vivo* and in rodent cells *in vitro*. No conclusion could be drawn with respect to its mutagenicity to bacteria.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of potassium bromate.

There is *sufficient evidence* in experimental animals for the carcinogenicity of potassium bromate.

Overall evaluation

Potassium bromate is *possibly carcinogenic to humans (Group 2B)*.

6. References

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