The BG RCI is the legal successor of BG Chemie since 2010

BG RCI
Berufsgenossenschaft
Rohstoffe und chemische Industrie

# TOXICOLOGICAL EVALUATIONS

BG RCI

Kurfürsten-Anlage 62 · D-69115 Heidelberg, Germany
Telefon: +49 6221 5108-28451
E-Mail: toxikologischebewertungen@bgrci.de
Internet: www.bgrci.de/toxicologicalevaluations

**TOXICOLOGICAL EVALUATION**

last updated: 11/2000

# Tetrafluoro-boric acid and its salts

# No. 136

CAS No. 16872-11-0
CAS No. 13755-29-8
CAS No. 13826-83-0
CAS No. 14075-53-7

BG Chemie
Berufsgenossenschaft der chemischen Industrie

BG Chemie
P.O.B. 10 14 80, 69004 Heidelberg, Germany
Telephone: +49 (0) 6221 523 400
E-Mail: praevention@bgchemie.de
Internet: www.bgchemie.de

# Tetrafluoroboric acid and its salts

This Toxicological Evaluation replaces a previously published version in volume 7 of the book series “Toxicological Evaluations” published by Springer.

Apart from the corrosion which is seen with free tetrafluoroboric acid, the systemic toxicity profile of these compounds is determined by the tetrafluoroborate anion.

## 1 Summary and assessment

According to a study published in 1949, sodium tetrafluoroborate is well absorbed in humans after repeated oral administration, and 100% is excreted in urine. Potassium tetrafluoroborate, according to an older study with intraperitoneal injection, accumulates in the thyroid gland of the rat within 2 hours of administration.

Single oral administration of tetrafluoroboric acid is harmful or toxic, depending on the source of information ($LD_{50}$ rat oral ranges from 464 to 1000 mg/kg body weight (51.5% solution) and from 100 to 200 mg/kg body weight (no details of purity); $LD_{50}$ mouse oral < 50 mg/kg body weight). In a safety data sheet on potassium tetrafluoroborate, an oral $LD_{50}$ value of 5854 mg/kg body weight is given for the rat. Upon acute dermal application, the $LD_{50}$ of tetrafluoroboric acid (21.7% pure) in guinea pigs is in the range from 2.5 to 5.0 ml/kg body weight. For intraperitoneal administration of tetrafluoroboric acid, $LD_{50}$ values are reported as 10 to 25 mg/kg body weight (rat) and < 10 mg/kg body weight (mouse), while values given for potassium tetrafluoroborate are 240 mg/kg body weight (rat), 590 mg/kg body weight (mouse) and 380 mg/kg body weight (rabbit). Following subcutaneous administration of sodium tetrafluoroborate to rats, the $LD_{50}$ is approx. 550 mg/kg body weight. Signs of intoxication observed after oral administration of tetrafluoroboric acid include dyspnoea, sedation, ataxia, lack of appetite, hyporeflexia, reduced muscle tone, squatting position and prone position.

In a 28-day study which was conducted in male and female rats in accordance with OECD guideline No. 407 and included a 14-day observation pe-

riod, potassium tetrafluoroborate was administered orally at dose levels of 0 (controls), 20, 80 and 320 mg/kg body weight. Substance-related changes were only seen in the females' haematological parameters (significant dose-dependent decreases in erythrocyte count and haematocrit value at and above 80 mg/kg body weight/day, significantly reduced haemoglobin value at 320 mg/kg body weight/day), all being completely reversible after a 14-day observation period. Thyroid hormone determinations at days 8, 28 and 42 were without findings, as was the histopathological examination of the thyroid glands at days 28 and 42. In this study, the *no observed effect level* for male rats was 320 mg/kg body weight, while that for female rats was 20 mg/kg body weight due to alterations in the haematological parameters.

Tetrafluoroboric acid (21.7% pure) has been observed to cause corrosive injury to the skin of guinea pigs. Potassium tetrafluoroborate has no irritant effect on rabbit skin and the rabbit eye.

In the Salmonella/microsome test conducted in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 as well as in *Escherichia coli* WP2uvrA with and without metabolic activation, tetrafluoroboric acid caused no gene mutations.

In an older study in rats, potassium tetrafluoroborate inhibited iodine uptake by the thyroid gland. In the 28-day study in rats described above, however, no effect of potassium tetrafluoroborate on the thyroid gland was noted.

Workers employed in the production and handling of tetrafluoroboric acid and its salts are reported to have shown no indications of dysthyreosis or of any complaints such as skin irritation, respiratory problems, chronic colds or lacrimation, nor were any cases of sensitisation observed.

Table 1 below provides a comparative overview of the available toxicological studies on tetrafluoroboric acid and its salts.

| Table 1. Overview of toxicological studies on tetrafluoroboric acid and its salts | | | | |
|---|---|---|---|---|
| Type of study | Tetrafluoroboric acid (CAS No. 16872-11-0) | Sodium tetrafluoroborate (CAS No. 13755-29-8) | Ammonium tetrafluoroborate (CAS No. 13826-83-0) | Potassium tetrafluoroborate (CAS No. 14075-53-7) |
| **Acute toxicity** | | | | |
| $LD_{50}$ oral | 51.5% acid: > 464 < 1000 mg/kg b.w. (rat)<br>100 to 200 mg/kg b.w. (rat)<br>< 50 mg/kg b.w. (mouse) | – | – | 5854 mg/kg b.w. (rat) |
| $LD_{50}$ dermal | 21.7% acid: 2.5 to 5.0 ml/kg b.w. (guinea pig) | – | – | – |
| $LD_{50}$ intraperitoneal | 10 to 25 mg/kg b.w. (rat)<br>< 10 mg/kg b.w. (mouse) | – | – | 240 mg/kg b.w. (rat)<br>590 mg/kg b.w. (mouse)<br>380 mg/kg b.w. (rabbit) |
| $LD_{50}$ subcutaneous | – | ca. 550 mg/kg b.w. (rat) | – | – |
| **Subacute toxicity** | | | | |
| 28-day study, oral | – | – | – | NOEL 320 mg/kg b.w. (male rat)<br>NOEL 20 mg/kg b.w. (female rat) |
| **Skin and mucous membrane effects** | | | | |
| Skin irritation | corrosive (guinea pig) | – | – | not irritating (rabbit) |
| Eye irritation | – | – | – | not irritating (rabbit) |
| **Genotoxicity** | | | | |
| in vitro Salmonella/microsome test | negative (*Salmonella typhimurium* TA 98, TA 100, TA 1535, TA 1537, TA 1538, *Escherichia coli* WP2uvrA) | – | – | – |
| – not determined<br>b.w. body weight<br>NOEL no observed effect level | | | | |

## 2 Name of substance

| | | |
|---|---|---|
| 2.1 | Usual name | Tetrafluoroboric acid<br>Sodium tetrafluoroborate<br>Ammonium tetrafluoroborate<br>Potassium tetrafluoroborate |
| 2.2 | IUPAC name | Tetrafluoroboric acid<br>Sodium tetrafluoroborate<br>Ammonium tetrafluoroborate<br>Potassium tetrafluoroborate |
| 2.3 | CAS No. | 16872-11-0 (tetrafluoroboric acid)<br>13755-29-8 (sodium tetrafluoroborate)<br>13826-83-0 (ammonium tetrafluoroborate)<br>14075-53-7 (potassium tetrafluoroborate) |
| 2.4 | EINECS No. | 240-898-3 (tetrafluoroboric acid)<br>237-340-6 (sodium tetrafluoroborate)<br>237-531-4 (ammonium tetrafluoroborate)<br>237-928-2 (potassium tetrafluoroborate) |

## 3 Synonyms, common and trade names

Borate(1-), tetrafluoro-, hydrogen
Borofluoric acid
Fluoboric acid
Hydrofluoboric acid
Hydrogen tetrafluoroborate
Tetrafluorborsäure

Apreton R
Borate(1-), tetrafluoro-, sodium
Natriumtetrafluoroborat
Sodium borofluoride
Sodium boron tetrafluoride

Ammonium borofluoride
Ammonium fluoborate
Ammonium fluoroborate
Ammonium tetrafluoroborate(1-)
Ammoniumtetrafluoroborat
Borate(1-), tetrafluoro-, ammonium

Avogadrite
Borate(1-), tetrafluoro-, potassium
Kaliumtetrafluoroborat
Potassium borofluoride
Potassium fluoborate
Potassium fluoroborate

## 4 Structural and molecular formulae

4.1 Structural formula

$H^+ [BF_4]^-$
$Na^+ [BF_4]^-$
$[NH_4]^+ [BF_4]^-$
$K^+ [BF_4]^-$

4.2 Molecular formula

$HBF_4$
$NaBF_4$
$NH_4BF_4$
$KBF_4$

## 5 Physical and chemical properties

5.1 Molecular mass, g/mol

87.81 (tetrafluoroboric acid)
109.79 (sodium tetrafluoroborate)
104.84 (ammonium tetrafluoroborate)
125.91 (potassium tetrafluoroborate)

5.2 Melting point, °C

Tetrafluoroboric acid: below –78 (50% pure) (Riedel-de Haën, 1990 a)
Sodium tetrafluoroborate: 384 (Riedel-de Haën, 1990 b)
Potassium tetrafluoroborate: 530 (Riedel-de Haën, 1995)

| | | |
|---|---|---|
| 5.3 | Boiling point, °C | Tetrafluoroboric acid: > 130 with decomposition (50% pure) (Kali-Chemie, 1990 a) |
| 5.4 | Vapour pressure, hPa | No information available |
| 5.5 | Density, g/cm³ | Tetrafluoroboric acid: 1.32 (at 25 °C, 43% pure)<br>1.38 (at 20 °C, 48% pure) (Kali-Chemie, 1989)<br>1.38 (at 20 °C, 50% pure) (Kali-Chemie, 1990 a)<br>Sodium tetrafluoroborate: 2.470 (at 20 °C) (Riedel-de Haën, 1990 b)<br>Ammonium tetrafluoroborate: 1.850 (at 20 °C) (Riedel-de Haën, 1990 c)<br>Potassium tetrafluoroborate: 2.500 (at 20 °C) (Riedel-de Haën, 1995) |
| 5.6 | Solubility in water | Tetrafluoroboric acid: Miscible in all proportions (Kali-Chemie, 1990 a)<br>Sodium tetrafluoroborate: 973 g/l (at 20 °C)<br>2100 g/l (at 100 °C) (Riedel-de Haën, 1990 b)<br>Ammonium tetrafluoroborate: 250 g/l (at 20 °C) (Riedel-de Haën, 1990 c)<br>Potassium tetrafluoroborate: 4.4 g/l (at 20 °C) (Riedel-de Haën, 1995) |
| 5.7 | Solubility in organic solvents | No information available |
| 5.8 | Solubility in fat | No information available |
| 5.9 | pH value | Tetrafluoroboric acid: 1 (50% aqueous solution) (Riedel-de Haën, 1990 a)<br>ca. 1 (at 8.7 g/l and 20 °C) (EC, 1996)<br>Sodium tetrafluoroborate: ca. 3 (1% solution) (Riedel-de Haën, 1990 b)<br>Ammonium tetrafluoroborate: ca. 3.5 (5% solution) (Riedel-de Haën, 1990 c)<br>Potassium tetrafluoroborate: ca. 5 (at 4 g/l and 20 °C) (Riedel-de Haën, 1995) |

| | | |
|---|---|---|
| 5.10 | Conversion factor | 1 ml/m³ (ppm) ≙ 3.58 mg/m³<br>1 mg/m³ ≙ 0.28 ml/m³ (ppm)<br>(Tetrafluoroboric acid)<br>1 ml/m³ (ppm) ≙ 4.48 mg/m³<br>1 mg/m³ ≙ 0.22 ml/m³ (ppm)<br>(Sodium tetrafluoroborate)<br>1 ml/m³ (ppm) ≙ 4.29 mg/m³<br>1 mg/m³ ≙ 0.23 ml/m³ (ppm)<br>(Ammonium tetrafluoroborate)<br>1 ml/m³ (ppm) ≙ 5.14 mg/m³<br>1 mg/m³ ≙ 0.19 ml/m³ (ppm)<br>(Potassium tetrafluoroborate)<br>(at 1013 hPa and 25 °C for the pure substances) |

# 6 Uses

The primary use of tetrafluoroboric acid is in the manufacture of tetrafluoroborate salts. Tetrafluoroboric acid is also used in electroplating and dipping solutions for surface treating of aluminium, as a pickling agent for hot rolled steel and as an etchant for silicon and glass in the electronics industry. Molten alkali-metal and ammonium tetrafluoroborates are good solvents for metal oxides and are used in fluxes for soldering and brazing. Tetrafluoroboric acid and alkali-metal fluoroborates are also used as catalysts in organic syntheses and polymerisation reactions (Falbe and Regitz, 1990; Schwetz and Lipp, 1989).

# 7 Experimental results

## 7.1 Toxicokinetics and metabolism

### *Sodium tetrafluoroborate*

Following daily oral intake of 6.4 mg sodium tetrafluoroborate by a volunteer for a period of 14 days, a daily average of 100% was excreted in the urine and 1.6% in the faeces. The fluoride content of the volunteer's food was not determined. Sodium fluoroborate is therefore well absorbed, but the fluoride which enters the body is not stored. The authors attributed this to slow

hydrolysis of the tetrafluoroborate ion. In another study with 3 volunteers and a study duration of 7 to 38 weeks, there were indications that fluoride which was absorbed in the form of sodium tetrafluoroborate was stored in the body. The amount was less than 10% of that absorbed into the bloodstream (no further details; Largent and Heyroth, 1949; Largent, 1954).

### *Potassium tetrafluoroborate*

Rats (approx. 200 g; 4 animals/group) were given a single intraperitoneal injection of 5 µg $^{18}$F-labelled potassium tetrafluoroborate (it was not specified whether per kilogram body weight or per rat). After 40, 60, 100 and 120 minutes, various organs were assessed for relative specific tetrafluoroborate activity (tissue/blood specific activity ratio). The results are shown in Table 2 below.

**Table 2. Relative specific activity of potassium $^{18}$F-tetrafluoroborate (tissue/blood activity ratio) in organs of rats following single intraperitoneal injection (mean values of 4 rats)**

| Time after injection (minutes) | 40 | 60 | 100 | 120 |
|---|---|---|---|---|
| Muscle | 1.93 | 1.65 | 1.90 | 1.42 |
| Liver | 1.27 | 1.34 | 0.99 | 1.24 |
| Spleen | 1.35 | 1.01 | 0.85 | 1.03 |
| Brain | 0.67 | 0.23 | 0.49 | 0.86 |
| Thyroid gland | 12.3 | 15.7 | 21.0 | 36.4 |

The highest activity was found in the thyroid gland, where it was 26- to 42-fold higher than in the other organs after 2 hours. Increases in dose to 50, 500 and 1000 µg potassium tetrafluoroborate did not increase the specific activity in the thyroid gland, but reduced it relative to the values found after administration of 5 µg, e.g. by about a factor of 20, 210 minutes after 1000 µg (Anbar et al., 1960).

In a further study by the same investigators on the distribution of potassium tetrafluoroborate in various tissues, male albino rats (weighing 110 to 150 g; aged 11 to 13 weeks) were each intravenously injected with 1 µmol $^{18}$F-labelled potassium tetrafluoroborate (no details of the specific radioactivity). At 120 minutes after injection, the following relative specific activities (activity per gram of tissue/activity in serum) were determined: liver 0.29,

spleen 0.37, kidney 0.60, lung 0.60, muscle 0.14, brain 0.03, femoral diaphysis 0.26, femoral epiphysis 0.29, incisors 0.27, cranial bone 0.27, cartilage 0.30. Further relative specific activities at 30, 120 and 240 minutes after injection were reported for serum/total injected dose as 1.75, 0.28 and 0.07, respectively, for muscle/serum as 0.14, 0.15 and 0.35, respectively, as well as for femoral epiphysis/serum as 0.35, 0.85 and 1.35, respectively, and for femoral epiphysis/femoral diaphysis as 1.0, 2.3 and 2.4, respectively (no further details; Anbar and Ernst, 1962).

## 7.2 Acute and subacute toxicity

### *Tetrafluoroboric acid*

The acute oral toxicity of tetrafluoroboric acid was investigated in groups of 5 male and 5 female rats (no details of the strain used; initial weights between 115 and 170 g) in accordance with OECD guideline No. 401. A 51.5-percent aqueous solution of tetrafluoroboric acid was used for testing. Dose levels were 10, 100, 464 and 1000 mg/kg body weight and the observation period was 14 days. The 10 mg/kg body weight dose was tolerated without signs of toxicity. Following 100 mg/kg body weight, dyspnoea, sedation and lack of appetite were observed, and in the males, half-closed eyes. The signs of toxicity were reversible after 24 hours. Following 464 mg/kg body weight, signs of intoxication included dyspnoea, sedation, half or completely closed eyes, hyporeflexia, ataxia, body tremor, reduced muscle tone, squatting position and prone position, vocalisation, slightly reduced locomotor activity and glassy eyes, but the dose was survived by all rats. Following 1000 mg/kg body weight, all animals died within 24 hours. Autopsy of the deceased rats revealed oedematous and highly haemorrhagic gastrointestinal walls as well as blood-piebalded livers. Dissection of the surviving rats showed no treatment-related findings. Thus the $LD_{50}$ of 51-percent tetrafluoroboric acid was between 464 and 1000 mg/kg body weight, or, according to the authors of the report, between 236.64 and 515 mg pure substance/kg body weight (Kali-Chemie, 1990 b).

For oral administration of tetrafluoroboric acid to rats (5 per group) followed by a 14-day observation period, an approximate $LD_{50}$ of 100 to 200 mg/kg body weight was determined. Clinical signs of toxicity observed included

weakness and ataxia. Deaths occurred between 35 minutes and one day after administration (no further details; Eastman Kodak, 1992).

For mice (5 per group), an approximate $LD_{50}$ was given as < 50 mg/kg body weight for oral administration of tetrafluoroboric acid. The observation period was 14 days. Clinical signs of toxicity included weakness, ataxia and twisting motions. Deaths occurred between 15 minutes and 9 days after administration (no further details; Eastman Kodak, 1992).

In guinea pigs (3 per group), the approximate $LD_{50}$ for occlusive dermal application of 21.7-percent tetrafluoroboric acid followed by a 14-day observation period was 2.5 to 5.0 ml/kg body weight. Deaths occurred after 2 to 3 days. At the application site, moderate oedema, dark grey and black discoloration as well as very soft and eroded tissue was observed. In the surviving animals, all soft tissue sloughed off deep into the flesh and hard dark scabs formed over the exposed muscular tissue which seemed to be healing well (no further details; Eastman Kodak, 1992). The substance thus exhibited corrosive effects under the testing conditions described above.

Following intraperitoneal administration of tetrafluoroboric acid to rats (5 per group), an approximate $LD_{50}$ of 10 to 25 mg/kg body weight was reported. The observation period was 14 days. Clinical signs of toxicity observed included weakness and ataxia. Deaths occurred between 27 minutes and 9 days after administration (no further details; Eastman Kodak, 1992).

### *Sodium tetrafluoroborate*

For sodium tetrafluoroborate, the acute subcutaneous $LD_{50}$ in the rat was reported as approx. 550 mg/kg body weight. Damage to the cardiac muscle and a drop in body temperature were noted (no further details; Druckrey et al., 1973).

### *Potassium tetrafluoroborate*

In a safety data sheet on potassium tetrafluoroborate, an oral $LD_{50}$ value of 5854 mg/kg body weight is given for the rat (no further details; Riedel-de Haën, 1995).

Following single intraperitoneal administration of potassium tetrafluoroborate, the $LD_{50}$ values determined in rats, mice and rabbits were 240 (130 to 460), 590 (460 to 750) and 380 (190 to 780) mg/kg body weight, respectively (no further details; Blaisdell, 1955).

In a dose-finding study for a 28-day study, groups of 5 male and 5 female Wistar rats (initial weights of the males and females were 190 to 205 g and 149 to 155 g, respectively) were treated by oral gavage with potassium tetrafluoroborate (99.4 % pure) at doses of 0 (controls), 50, 157 and 500 mg/kg body weight in polyethylene glycol 400 on 5 consecutive days. No clinical signs of toxicity were seen. Body weight development of the top dose animals was slightly, but not statistically significantly less than that of the control group. Absolute liver weights were reduced in the top dose males and in the females receiving doses of and above 157 mg/kg body weight. Absolute testicular weights in the 500 mg/kg group were lower than controls, while absolute and relative ovary weights were increased from 157 mg/kg body weight. Upon macroscopic examination, 9 out of 10 top dose animals were observed to have signs of gastric mucosal corrosion (pale or slightly reddish erosions, detachable whitish coating; Biopharm, 1995).

In the subsequent 28-day study conducted in accordance with OECD guideline No. 407, groups of 5 male and 5 female Wistar rats (average initial weights of the males and females 133.7 to 137.4 g and 124.9 to 129.0 g, respectively) received potassium tetrafluoroborate (100.1% pure, solution in deionised water) by oral gavage at dose levels of 0 (controls), 20, 80 and 320 mg/kg body weight. In addition, the study included satellite groups of 5 males and 5 females per dose group for interim sacrifice after 8 days as well as another 5 males and 5 females in the control and the top dose groups for a 14-day recovery period. The levels of the thyroid hormones, thyroxin, triiodothyronine and thyroid-stimulating hormone, were determined in all groups at days 8 and 28 as well as at the end of the recovery period. The scope of the histopathological examination complied with OECD guideline No. 408, with the thyroid and parathyroid glands from all dose groups being examined by light microscopy. There were no deaths during the study. Behaviour, clinical picture, body weight development and food and water consumption remained unaffected. Clinical chemistry and urinalysis parameters revealed no treatment-related effects. In none of the dose groups and at no time point investigated were there any treatment-related alterations in thyroid hormone levels. The haematology results revealed a

slight, but statistically significant reduction in erythrocyte count and haematocrit value in the females of the mid and high dose groups. In the high dose females, decreased haemoglobin values were noted. The values obtained for mean corpuscular volume were not affected. By the end of the 14-day recovery period, the haematological parameters had returned to control values. No changes in organ weights were observed. Gross pathology and histopathological examination of the organs, including the thyroid and parathyroid glands, were without findings. Thus, the *no observed effect level* for the male rats was 320 mg/kg body weight, while that for the female rats was 20 mg/kg body weight due to alterations in the haematological parameters (Hoechst, 1997).

## 7.3 Skin and mucous membrane effects

### *Tetrafluoroboric acid*

Tetrafluoroboric acid (21.7% pure) caused corrosive injury to the guinea pig skin (cf. Section 7.2; Eastman Kodak, 1992).

### *Potassium tetrafluoroborate*

The skin irritancy of potassium tetrafluoroborate (no indication of purity) was tested in 3 female rabbits (New Zealand White; 2.57 to 2.70 kg) in accordance with OECD guideline No. 404. A 4-hour semi-occlusive exposure to 500 mg of the test substance made into a paste with 0.5 ml distilled water produced no irritation (the primary irritation index on the Draize scale was 0.0). Potassium tetrafluoroborate was therefore classified as non-irritant to rabbit skin (SafePharm, 1992 a).

Application of 400 mg potassium tetrafluoroborate/kg body weight to rabbit skin produced no signs of irritation or toxicity (no further details; Blaisdell, 1955).

In an eye irritation study carried out in accordance with OECD guideline No. 405, approx. 99 mg potassium tetrafluoroborate (no indication of purity) caused minimal to moderate irritation of the conjunctiva in rabbits (New Zealand White; 2 females, 1 male; 2.69 to 2.89 kg), which was reversible 24 to 48 hours after treatment. The iris and cornea were normal. According

to a modification of the classification system of Kay and Calandra (J. Soc. Cosmet. Chem., 13, 281–289 (1962)), the substance was evaluated as slightly irritating to the rabbit eye, while according to the Commission Directive 91/325/EEC it was not irritating to the rabbit eye (SafePharm, 1992 b).

Application to the rabbit eye of up to 3 mg potassium tetrafluoroborate produced no grossly observable irritation (no further details; Blaisdell, 1955).

## 7.4 Sensitisation

No information available.

## 7.5 Subchronic and chronic toxicity

### *Potassium tetrafluoroborate*

Male and female Wistar rats (no details of the number of animals/group) were given potassium tetrafluoroborate in their drinking water for a period of 3 months. The dose was equivalent to 10 mg fluoride ions/l drinking water. A control group was included. The scope of the study encompassed body weight development, degree of depigmentation of the incisor enamel at 4 time points during the study (no further details) and determination of organ weights, and in 3 males and 3 females per group it included histopathological examination of the liver, kidney, adrenal glands, spleen, heart and testes. Body weight development was similar to that of the controls. No depigmentation of the incisors was observed. Relative organ weights did not differ from controls. In regard of the heart and testes, no histopathological changes were noted. According to the investigators' observations, the livers of half of the animals exhibited dilatation of the blood vessels and, occasionally, indurations. The spleens were also described as showing marked vascular dilatation and loss of basophilia of the splenic nodules with subsequent loss of structure. With respect to the kidneys, half of the animals displayed parenchymal indurations, 2 of the animals showing dilatation of the distal tubules. In one third of the kidneys examined, the peripheral vessels and the interstitial tissue were richly perfused. The adrenal glands were reported to exhibit marked changes in the parenchyma (which according to the authors indicated an increased activity of the cells in the fascicular zone). The investigators considered the histopathological chan-

ges to be substance-related (no further details; Janecek et al., 1974). Insufficient documentation of the experimental setup and the results (e.g. no details of group size or analytical checks) render the study unsuitable for the assessment of potassium tetrafluoroborate toxicity following subchronic oral administration.

## 7.6 Genotoxicity

### 7.6.1 In vitro

***Tetrafluoroboric acid***

Tetrafluoroboric acid (as a 42% aqueous solution) was tested for mutagenic activity in the Salmonella/microsome assay in *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 as well as in *Escherichia coli* WP2uvrA, with and without metabolic activation (S9 mix from rat liver induced with polychlorinated biphenyl (KC 500)). The test concentrations were in the range from 1 to 5000 µg/plate. Even at the highest concentration tested, no mutagenic activity was seen. No bacteriotoxicity data were reported (Shimizu et al., 1985).

### 7.6.2 In vivo

No information available.

## 7.7 Carcinogenicity

No information available.

## 7.8 Reproductive toxicity

No information available.

## 7.9 Effects on the immune system

No information available.

## 7.10 Neurotoxicity

No information available.

## 7.11 Other effects

### *Potassium tetrafluoroborate*

In the context of studies on the localisation of intracranial space-occupying pathological lesions, $^{18}$F-labelled potassium tetrafluoroborate was investigated as one of several substances. In rats injected with $^{18}$F-labelled potassium tetrafluoroborate (presumably via the intraperitoneal route; no further details), the relative specific activities shown in Table 3 were ascertained for the various tissues investigated (no further details; Askenasy et al., 1962).

**Table 3. Relative specific activities in tissues of the rat after single injection of potassium $^{18}$F-tetrafluoroborate**

| Relative specific activity | Time after injection | | |
|---|---|---|---|
| | 30 minutes | | 120 minutes |
| Blood/brain | 55 | | 44 |
| Muscle/brain | 3.6 | | 6.4 |
| Cranial bone/blood | 0.35 | | 0.26 |
| Blood after 30 minutes/blood after 120 minutes | | 6.2 | |
| Percent of injected dose in the intestines | | 2.6 | |

Rats (100 to 110 g) were given a single intraperitoneal injection of 0.1 ml 1-percent propylthiouracil solution in order to inhibit the formation of protein-bound iodine in the thyroid gland. One hour later, they were injected intraperitoneally with 0.1 ml $^{131}$iodine iodide solution (40 mc/ml) and another 15 minutes later with 0.5 ml saline solution containing 25 µmol potassium tetrafluoroborate (it was not specified whether this was per kilogram body weight or per animal). At 30, 60, 90 and 120 minutes after the iodide injection, the iodine activity in the isolated thyroid gland was measured. Potassium tetrafluoroborate inhibited iodine uptake by the thyroid gland by 89.2%, 93.7%, 92.6% and 86.5% at 30, 60, 90 and 120 minutes, respectively (Anbar et al., 1959).

Blood serum samples of 12 ml were obtained from healthy donors and Wistar rats and incubated with $^{125}$iodine-labelled thyroxin at room temperature for one hour. Subsequently, 1 ml distilled water or 1 ml aqueous potassium tetrafluoroborate solution was added, and after another 1-hour incubation at room temperature the concentration of free thyroxin was ascertained. Based on a graphical representation of the data, potassium tetrafluoroborate increased the serum levels of free thyroxin in the human and rat samples from approx. 0.025% (controls) to approx. 0.031% and from approx. 0.041% to 0.058%, respectively. The greater increase in free thyroxin seen in the rat samples was attributed by the authors to differences in thyroxin-binding proteins. In in vivo studies in male Wistar rats (8 per group), however, oral administration of potassium tetrafluoroborate did not enhance the level of free thyroxin compared with a control group which was given distilled water (no further details; Michajlovskij and Langer, 1974).

# 8 Experience in humans

Tetrafluoroboric acid and sodium, ammonium and potassium tetrafluoroborate are not listed in the index of allergens compiled by the IVDK (Informationsverbund Dermatologischer Kliniken, Information Network of Departments of Dermatology for the surveillance and scientific evaluation of contact allergies in Germany). They were not tested. Owing to their structures, the compounds are considered unlikely to have a skin-sensitising potential (IVDK, 1998).

The handling of tetrafluoroboric acid and potassium tetrafluoroborate in the context of production and processing have not led to any known complaints, such as skin irritation, respiratory problems, chronic colds or lacrimation, in workers employed in these areas. There are no indications that there may have been cases of sensitisation (Solvay, 1998).

In the production of tetrafluoroboric acid and its salts there have been no cases of sensitisation amongst employees in the daily handling of these substances (Riedel-de Haën, 1998).

In employees working with tetrafluoroboric acid and its derivatives and undergoing regular medical examinations, there have been no indications of enlargement or dysfunction of the thyroid gland over a period of more than 20 years (Solvay, 1992 a, b).

In another chemical plant, 6 workers who had frequent contact with tetrafluoroboric acid regularly underwent medical examination. None of them had goitre or signs of hypothyroidism. The $T_3$ and $T_4$ levels were in the normal range (Riedel-de Haën, 1992).

A toxicokinetic study of sodium tetrafluoroborate in humans is discussed in Section 7.1.

# 9 Classifications and threshold limit values

No information available.

# References


Anbar, M., Guttmann, S., Lewitus, Z.
Effect of monofluorosulphonate, difluorophosphate and fluoroborate ions on the iodine uptake of the thyroid gland
Nature, 183, 1517–1518 (1959)

Anbar, M., Guttmann, S., Lewitus, Z.
The accumulation of fluoroborate ions in thyroid glands of rats
Endocrinology, 66, 888–890 (1960)

Anbar, M., Ernst, N.
A distribution study of $F^{18}$-labelled cationic fluorocomplexes in rats
Int. J. Appl. Radiat. Isotop., 13, 47–51 (1962)

Askenasy, H.M., Anbar, M., Laor, Y., Lewitus, Z., Kosary, I.Z., Guttmann, S.
The localization of intracranial space-occupying lesions by fluoroborate ions labelled with fluorine 18
Am. J. Roentgenol., 88, 350–354 (1962)

Biopharm (Pharmakologische Forschungsgesellschaft Biopharm GmbH, Berlin)
5-Tage-Dosisfindungsstudie mit oraler Applikation von Kaliumtetrafluoroborat (BG-Nr.: 136; CAS-Nr.: 14075-53-7) an Ratten
Unpublished amendment to Study report 008TOX93 (1995)
On behalf of BG Chemie

Blaisdell, C.T.
Chemical Corps Medical Laboratories Research Report No. 351, March 1955
Cited in: Levinskas, G.J.
Toxicology of boron compounds
In: Adams, R.M. (ed.)
Boron, metallo-boron compounds and boranes, 693–737
Interscience Publishers (1964)

Druckrey, H., Stekar, J., Hünig, S.
Carcinogene Wirkung von Äthoxy-diazenium-Salzen (O-Äthyl-dialkylnitrosimmonium-Salzen) an Ratten
Z. Krebsforsch., 80, 17–26 (1973)

Eastman Kodak Company, Rochester, New York
Letter from Eastman Kodak Co to USEPA regarding toxicity studies of hydrogen tetra-fluoroborate (-1) with cover letter dated 092492
NTIS/OTS 0570943

EC (European Commission), Existing Chemicals Bureau
Joint Research Centre, Ispra, Italy
IUCLID data set tetrafluoroboric acid
CD-ROM, ed. I (1996)

Falbe, J., Regitz, M. (eds.)
Römpp Chemie Lexikon
9th ed., vol. 2, 1409–1410
Georg Thieme Verlag, Stuttgart, New York (1990)

Hoechst AG, Hoechst Marion Roussel, Preclinical Development Drug Safety
Kaliumtetrafluoroborat – Testing for subacute oral toxicity (28 applications within 29 days) in the male and female Wistar rat
Unpublished report No. 97.0205 (1997)
On behalf of BG Chemie

IVDK (Informationsverbund Dermatologischer Kliniken)
Written communication to BG Chemie of 28.03.1998

Janecek, J., Cervenka, R., Jirik, V.
Biologische Wirkung von Fluorverbindungen in Trinkwasser (German translation of the Czech)
Cesk. Hyg., 19 (3), 113–126 (1974)

Kali-Chemie AG
Grunddatensatz für Altstoffe – Tetrafluorborsäure (1989)

Kali-Chemie AG
DIN safety data sheet Tetrafluoroboric acid (1990 a)

Kali-Chemie AG, Pharmaceutical Division, Department of Biological Development
Toxicity of tetrafluorboric acid ($HBF_4$; CAS No. 16872) in rats after single oral administration
Unpublished report (1990 b)

Largent, E.J.
Metabolism of inorganic fluorides
In: Fluoridation as a public health measure
American Association for the Advancement of Science, Washington, D.C., p. 49–78 (1954)

Largent, E.J., Heyroth, F.F.
The absorption and excretion of fluorides. III. Further observations on metabolism of fluorides at high levels of intake
J. Ind. Hyg. Toxicol., 31 (3), 134–138 (1949)

Michajlovskij, N., Langer, P.
Increase of serum free thyroxine following the administration of thiocyanate and other anions in vivo and in vitro
Acta Endocrinol., 75, 707–716 (1974)

Riedel-de Haën AG
DIN safety data sheet tetrafluoroboric acid 50% (1990 a)

Riedel-de Haën AG
DIN safety data sheet sodium tetrafluoroborate pure (1990 b)

Riedel-de Haën AG
DIN safety data sheet ammonium tetrafluoroborate (1990 c)

Riedel-de Haën AG
Written communication to BG Chemie of 13.05.1992

Riedel-de Haën AG
EU safety data sheet potassium tetrafluoroborate ultrapure (1995)

Riedel-de Haën AG
Written communication to BG Chemie of 23.07.1998

SafePharm Laboratories Limited, Derby, U.K.
Potassium tetrafluoroborate: acute dermal irritation test in the rabbit
Unpublished report, Project Number 121/175 (1992 a)
On behalf of Riedel-de Haën AG

SafePharm Laboratories Limited, Derby, U.K.
Potassium tetrafluoroborate: acute eye irritation test in the rabbit
Unpublished report, Project Number 121/176 (1992 b)
On behalf of Riedel-de Haën AG

Schwetz, K.A., Lipp, A.
Boron carbide, boron nitride, and metal borides
In: Ullmann's encyclopedia of industrial chemistry
5th ed., vol. A4, p. 295–330
VCH Verlagsgesellschaft mbH, Weinheim (1989)

Shimizu, H., Suzuki, Y., Takemura, N., Goto, S., Matsushita, H.
The results of microbial mutation test for forty-three industrial chemicals
Jpn. J. Ind. Health, 27, 400–419 (1985)

Solvay (Solvay Fluor und Derivate GmbH, Werk Wimpfen)
Written communication to BG Chemie of 27.02.1992 a

Solvay (Deutsche Solvay Werke GmbH, Hannover, ZB Umwelt/Sicherheit)
Written communication to BG Chemie of 01.04.1992 b

Solvay Deutschland GmbH, Umweltschutz und Sicherheit
Written communication to BG Chemie of 09.06.1998