Danish Ministry of the Environment
Environmental Protection Agency

2- Mercapto-benzothiazole (MBT)

Evaluation of health hazards and proposal of a health-based quality criterion for ambient air

Environmental Project No. 1530, 2014

Title:

2- Mercapto-benzothiazole (MBT)

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Content

Preface

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to 2-Mercaptobenzothiazole (MBT) and proposal of a health based quality criterion in ambient air. This resulted in 2001 in the present report, which was prepared by Elsa Nielsen, Grete Østergaard and John Christian Larsen, The Institute of Food Safety and Toxicology, Danish Veterinary and Food Administration, i.e. the present Division of Toxicology and Risk Assessment, National Food Institute, Technical University of Denmark.

The report has been subjected to review and discussion and has been endorsed by a steering committee consisting of representatives from the following Danish authorities:

The Danish Working Environment Authority,
The National Board of Health, Denmark,
The Danish Public Health Medical Officers
The Danish Environmental Protection Agency

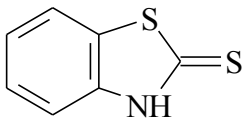
The Danish Environmental Protection Agency
Copenhagen, January 2014.

1 General description

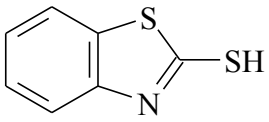
1.1 Identity

Molecular formula: $C_7H_5NS_2$

Structural formula:



2-benzothiazolethione



2-benzothiazolethiole

Molecular weight: 167.25

CAS-no.: 149-30-4

Synonyms: MBT
Benzothiazole-2-thiol
2(3H)-Benzothiazolethion
2-Benzothiazolethiol
2-Benzothiazolyl mercaptan
Accelerator-M

1.2 Physical / chemical properties

Description: MBT is a pale yellow, crystalline substance with an unpleasant odour and a bitter taste. MBT can occur in two tautomeric forms, see above. Both in solution as well as in the crystal the equilibrium is almost completely on the side of 2-benzothiazolethione.

Purity: 94-97%.

Melting point: 180.2 - 181.7 °C

Boiling point: Decomposes above 260 °C

Density: 1.42 g/ml (at 20°C).

Vapour pressure: 1.9×10^{-4} mmHg (2.5×10^{-2} Pa) at 25°C.

Concentration of saturated vapours: 0.25 ppm (at 20°C and 760 mmHg)

Flash point: 243 °C

Solubility:	Water: 117 mg/l (at 20°C). MBT has a weakly acidic reaction in aqueous solution. MBT is soluble in acetone and slightly soluble in alcohol, ether, benzene, and glacial acetic acid.
$logP_{octanol/water}$:	Experimental value: 1.61 - 2.43. Calculated value: 2.84.
Henry's constant:	4.2×10^{-6} Pa x m^3/mole (calculated value).
pK_a-value:	7.03 (in aqueous buffer solution).
Stability:	The stability of MBT in aqueous solutions is influenced by iron ions. While it is stable in the presence of iron ions in neutral or alkaline solutions, MBT is reduced to benzothiazole in acidic solutions and hydrogen sulfide is set free. MBT is readily oxidizable, especially by ozone.
Incompatibilities:	When heated, MBT may react with oxidising materials and emit (unspecified) toxic decomposition products.
Odour threshold, air:	-
Odour threshold, water:	1.76 mg/l (BUA 1997).
Taste threshold, water:	-
References:	BIBRA (1990), BUA (1997), IUCLID (2000).

1.3 Production and use

The technical synthesis of MBT is carried out through the conversion of 1) aniline, carbon disulfide and sulfur; 2) benzothiazole and sulfur; or 3) aniline, carbon disulfide, benzothiazole and sulfur. During these reactions, hydrogen sulfide, benzothiazole, dimercaptobenzothiazole and sulfurous resins arise as by-products. (BUA 1997).

MBT is primarily used in the rubber industry as a non-volatile vulcanisation accelerator. MBT reacts with zinc oxide and sulfur to form an activated complex, which leads to cross-linkage via sulfur bridges as a result of the reaction with the long-chain rubber molecules. Following vulcanisation, MBT can be bonded in the vulcanizate or may be present as a substance incorporated in the polymer. The concentration of free MBT in the final product is dependent on the vulcanisation conditions and the vulcanisation auxiliary substances used apart from MBT.
MBT is also used as an intermediate in the production of other accelerators, some of which may decompose during vulcanisation and emit MBT. Furthermore, MBT is used in the synthesis of the pesticide methabenzothiazuron (1-benzothiazole-2-yl-1,3-dimethylurea).
(BUA 1997).

1.4 Environmental occurrence

MBT entering the environment during the industrial use is mainly with waste water and only to a smaller extent with waste air or as a component of industrial waste. Furthermore, MBT is discharged directly into the environment during the use of the pesticide methabenzothiazuron and indirectly primarily from rubber products. (BUA 1997, HSDB 1998).

1.4.1 Air

As a vulcanization accelerator in the rubber industry, MBT may be discharged into the atmosphere in the form of particles during the processing of substances. MBT emission in the air around workplaces has been reported with older, eastern European plants; however, no quantitative data are available. (BUA 1997).

1.4.2 Water

No data on concentrations of MBT in surface water, ground water, or drinking water have been found.

1.4.3 Soil

No data on concentrations of MBT in soil have been found.

1.4.4 Foodstuffs

In Japan, the migration of MBT was investigated in 12 rubber articles intended for contact with food products or consumer goods. MBT was found in 5 samples in amounts between 12.3 and 85.6 mg/kg. (Baba 1980 - quoted from BUA 1997).

1.5 Environmental fate

1.5.1 Air

In Japan, the migration of MBT was investigated in 12 rubber articles intended for contact with food products or consumer goods. MBT was found in 5 samples in amounts between 12.3 and 85.6 mg/kg. (Baba 1980 - quoted from BUA 1997).

1.5.2 Water

If released in water, MBT is partially dissociated and may partially adsorb to sediment, especially in acidic water. MBT will rapidly photodegrade in surface water. Biodegradation is apparently very slow and it is not expected to volatilise appreciably. (HSDB 1998, BUA 1997).

1.5.3 Soil

MBT has a low to moderate mobility in soil. Leaching is more likely to occur in alkaline soil. Biodegradation is generally not likely to occur, but may occur when

low concentrations are released to acclimated soil; the half-lives in three standard soils ranged from 92 to 248 days. (HSDB 1998).

1.5.4 Bioaccumulation

Various test results and the values for $\log P_{o/w}$ indicate that the bioaccumulation potential of MBT is low (BUA 1997).

1.6 Human exposure

The general population may be exposed to MBT in rubber products including shoes, gloves, scuba diving masks, wet suits, swim caps and goggles, and many cosmetic products. Infants may be exposed through contact with comforters and teats for baby feeders. In addition, MBT may enter the human organism through the use of contaminated injection solutions and x-ray contrast media. (HSDB 1998, BUA 1997).

2 Toxicokinetics

2.1 Absorption, distribution, and elimination

2.1.1 Inhalation

No data have been found.

2.1.2 Oral intake

Fischer-344 rats (20 males and 20 females per group) were given a single dose of 0.592 or 55.5 mg ^{14}C-labelled MBT/kg b.w. by stomach tube. Four males and 4 females were killed 8, 24, 48, 72, and 96 hours after administration and blood, urine and faeces were collected for radioactivity measurement. Urine from 1 animal per group was collected at 8 hours after administration, and the metabolites were analysed by HPLC. On average, 83-96% of the radioactivity was excreted in the urine and 4-9% in the faeces within 96 hours after dosing. At this time, 0.4-2% was still detectable in the erythrocytes. Seven metabolites were found in the urine, of which 2 were major metabolites (no further details are available on the metabolites). (Hill 1986 - quoted from BUA 1997).

Two male rats were given a single oral dose of 50 mg 2-^{35}S-MBT. Their urine and faeces were collected and extracted 24, 48, and 72 hours after administration. In the urine, 79.4% of the radioactivity was found and 1.4% in the faeces. Besides unchanged MBT, the following metabolites were detected: MBT-sulfate, MBT-glucuronide, 2,2'-dibenzothiazole disulfide and 2-benzothiazole mercapturic acid; the majority (90%) consisted of the parent compound or the metabolite 2,2'-dibenzothiazole disulfide. (Fukuoka & Tanaka 1987 - quoted from BUA 1997).

Male and female Fischer-344 rats (number not specified) were given 0.509 mg MBT/kg b.w. in corn oil by stomach tube, daily for 14 days, followed by a single dose of ^{14}C-labelled MBT (0.503 mg/kg b.w.). Up to approximately 90% of the radioactivity was excreted in the urine and up to approximately 10% in the faeces. The highest specific radioactivity was measured in the thyroid gland. (El Dareer et al. 1989 - quoted from BUA 1997).

2.1.3 Dermal contact

About 16-17% of the radioactivity from a dermal dose of 0.503 mg ^{14}C-labelled MBT/kg b.w. was absorbed through the skin of rats, and the majority (91-94%) was excreted in the urine. A higher percentage (33.4%) of the radioactivity was absorbed through guinea pig skin. (El Dareer et al. 1989 - quoted from BUA 1997 and from BIBRA 1990).

Following a single dose of approximately 11 mg ^{14}C-labelled MBT/kg b.w. applied to the intact or abraded skin of guinea-pigs, the absorption through the abraded skin was higher (37%) than through the intact skin (9%). The substance was almost completely eliminated in the urne and the faeces. The highest level of radioactivity

was present in the thyroid gland, followed by the blood and the kidneys. (Nagamatsu et al. 1979 - quoted from BUA 1997).

2.1.4 Other routes

The metabolites benzothiazole-2-^{35}S-mercaptoglucuronide and ^{35}S-sulfate, together with non-radioactive benzothiazole-2-mercapturic acid, were detected in the urine of male rats for up to 14 days after a single intraperitoneal injection of 590 mg 2-^{35}S-MBT/kg b.w. (Colucci & Buyske 1965 - quoted from BUA 1997).

A single dose of 0.602 mg ^{14}C-labelled MBT was injected intravenously into the tail vein to groups of 28 male and 28 female Fischer rats. Blood samples, urine, and faeces were collected at various time intervals after dosing. After 72 hours, the rats had excreted 91-96% in the urine and 4-15% in the faeces. About 1.5-1.75% of the radioactivity was still present in the erythrocytes. The range of metabolites detected was comparable with that found after oral administration. (El Dareer et al. 1989 - quoted from BUA 1997).

2.2 Toxicological mechanisms

2.2.1 Sensitising effect

Based on *in vitro* measurements it has been suggested that the SH-group of MBT reacts with the carboxyl group of free amino acids present in the epidermis by oxidation and/or thioester formation, so that the hapten MBT becomes an allergen (Wang & Tabor 1988 - quoted from BUA 1997).

3 Human toxicity

3.1 Short and long term toxicity

No data on human toxicity following inhalation or oral intake have been found.

3.1.1 Dermal contact

3.1.1.1 Irritation

Two out of 1141 patients with suspected allergic contact dermatitis given covered 48/72-hour patch tests with 1% MBT in petrolatum exhibited reactions considered by the investigators to be irritant in nature (Storrs et al. 1989 - quoted from BIBRA 1990).

3.1.1.2 Sensitisation

MBT is a potent contact allergen and is the main allergen involved in rubber allergy. For the normal population, the occurrence of MBT sensitisation in different countries has been reported to be in the range of 0.9 to 7.8%. (Schweisfurth 1995).

In a human maximisation test, 9 of 24 test subjects (38%) showed a positive response (sensibilisation). The induction concentration was 25% MBT, and sodium laurylic sulphate pre-treatment was used. Provocation was performed with 10% MBT. (Kligman 1966 - quoted from Nordic Council of Ministers 1991).

The prevalence of patch test responses to 16 allergens, including MBT (2%), was studied in 1200 patients (presumably dermatological patients, although this is not stated) from various locations in North America. Five percent of the study population exhibited sensibilisation to MBT.
Among 4824 Scandinavian patients, a 2% response rate was found using a similar test method (2% MBT).
(Marzuli & Maibach - quoted from Nordic Council of Ministers 1991).

The yearly incidence of MBT sensibilisation among hospital patients during the years 1971-76 was 1.2-2.8% (Cronin 1980 - quoted from Nordic Council of Ministers 1991).

Among 810 contact dermatitis patients, 55 patients (6.8%) showed sensitisation to "rubber additives". Further testing of the 55 rubber additives sensitised patients revealed that 18.1% reacted to mercaptomix[1]. (Song et al. 1979 - quoted from Nordic Council of Ministers 1991). [1]

[1] "Mercaptomix" is used in a standard battery for contact allergy. Mercaptomix contains 4 mercaptanes: MBT (mercaptobenzothiazole), MMBT (morpholinylmercaptobenzothiazole), MBTS (dibenzothiazyl disulfide), and CBS (cyclohexylbenzothiazyl sulphenamid).

During a 12-year period, a total of 106 patients with rubber-related contact dermatitis were tested with a patch test using several rubber additives including MBT. Twenty-four percent showed sensibilisation to MBT. It was concluded that MBT and TMT (tetramethylthiuram) are the main sensibilising agents involved in rubber allergy. (Wilson 1969 - quoted from Nordic Council of Ministers 1991).

Among 1088 dermatological patients tested in 1971 in a standard test battery, 1% showed sensitisation to MBT (2%) (Ziegler & Süss 1975 - quoted from Nordic Council of Ministers 1991 and from BUA 1997).

Among 6621 patients from 8 different countries, the mean occurrence of responses to epicutaneous testing of MBT was 2.9% (Cronin 1980 - quoted from Nordic Council of Ministers 1991).

Among 18 workers exposed occupationally to MBT-containing dust, 6 experienced skin problems related to dust exposure. A patch test was not performed. (National Institute for Occupational Safety and Health 1979 - quoted from Nordic Council of Ministers 1991).

Among 11 surgeons suffering from contact dermatitis in relation to use of surgical gloves, 7 showed a positive patch test response to MBT (Fisher 1975 - quoted from Nordic Council of Ministers 1991).

Among 50 spinal injury patients using uridoms and experiencing penile skin problems, 22% showed sensibilisation to mercaptomix[1]. Among 114 other patients using uridoms, a 13% occurrence of subjective symptoms possible related to rubber allergy was reported in a questionnaire survey. (Brandsbury 1975 - quoted from Nordic Council of Ministers 1991).

Among 12 cases of contact dermatitis related to occupational exposure to MBT-containing cutting oil, 7 subjects showed a positive response to MBT (1%) in a patch test (Fregert & Skog - quoted from Nordic Council of Ministers 1991).

In 3125 (presumably dermatological) North American patients, a 3.0% occurrence of sensibilisation to mercaptomix[1] was found (Büehler 1985 - quoted from Nordic Council of Ministers 1991).

When 145 allergy sufferers were tested with MBT (2% in vaseline), 89 reacted positively (Foussereau & Cavalier 1977 - quoted from BUA 1997).

3.2 Reproductive and developmental effects

No data have been found.

3.3 Mutagenic and genotoxic effects

No data have been found.

3.4 Carcinogenic effects

Mortality (1955-1996) and cancer morbidity experience (1971-1992) of a cohort of 2160 male production workers from a chemical factory (in north Wales) manufacturing chemicals for the rubber industry, with special reference to MBT,

aniline, phenyl-ß-naphthylamine and *o*-toluidine, were investigated. All subjects had at least 6 months employment at the factory and some employment in the period 1955-1984. Detailed job histories and estimates of individual cumulative exposure to MBT and its derivatives were obtained (no further details in the abstract).
Based on serial rates for the general population of England and Wales, observed mortality for the total cohort was close to expectation for all causes (observed deaths 1131, expected deaths 1114.5, standardised mortality ratio (SMR) 101), and for all cancers (observed 305, expected 300.2, SMR 102). There was a significant excess mortality from cancer of the bladder in 605 subjects potentially exposed to one or more of the four chemicals being investigated (observed 9, expected 3.25, SMR 277). In a separate analysis, no positive trend for risk of bladder cancer and cumulative exposure to MBT was found.
(Sorahan et al. 2000 - quoted from TOXLINE).

A study of workers exposed to MBT at a rubber chemical plant (in Nitro, West Virginia) found high rates of lung cancer, prostate cancer, and bladder cancer in these workers who also had potential exposure to 4-aminobiphenyl (PAB), a potent bladder carcinogen. In an update of this study, the mortalities of 1059 full time white male production workers employed at the plant from 1955 to 1977 were examined. It was found that MBT workers had expected rates of lung cancer (SMR 1.0) and prostate cancer (SMR 0.9). There was an excess of bladder cancer among MBT workers with definite exposure to PAB (SMR 27.1) and MBT workers with potential exposure to PAB (SMR 4.3). There were no deaths from bladder cancer among workers with no exposure to PAB (SMR 0.0). (Collins et al. 1999 - quoted from TOXLINE).

4 Animal toxicity

4.1 Single dose toxicity

The acute toxicity of MBT is low. The symptoms of MBT poisoning in animals include peripheral vasodilatation, salivation, lachrymation, and tonic/clonic spasms. (BUA 1997).

4.1.1 Inhalation

Ptosis and reduced movement occurred in rats exposed to 1270 mg/m^3 MBT as dust for 4 hours; the effects were reversible. No anatomical or pathological changes were seen at autopsy. (Ciba Geigy 1985 - quoted from BUA 1997).

Exposure of rats to MBT dust at atmospheric concentrations of 350 to 400 mg/m^3, 2 hours a day for 15 days resulted in weight loss. No adverse effects were observed on histopathological examination of the lungs and nervous system (no further details). (Vorob'eva & Mezentseva 1962 - quoted from BUA 1997 and from BIBRA 1990).

4.1.2 Oral intake

Oral LD_{50}-values of 1680-3800 mg/kg b.w. have been reported for rats; of 1850-2000 mg/kg b.w. for mice; of 1680 mg/kg b.w. for guinea pigs, and of 7500-8750 mg/kg b.w. for rabbits (BUA 1997, BIBRA 1990, IUCLID 2000).

In a range-finding study rats and mice (5 animals of each sex per group) were given MBT in corn oil by stomach tube 12 times (on 5 days per week). Rats were given 0, 165, 313, 625, 1250, or 2500 mg/kg b.w. per day, and mice 0, 187.5, 375, 750, 1500, or 3000 mg/kg b.w. per day. (Dieter 1988 - quoted from BUA 1997).
In rats, body weight gain was reduced by up to 14% in the highest dose group (2500 mg/kg b.w.); no other treatment-related effects were observed.
In mice, all of the high-dose animals died (3000 mg/kg b.w.), as did 4/5 females in the 1500 mg/kg b.w. group. These animals exhibited lethargy and prostration after treatment by stomach tube.

A range-finding test in mice established a maximum tolerated dose (the dose which caused no deaths) of 100 mg/kg b.w. on single or repeated (daily for 6 or 19 days) oral administration of MBT in 0.5% gelatine (Innes et al. 1969 - quoted from BUA 1997).

Rats (5 males per group) were given feed containing 0, 0.1, or 1% MBT (equivalent to 0, 91, or 866 mg/kg b.w./day) for 11 days. Reductions in body weight gain and feed consumption were observed. The absolute and relative liver weights were increased in high-dose animals. The treated groups showed no differences from the control group in terms of behaviour, haematological and clinical-chemical parameters, and there were no changes evident on pathological and histopathological examination. (Eastman Kodak 1985 - quoted from BUA 1997).

4.1.3 Dermal contact

A dermal LD_{50}-value in excess of 7940 mg /kg b.w. has been reported in rabbits (BUA 1997, BIBRA 1990, IUCLID 2000).

Daily application of neat MBT to the intact abdominal skin of rabbits for 10 days caused slight hyperaemia after each application (no further details) (Dow 1985 - quoted from BUA 1997).

4.1.4 Skin irritation

MBT (500 mg) was applied to the intact or abraded skin of white New Zealand rabbits as a finely-milled powder in water and kept under occlusive cover for 24 hours. Skin reactions were evaluated at 24 and 72 hours. MBT did not cause any primary skin irritation. (Monsanto 1985 - quoted from BUA 1997).

Guinea-pigs treated topically with an aqueous paste of MBT (dose not specified) and evaluated 24 hours after application revealed no indications of a skin reaction (no further details) (Du Pont 1948 - quoted from BUA 1997).

4.1.5 Eye irritation

MBT (500 mg) was applied to the intact or abraded skin of white New Zealand rabbits as a finely-milled powder in water and kept under occlusive cover for 24 hours. Skin reactions were evaluated at 24 and 72 hours. MBT did not cause any primary skin irritation. (Monsanto 1985 - quoted from BUA 1997).

Guinea-pigs treated topically with an aqueous paste of MBT (dose not specified) and evaluated 24 hours after application revealed no indications of a skin reaction (no further details) (Du Pont 1948 - quoted from BUA 1997).

4.1.6 Skin sensitisation

A maximisation test has been performed using 20 guinea pigs. During the induction phase, 0.1 ml of a 1% MBT solution was applied intradermally and 0.1 ml of a 25% solution was applied epicutaneously. Freunds complete adjuvant was used. In the provocation test, 15% MBT was applied epicutaneously and the response was evaluated at 48 and 72 hours. Eight guinea pigs (40%) showed a positive response. (Magnusson & Kligman 1969 - quoted from Nordic Council of Ministers 1991).

In a guinea pig maximisation test (24 guinea pigs) of MBT, 20% of the animals showed a positive response (Ziegler & Süss 1975 - quoted from Nordic Council of Ministers 1991).

In four groups of 10 guinea pigs, 2-7 animals per group were sensibilised to MBT following epicutaneous application in a Buehler test. In this study, cross-sensibilisation to MMBT (morpholinylmercaptobenzothiazol, structurally related to MBT) was demonstrated in the majority of animals reacting to MBT. (Wang & Suskind 1987 - quoted from Nordic Council of Ministers 1991).

Groups of 10 guinea pigs were tested for sensibilisation to MBT by using the guinea pig maximisation test, the Siat procedure, and a modified Draize test. In the

guinea pig maximisation test, 6 animals showed a positive response, whereas negative responses were observed using the other two test procedures. (Goodwin et al. 1980 - quoted from Nordic Council of Ministers 1991).

In a guinea pig maximisation test, 12 guinea pigs received a subcutaneous injection of MBT (dose not specified) in the neck, followed y an injection of Freund's adjuvant. Eight days later they were pretreated locally with sodium lauryl sulfate and on the following day, MBT was aplied topically for 48 hours (dose not specified). Two weeks later a patch test was carried out. Oedema and erythema were observed in 5 out of 12 of the guinea-pigs after 24, 48, 72, and 144 hours. MBT was concluded to have a sensitising potential in this study. (Ziegler et al. 1972 - quoted from BUA 1997).

4.1.7 Other routes

Male mice were given intraperitoneal injections of MBT (300 mg/kg b.w.). Shortly after the administration of MBT, the mice suffered from extreme weakness accompanied by ptosis, which lasted for more than 2 hours. Brain catecholamine concentrations were measured after 1, 2, and 4 hours. The content of noradrenaline was reduced by 60% compared with controls at 1 and 2 hours, and returned to normal after 4 hours. The dopamine level was increased by 24% at 2 hours and returned to normal after 4 hours. At this time the mice had recovered from the weakness. (Johnson et al. 1970 - quoted from BUA 1997).

4.2 Repeated dose toxicity

4.2.1 Inhalation

No data have been found.

4.2.2 Oral intake

Rats and mice (10 animals of each sex per group) were given MBT by gavage in corn oil, 5 days per week for 13 weeks. Rats were given 0, 188, 375, 750, or 1500 mg/kg b.w. per day and mice 0, 94, 188, 375, 750, or 1500 mg/kg b.w. per day. (NTP 1988).
In rats, no compound-related deaths occurred. The animals displayed irritable behaviour that was more pronounced with increasing dose and was characterised as resistance to gavage. Body weight gain was reduced with increasing dose, with a maximum change of 15% compared with vehicle controls. Absolute and relative liver weights were increased in male at the two highest dose levels (750 and 1500 mg/kg b.w. per day) and in all groups of treated females, however, no microscopic pathologic changes were noted in any tissue.
In mice, more than half of the high-dose animals died. Body weight gain was not affected. Clinical signs were dose related and included lethargy and rough coats in animals dosed with 375 mg/kg b.w. per day and lachrymation, salivation, and clonic seizure in some animals of the two highest dose levels (750 and 1500 mg/kg b.w. per day). The relative liver weight of dosed groups were higher than those of the vehicle controls. No compound-related gross or microscopic pathologic effects were observed.

In two-year studies, rats and mice (50 animals of each sex per group) were given MBT in corn oil by gavage, 5 days per week for 103 weeks. Male rats were given 0, 375, or 750 mg/kg b.w. per day and female rats 0, 188, or 375 mg /kg b.w./day. Mice were given 0, 375, or 750 mg/kg b.w. per day. (NTP 1988).
In rats, post-gavage lethargy and prostration occurred frequently in dosed animals. Survival of dosed male rats was significantly lower than that of the vehicle controls after week 85 (low-dose males) and after week 83 (high-dose males). Mean body weights of dosed rats were similar to or greater than those of the vehicle controls. The severity of nephropathy was increased in dosed male rats. Ulcers and inflammation of the forestomach were prevalent in dosed rats, as were increased incidences of epithelial hyperplasia and hyperkeratosis in male rats. The occurrence of cystic follicles in the thyroid gland were increased (not statistically significant) in treated animals when compared with the control group (males: 6/50, 8/50, 12/49; females: 4/50, 3/50, 6/50 in control, low- and high-dose groups, respectively).
In mice, post-gavage lethargy and prostration occurred frequently in dosed animals. Survival of high-dose females was significantly lower than that of the vehicle controls after week 27. Minor reductions in body weight gain occurred between weeks 3 and 64, with recovery thereafter. No increases in treatment-related non-neoplastic lesions observed.

In rabbits treated orally with 20 mg MBT/kg b.w. every other day for 2 months, and then daily for 1.5 months, histological examination revealed slight changes in the liver, kidneys, and lungs (no further details). There were no effects on general well-being, behaviour, liver function or the blood. (Vorob'eva & Mezentseva 1962 - quoted from BUA 1997).

No effects were seen in dogs that received 120 ppm MBT in their feed (approximately 3 mg/kg b.w. per day) for 1 year (Lehmann 1965 - quoted from BUA 1997 and BIBRA 1990).

4.3 Reproductive and developmental effects

4.3.1 Generation studies

In a two-generation study in Sprague-Dawley rats, the effects of MBT on reproductive performance and fertility were examined. Male and female rats (28 animals of each sex per group) were administered dietary MBT in concentrations of 0, 2500, 8750, or 15000 ppm (equivalent to 0, 179, 625, or 1071 mg/kg b.w. per day). The premating exposure period was 10 weeks for both sexes. Exposure continued through gestation and lactation until sacrifice approximately 88 days post weaning (this is presumed to be the age of the F1 generation). Survival, clinical signs, reproductive indices, litter size, and pup birth weight and viability were comparable for control and treated animals of all generations. Body weights were significantly reduced for high-dose F0 animals prior to breeding, and for F1 pups from the mid- and high-dose groups and F2 pups from all treated groups beginning at day 14 of lactation and continuing until sacrifice. Treatment-related weight and histopathological changes were seen in kidneys (primarily in males) of F0 and in livers and kidneys of F1 parental rats. (Mercieca et al. 1991 - quoted from TOXLINE, Monsanto 1991 - quoted from IUCLID 2000).

There were no indications of effects on reproduction or lactation in a three-generation study in rats that received up to 120 ppm MBT in their feed (ca. 6

mg/kg b.w. per day) (Lehman 1965 - quoted from BUA 1997 and from BIBRA 1990).

4.3.2 Developmental toxicity / teratogenicity

In a range-finding study, pregnant rats were given 0, 300, 600, 1000, 1500, or 2200 mg/kg b.w. per day by gavage on day 6-15 of gestation (group size not specified). At 1500 and 2200 mg/kg b.w. per day, maternal toxicity (body weight decrease, mortality at 2200 mg/kg b.w. per day) was observed. There were no external abnormalities in foetuses. (Monsanto 1991 - quoted from IUCLID 2000).

Female Sprague-Dawley rats were given 300, 1200, or 1800 mg/kg b.w. per day of MBT in corn oil by stomach tube from day 6 to 15 of pregnancy. On day 20 of pregnancy the foetuses were removed by Caesarean section, weighed and examined for external, visceral and skeletal abnormalities. Maternal toxicity (salivation, blood-caked mouths, coloured urine, and reduced activity, body weight and feed consumption) was observed at the two highest dose levels. MBT did not cause embryotoxic or teratogenic effects at this dose range. (Springborn Life Sciences 1989a - quoted from BUA 1997, Rodwell et al. 1990 - quoted from TOXLINE).

MBT was tested for embryotoxicity in the course of a dominant lethal assay. One group of female rats (11 animals) received 200 mg/kg b.w. orally before pregnancy on days 1 and 3 of oestrus, the second group (15 animals) on days 4 and 11 of pregnancy. Male rats which were mated with the first group received the same dose twice before mating, at intervals of 3 days. The second group was mated with untreated males. MBT treatment increased the length of the oestrous cycle of the dams. A significant reduction in foetal weight and fertility (number of live foetuses per dam) occurred, independent of whether the females were treated before or during pregnancy. Total embryo mortality increased significantly. (Alexandrov 1982 - quoted from BUA 1997).

MBT in 1% methyl cellulose was given to groups of 20 pregnant rabbits in doses of 0, 50, 150 or 300 mg/kg b.w. per day by stomach tube from day 6 to 18 of pregnancy. On day 29 of pregnancy, the foetuses were removed by Caesarean section and examined for external, visceral, and skeletal anomalies. At the highest dose level, a slight reduction in maternal body weight and a slight increase in absolute and relative liver weight were observed. MBT was not embryotoxic or teratogenic at these doses. (Springborn Life Sciences 1989b - quoted from BUA 1997, Rodwell et al. 1990 - quoted from TOXLINE).

No foetal toxicity, malformations, or maternal toxicity were observed when 10-15 pregnant rats were given daily intraperitoneal injections of 200 mg MBT/kg b.w. per day (in oil) from day 1 to 15 of pregnancy (Hardin et al 1981 - quoted from BUA 1997 and from BIBRA 1990).

4.4 Mutagenic and genotoxic effects

4.4.1 *In vitro* studies

4.4.1.1 Bacterial assays

MBT has been tested in the Salmonella/microsome test (strains TA1535, TA1537, TA1538, TA98 and TA100) with and without metabolic activation (S9-mix) at concentrations up to 300 µg/plate with negative results. Concentrations from 333 µg/plate were bacteriotoxic. (Pharmacon Research International 1984 - quoted from BUA 1997).
Similar results have, according to BUA (1997), been reported in an earlier, comparable study (Bionetics 1976 - quoted from BUA 1997).

MBT was not mutagenic in *Salmonella typhimurium* strains (TA98, TA100, TA1535, TA1537) when tested at concentrations up to 10000 µg/plate in the presence or absence of metabolic activation (S9 from rat or hamster liver). Toxicity was observed from 333 µg/plate. (NTP 1988).

MBT was not mutagenic in *Escherichia coli* strain SD-4-73 (no further details (Szybalski 1958 - quoted from BUA 1997 and from NTP 1988).

4.4.1.2 Tests in fungi

MBT gave no indications of an increase in the number of revertants when tested for induction of mitotic gene conversion in *Saccharomyces cerevisiae* strain D4 with and without metabolic activation (S9-mix) (Monsanto 1985 - quoted from BUA 1997).

4.4.1.3 Mammalian cell assays

A forward mutation test in Chinese Hamster Ovary (CHO) cells gave negative results when MBT was tested at concentrations up to 300 µg/ml (metabolic activation) and up to 50 µg/ml (without metabolic activation). Doses of 100 µg/ml (without metabolic activation) and 1000 µg/ml (with metabolic activation) were toxic to the cells. (Pharmacon Research International 1984 - quoted from BUA 1997 and from NTP 1988).

In L5178Y mouse lymphoma cells, both negative and positive results have been reported.
Negative results were obtained when MBT was tested at concentrations up to 100 µg/ml with and without metabolic activation (no further details) (Monsanto 1978 - quoted from IUCLID 2000). Small increases in mutant frequency were observed but only at concentrations that also produced cytotoxicity when MBT was tested at concentrations up to 150 µg/ml with metabolic activation and up to 100 µg/ml without metabolic activation (Monsanto 1986 - quoted from IUCLID 2000).
MBT induced thymidine kinase mutants in the presence of metabolic activation (S9 from rat liver) when tested at concentrations from 5-20 µg/ml but not in the absence of metabolic activation when tested at concentrations up to 100 µg/ml (NTP 1988).

The ability of MBT to induce chromosomal aberrations was tested in Chinese Hamster Ovary (CHO) cells at concentrations of 10 to 30 µg/ml (without metabolic activation) and of 352 to 500 µg/ml (with metabolic activation, S9 from rat liver). In the presence of metabolic activation, there was an increase in chromosomal aberrations at concentrations of 374 µg/ml and above; chromosomal aberrations were not observed without metabolic activation. (NTP 1988; Dieter 1988, Anderson et al. 1990 - both quoted from BUA 1997).

The induction of sister chromatid exchanges (SCEs) was studied in CHO cells with and without metabolic activation (S9 from rat liver) at the same dose levels as used in the tests for chromosomal aberrations. With metabolic activation, an increased incidence of the relative number of SCEs/cell was observed; without metabolic activation, there was no induction of SCEs. (NTP 1988; Dieter 1988, Anderson et al. 1990 - both quoted from BUA 1997).

4.4.2 *In vivo* studies

In a micronucleus test in CD1 mice, a dose of 300 mg MBT/kg b.w. was given by intraperitoneal injection on 2 consecutive days, and 1000 polychromatic erythrocytes/mouse were screened for micronuclei. MBT was negative in this study. (Pharmacon Research International 1984 - quoted from BUA 1997 and from NTP 1988).

Male Sprague-Dawley rats (28 animals per group) received MBT at dietary concentrations of 0, 2500, 8750 and 15000 ppm (equivalent to 0, 125, 440, or 750 mg/kg b.w. per day) for 13 weeks before mating and then throughout the 2-week mating period. A positive control group received the basal diet and, 7 days before the mating period, a single dose of 100 mg cytoxan/kg b.w. Each male was paired with 2 nulliparous females for 2 weeks. Administration of the medium and high concentrations led to reductions in food consumption and body weight. The females were killed on day 13 of pregnancy, and the number of dead embryos and live foetuses was recorded; no dominant lethal effect was found in the MBT-treated groups compared with the controls. (Springborn Life Sciences 1989 - quoted from BUA 1997).

4.4.3 Covalent binding to DNA

An investigation of a possible genotoxic mechanism for the carcinogenicity of MBT was conducted by examining the covalent binding of MBT to DNA from rat tissues. Male and female Fischer 344 rats were given a single dose of 375 mg ^{14}C-labelled MBT /kg b.w. by gavage and were killed 8 hours later. The DNA was extracted from the liver, adrenal glands, pancreas, pituitary gland and bone marrow, and the DNA-bound radioactivity was determined. There was only a low and insignificant degree of binding of radioactivity to the DNA of the examined tissues. (Monsanto 1989 - quoted from BUA 1997).

4.5 Carcinogenic effects

4.5.1 Inhalation

No data have been found.

4.5.2 Oral intake

In two-year studies, rats and mice (50 animals of each sex per group) were given MBT in corn oil by gavage, 5 days per week for 103 weeks. Male rats were given 0, 375, or 750 mg/kg b.w. per day and female rats 0, 188, or 375 mg /kg b.w. per day. Mice were given 0, 375, or 750 mg/kg b.w. per day. (NTP 1988).

Table 4.5 Tumour incidences in rats (from NTP 1988)

Tumour	Sex	Control	188 mg/kg b.w. per day (females only)	375 mg/kg b.w. per day	750 mg/kg b.w. per day (males only)
Mononuclear cell leukaemia	male	7/50		16/50	3/50
	female	6/50	14/50	9/50	
Pituitary gland:					
hyperplasia	male	10/50		17/50	12/48
	female	8/49	10/50	6/50	
adenoma	male	14/50		21/50	12/48
	female	15/49	24/50	25/50	
adenocarcinoma	female	1/49	0/50	0/50	
adenoma or adenocarcinoma	female	16/49	24/50	25/50	
Adrenal gland:					
medullary hyperplasia	male	9/50		14/50	10/49
	female	5/50	8/50	2/50	
pheochromocytoma	male	18/50		25/50	22/49
	female	1/50	5/50	6/50	
malignant pheochromocytoma	male	0/50		2/50	2/49
pheochromocytoma or malignant pheochromocytoma	male	18/50		27/50	24/49
Pancreas:					
acinar cell hyperplasia	male	5/50		15/50	7/49
acinar cell adenoma	male	2/50		13/50	6/49
Preputial gland:					
adenoma	male	0/50		4/50	4/50
carcinoma	male	1/50		2/50	1/50
adenoma/carcinoma	male	1/50		6/50	5/50

The incidences of a variety of tumours were increased in dosed rats (table 4.5); some of the increased incidences were not dose related. In low-dose male rats, increased incidences ($p<0.01$) were observed for mononuclear cell leukaemia and pancreatic acinar cell adenomas. Increased tumour incidences with dose-related trends ($p<0.05$) included pituitary gland adenomas in females, preputial gland adenomas or carcinomas (combined) in males, adrenal gland pheochromocytomas

or malignant pheochromocytomas (combined) in males, and pheochromocytomas in females. These tumours were observed at significantly higher incidences ($p \leq 0.05$) in the high dose groups than in the vehicle controls.
In male rats, mesotheliomas occurred with a significant positive trend, although the incidences in the dosed groups were not statistically significantly increased compared to controls.
In mice, an increased incidence of hepatocellular adenomas or carcinomas (combined) was observed only in low dose females; no significant increases in tumour incidences were seen in male mice.
Under the conditions of these studies, NTP has concluded that there was "some evidence of carcinogenic activity" for male and female rats; "no evidence of carcinogenic activity" for male mice; and "equivocal evidence of carcinogenic activity" for female mice.
Non-neoplastic findings are given in part 4.2.

Mice of two strains (36 mice per group) received 100 mg MBT/kg b.w. per day by stomach tube from day 7 to 28 of life and then 323 ppm MBT in their feed (equivalent to approximately 50 mg/kg b.w. per day) for 17 months (Bionetics Research Laboratories 1968 - quoted from BIBRA 1990; Innes et al. 1979 - quoted from BUA 1997).
According to BIBRA (1990), there was a "suspicion of a treatment-related increase in the incidence of "reticulum cell sarcoma" (probably malignant lymphomas).
According to BUA (1997), "there was no significant increase in the incidence of tumours".

5 Regulations

5.1 Ambient air

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5.2 Drinking water

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5.3 Soil

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5.4 Occupational Exposure Limits

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5.5 Classification

MBT is classified for sensitising effects (R43 - may cause sensitisation by skin contact) and for environmental effects (N; R50/53 - very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (MM 2000).

XXIth recommendation of the Plastics Commission of the Federal Health Office: commodities on the basis of rubber from natural and synthetic rubber (status: 1 December 1986):
For the production of commodities based on natural and synthetic rubber, MBT is permissible as a vulcanisation accelerator according to the aforementioned recommendation with a maximum amount of 0.05%. With articles of the special category (toys, balloons, bottle teats) the additional amount of MBT is to be limited such that accelerators containing sulfur are not detectable in the extracts (BUA 1997).

5.6 IARC

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5.7 US-EPA

-

6 Summary and evaluation

6.1 Description

2-Mercaptobenzothiazole (MBT) is a crystalline substance with a low solubility in water (117 mg/l at 20°C) and a low vapour pressure. An odour threshold in water of 1.76 mg/l has been reported.

6.2 Environment

MBT enters the environment during industrial production and use mainly with waste water, during the use of the pesticide methabenzothiazuron, and via emission from rubber products. No data on environmental concentrations have been found. When released to the atmosphere, MBT is primarily removed by gravitational settling.

6.3 Human exposure

The general population may be exposed to MBT in rubber products.

6.4 Toxicokinetics

MBT is readily and almost completely (more than 90%) absorbed after oral and parenteral administration; absorption through intact skin is around 9 to 17%. Metabolism and elimination is almost complete within 96 hours; however, up to 2% was still detectable in the erythrocytes. Elimination is primarily via the urine (approximately 90%) and the parent compound, MBT-glucuronide, MBT-sulfate, 2-benzothiazole mercapturic acid, and the dimer 2,2'-dibenzothiazole disulfide have been identified with the parent compound and the dimer accounting for around 90% of the excreted substances.

6.5 Human toxicity

MBT is a potent contact allergen which is considered to be the main allergen involved in rubber allergy. MBT was shown to be a sensitiser in a human maximisation test. In several large studies of patients from various countries, 2-5% of the study population exhibited sensitisation to MBT. Among patients with rubber-related contact dermatitis, the percentage reacting to MBT was 20-60%.

Two epidemiological studies of workers exposed to rubber chemicals, including MBT, have shown an increased risk of bladder cancer. However, the data do not indicate that MBT is self is a bladder carcinogen.

6.6 Animal toxicity

6.6.1 Single dose toxicity

The acute toxicity of MBT is low with an LC_{50}-value above 1270 mg/m^3 in rats (4 hours exposure to MBT as dust); oral LD_{50}-values of 1680-3800 mg/kg b.w. for rats, of 1850-2000 mg/kg b.w. for mice, of 1680 mg/kg b.w. for guinea pigs; and of 7500-8750 mg/kg b.w. for rabbits; and a dermal LD_{50}-value in excess of 7940 mg/kg b.w. in rabbits. The symptoms of MBT poisoning in rodents included peripheral vasodilatation, salivation, lachrymation, and tonic/ clonic spasms.
MBT does not seem to be a primary skin irritant; it is slightly irritating to the eyes. MBT was positive for skin sensitising effect in several guinea pig maximisation tests, and in one Buehler test.

6.6.2 Repeated dose toxicity

In repeated dose toxicity studies (13-week and 2-year studies) in rats and mice with oral dosing (dose range 94 to 1500 mg/kg b.w. per day), lethargy in relation to daily dosing was observed in both animal species. In the 2-year rat study, inflammation and ulceration of the forestomach, epithelial hyperplasia and hyperkeratosis (males only) and nephropathy (males only) were observed in dosed animals, whereas in the 2-year mouse study, no compound-related nonneoplastic lesions were observed. In the 13-week study of rats, reduced body weight gain and increased liver weight (from 750 mg/kg b.w. per day) were observed; in mice, increased liver weight of dosed groups was observed.
In a teratogenicity study in rats, doses of 1200 or 1800 mg/kg b.w. per day caused maternal toxicity manifested as salivation, blood-caked mouths, coloured urine, reduced activity, and reduced body weight and feed consumption, while a dose of 300 mg/kg b.w. per day apparently did not.

6.6.3 Reproductive and developmental effects

In rats given very high doses (3000 mg/kg b.w. per day for 13 weeks), sloughing of the epithelial cells of seminal vesicles was observed in males.
In a three-generation study in rats, no indications of effects on reproduction or lactation were observed at a dietary dose level of around 6 mg/kg b.w. per day. Higher dietary doses (179-1071 mg/kg b.w. per day) were given in a two-generation study in rats; no adverse effects were registered in the offspring.
No external abnormalities were observed in the offspring of female rats exposed on gestational day 6-15 to oral doses of 300-2200 mg/kg b.w. per day. In another teratogenicity study in rats, no embryotoxic or teratogenic effects were observed in spite of marked maternal toxicity following oral administration of 300-1800 mg/kg b.w. per day on day 6-15 of gestation. In a rabbit teratogenicity study (oral doses of 0-300 mg/kg b.w. per day from day 6 to day 18 of pregnancy), slight maternal toxicity but no adverse foetal effects were observed at the highest dose level.
In a dominant lethal assay in rats, increased length of the oestrous cycle of the dams, reduced fertility, increased total embryo mortality, and reduced foetal weight were observed when MBT (200 mg/kg b.w.) was administered to female rats on day 1 and 3 of oestrus or on day 4 and 11 of pregnancy.

6.6.4 Mutagenic and genotoxic effects

MBT was not mutagenic when tested in *Salmonella typhimurium*, in *Eschericia coli*, in *Saccharomyces cerevisiae*, and in a forward mutation test in CHO cells. In mouse lymphoma cells, both negative and positive results have been reported. In the presence of metabolic activation, MBT increased the frequency of chromosomal aberrations and sister chromatid exchanges in CHO cells.
MBT was negative in two *in vivo* tests (a mouse micronucleus test and a dominant lethal test in rats). In a study examining the covalent binding of MBT to DNA in rat tissues, there was only a low and insignificant binding to the DNA of the examined tissues (liver, pancreas, bone marrow, adrenal or pituitary gland).

6.6.5 Carcinogenic effects

Carcinogenicity studies with oral exposure (gavage in corn oil) have been performed in rats and mice by NTP. The incidences of a variety of tumours were increased in dosed rats; some of the increased incidences were not dose related. In mice, an increased incidence of hepatocellular adenomas or carcinomas (combined) was observed in low dose females only; no significant increases in tumour incidences were seen in male mice.

6.7 Evaluation

MBT is a skin sensitiser. This is well-documented by both human and animal data. A human maximisation test has shown that 38% of the test subjects could be sensitised. In two guinea pig maximisation tests, 40% and 60% of the test animals were sensitised. In several studies of patients, 2-5% of the study population exhibited sensitisation to MBT. The percentage of MBT sensitisation among individuals suffering from rubber-related contact dermatitis is much higher (20-60%).
No data are available to evaluate whether MBT is a respiratory sensitiser.

With respect to general toxicity after repeated exposure, oral administration of MBT to rats and mice results in body weight reduction and effects on the liver and kidneys (rats only); at high dose levels, seizures and death are observed. MBT seems to have a pharmacological CNS depressant effect since lethargy in relation to dosing has been observed in both rats and mice. Lethargy and reduced body weight have been observed at oral doses from around 180 mg/kg b.w. per day in rats and from around 95 mg/kg b.w. per in mice; a NOAEL for these effects cannot be determined from the available studies.

MBT has not shown reproductive toxicity when tested in a two-generation rat study at doses (179-1071 mg/kg b.w. per day) which caused signs of general toxicity. A three-generation rat study also showed no reproductive effects; however, the dose was very low (6 mg/kg b.w. per day) compared with the doses causing toxicity, and this study is therefore considered inconclusive.
MBT did not show clear developmental toxicity in rats given oral doses from 300 to 2200 mg/kg b.w. per day (on gestation days 6-15) or in rabbits given oral doses of up to 300 mg/kg b.w. per day (on gestation days 6-18). In spite of marked maternal toxicity at the higher dose levels in the two studies in rats, no foetal malformations were observed.
In a dominant lethal assay in rats, increased length of the oestrous cycle of the dams, reduced fertility, increased total embryo mortality, and reduced foetal weight

were observed when MBT (200 mg/kg b.w.) was administered to female rats on day 1 and 3 of oestrus or on day 4 and 11 of pregnancy.

MBT has produced equivocal results when tested for genotoxicity *in vitro*. MBT has not shown any genotoxic potential in bacteria or fungi when tested both in the presence or absence of metabolic activation. In mouse lymphoma cells, MBT produced gene mutations in the presence of a metabolic activation system in one study, while no effect was reported in another study. In CHO cells, MBT produced clastogenic effects, measured as chromosomal aberrations and sister chromatid exchanges, at fairly high concentrations in the presence of a metabolic activation system. In two *in vivo* tests, MBT was negative in a dominant lethal test in rats and in a mouse micronucleus test.
In a study, designed to examine the covalent binding of MBT to DNA in the rat tissues in which tumours were observed in a chronic study (liver, pancreas, bone marrow, adrenal or pituitary gland), only a low and insignificant binding to the DNA of these tissues was observed.
The available data do not clearly resolve whether MBT is a genotoxic substance or not. The positive responses in the mammalian cells *in vitro* point to a clastogenic potential in combination with metabolic activation. In the absence of significant covalent binding to DNA in target tissues *in vivo* and mutagenic effects in bacteria *in vitro*, it can be speculated that the effects seen in mammalian cells *in vitro* are produced by reactive species, most likely reactive oxygen species, generated throught redox cycling of MBT in the metabolic activation system. MBT was also negatiave in the two *in vivo* tests. The rat dominant lethal test is considered of low sensitivity, while the negative result in the mouse micronucleus test combined with the tendency of MBT to persist in red blood cells (shown in toxicokinetic studies) indicate a low order of genotoxic potential of MBT *in vivo*, if any.

The rat study performed under the US National Toxicology Program showed an increase in the number of tumours in various organs of MBT-treated animals. As MBT has not convincingly shown genotoxic properties *in vivo*, the observed tumourigenic effect may be secondary to a prolonged adverse effect of treatment on the respective organs. Based on the available studies, a no observed adverse effect level (NOAEL) cannot be established. It cannot be excluded that MBT may have a carcinogenic potential in humans.

6.7.1 Critical effect and NOAEL

Based on the available data, the critical effect in humans following exposure to MBT is considered to be the sensitising effect observed in both humans and experimental animals following dermal contact with MBT. No data are available to elucidate whether MBT is a respiratory sensitiser. Furthermore, the available data do not indicate at which concentrations or dose levels the skin sensitising effect is exerted; however, it is considered that the sensitising effect may be exerted in humans at very low concentrations or dose levels, at least in sensitised individuals.

The available data are considered inadequate for the purpose of setting af health based C-value for the critical effect of MBT, the sensitising effect.
However, it is proposed to place MBT in Main Group 1 with a C-value lower than 0.001 mg/m^3 for the following reasons:
Main Group 1 is assigned those chemical substances that are known to be especially injurious to health or especially dangerous to the environment (MST 1990). Sensitisation to a chemical substance is a very serious health effect. Several studies of patients have revealed that 2 to 5% of the study population have

exhibited sensitisation to MBT following skin contact. Furthermore, MBT might be a respiratory sensitiser.
A C-value lower than 0.001 mg/m^3 is proposed because the sensitising effect may be exerted in humans at very low concentrations or dose levels, at least in sensitised individuals.

6.7.2 C-value

0.001 mg/m^3, Main Group 1

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TOXLINE.

2- Mercaptobenzothiazole (MBT)

The Danish Environmental Protection Agency has requested an evaluation of health hazards by exposure to 2- Mercaptobenzothiazole (MBT). This resulted in 2001 in the present report which includes a health-based quality criterion for the substance in ambient air.

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