Mercaptobenzothiazole and its salts: Human health tier II assessment

05 February 2016

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
2(3H)-Benzothiazolethione	149-30-4
2(3H)-Benzothiazolethione, zinc salt	155-04-4
2(3H)-Benzothiazolethione, sodium salt	2492-26-4

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to

human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this category are 2-mercaptobenzothiazole (MBT) and its sodium and zinc salts, NaMBT and ZnMBT, respectively. The chemical MBT, is a weak acid that forms salts in basic solutions with a variety of metal ions. The chemicals, NaMBT and ZnMBT hydrolyse to form the parent acid MBT. The physico-chemical properties of these chemicals are not expected to vary greatly. The systemic toxicity of these chemicals are expected to be similar and will be driven predominantly by MBT and, as such, they are grouped together for human health risk assessment (NIOSH, 2014; NTP, 1988; SCCP, 2005).

Import, Manufacture and Use

Australian

Sodium MBT has reported commercial use under previous mandatory and/or voluntary calls for information.

International

The following international uses have been identified through the European Union (EU) Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) dossiers; Galleria Chemica; the Substances and Preparations in Nordic countries (SPIN) database; the United States (US) Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR); the US National Library of Medicine's Hazardous Substances Data Bank (HSDB); the European Commission Scientific Committee on Consumer Products Report (SCCP, 2005); National Institute for Occupational Safety and Health Report (NIOSH, 2014) and the US High Volume Information System (HPVIS) robust summaries on benzothiazole-and morpholine-based thiazoles.

NaMBT has reported domestic use as an ingredient in automotive products (radiator cleaner at 1.0-1.5 %).

The chemicals have reported commercial use as corrosion inhibitors.

The chemicals have reported site-limited uses, including:

- as a vulcanisation accelerator for rubber;
- as additives in greases;
- as antifreezing agents; and
- in cutting fluids.

The chemicals have reported non-industrial uses, including:

- as a veterinary medication;
- as fungicides.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Worker Health and Safety Controls

Hazard Classification

The chemical, MBT is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

- Xi; R43 (sensitisation)

Exposure Standards

Australian

No specific exposure standards are available.

International

The following exposure standards are identified for MBT (Galleria Chemica):

An exposure limit of 4-5 mg/m^3 time weighted average (TWA) and maximum concentrations in the workplace air (MAK) in different countries such as Germany, Russia, Canada (Yukon), Norway and Switzerland.

Temporary Emergency Exposure limits (TEELs) defined by the US Department of Energy (DOEs) for MBT is reported as:

TEEL-1 = 8.2 mg/m^3;

TEEL-2 = 8.2 mg/m^3; and

TEEL-3 = 20 mg/m^3.

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 1 mg/m^3 TWA.

Health Hazard Information

In acidic conditions, ZnMBT dissociates to the parent acid MBT and zinc cation. Zinc is one of the most important trace elements in the human body, and is important in homeostasis, immune function, oxidative stress in apotosis and in ageing. A common risk to human health is zinc deficiency, which is associated with significant disorders such neurological disorders, autoimmune diseases, and age-related degenerative diseases (Chasapis et al, 2011). It is expected that, after ingestion, all zinc compounds dissociate into the zinc cation. Given the essential role of zinc ions in normal physiological functions, they are not considered toxicologically relevant except at high levels. Additionally, no critical systemic chronic effects were observed based on the NICNAS assessment of soluble zinc salts (NICNAS). The sodium cation is present in high quantities in the normal human diet and is considered to be low concern (NICNAS, 2012).

Toxicokinetics

Based on the available data, the chemicals in this group are expected to be readily absorbed following oral and inhalation exposure and to a lesser extent following dermal exposure (REACHa; REACHb; REACHc).

Acute Toxicity

Oral

The chemicals have low acute toxicity based on results from animal tests following oral exposure. The median lethal dose (LD50) in rats for each chemical is >2000 mg/kg bw. Observed sub-lethal effects included lethargy, increasing weakness, reduced appetite, changes in motor activity, collapse and death.

Sprague Dawley (SD) rats (5 animals/dose) were administered MBT at 3160, 3610, 3980, or 5010 mg/kg bw by gavage. All animals in the 3610 and 5010 mg/kg bw dose groups died within one to three days of treatment. Clinical signs included reduced appetite and increasing weakness, collapse and death. Lung hyperaemia (excess of blood), slight liver discolouration and gastrointestinal inflammation were observed in the autopsy of the deceased animals. The reported LD50 was 3800 mg/kg bw (REACHa).

In another study, SD rats (5 animals/dose) were administered ZnMBT at 5000, 6310, 7940 or 10000 mg/kg bw by gavage. All animals in the 10000 mg/kg bw/group died one to two days after the treatment. Autopsy examination of the deceased animals showed haemorrhagic areas in the lungs, liver hyperaemia and gastrointestinal inflammation. Sub-lethal effects included reduced appetite and activity, increasing weakness and collapse. The reported LD50 was 7500 mg/kg bw (REACHc).

In another study, NaMBT was administered to Wistar rats (10 animals/sex/dose) at 400, 800, 1600, 2480, 2800, 3200 or 4000 mg/kg bw by gavage. Clinical signs included sedation, breathing disturbance and myoclonus (spasmodic jerky contraction of muscles). The reported LD50 was 2100 mg/kg bw (REACHb).

Dermal

The chemicals have low acute toxicity based on results from animal tests following dermal exposure. The LD50 in rabbits for MBT and NaMBT is >2000 mg/kg bw. Observed sub-lethal effects included changes in motor activity and reduced appetite.

New Zealand White rabbits (2 animals/sex/dose) were applied MBT in corn oil under semiocclusive conditions at 5010 or 7940 mg/kg bw for 24 hours. No mortalities were reported. Clinical signs included reduced appetite and activity for 1 to 2 days after treatment. The reported LD50 was >7940 mg/kg bw (REACHa; REACHc).

In another study, NaMBT was applied on the skin of New Zealand White rabbits (1-3 animals/sex/dose) under semiocclusive conditions at 3160, 5010 or 7940 mg/kg bw for 24 hours. Clinical signs included weight loss, increasing weakness, tremors, convulsions, salivation, collapse and death in a few animals. One animal in the 7940 mg/kg bw group died 3 hours after the treatment and one animal died one day after the treatment. Autopsy of the animal that died at 3 hours after treatment showed haemorrhagic areas in the lungs, liver, spleen and kidney discolouration, enlarged gall bladder and gastrointestinal inflammation. The reported LD50 was >5010 mg/kg bw (REACHb).

Inhalation

The chemicals have low acute toxicity in an animal test following inhalation exposure. The median lethal concentration (LC50) for MBT is >1270 mg/L .

Charles River rats (5 animals/sex/dose) were exposed to MBT at 1270 mg/L by whole body inhalation exposure for a 4 hour duration. No mortalities were reported. Clinical signs included ptosis and hypoactivity. The reported LC50 was >1270 mg/L air (REACHa).

Corrosion / Irritation

Corrosivity

Based on experimental data for NaMBT from skin and eye irritation studies in animals (particularly scar formation and corneal necrosis) and observations in humans, there is sufficient evidence to warrant hazard classification.

NaMBT is corrosive to the skin in animal and human tests following dermal exposures due to its high pH (NIOSH, 2014).

Animal studies

In a skin irritation study, New Zealand White rabbits (6 animals) were treated with NaMBT (45% solution, pH > 12) for 4 hours via semiocclusive application to intact skin and observed for up to 7 days. The chemical was corrosive with a mean overall irritation score of 8 (out of a maximum irritation score of 8). The effects were not reversible within 7 days (REACHb).

In another skin irritation study, a 50 % NaMBT solution was applied to intact and abraded skin of New Zealand White rabbits (6 animals) for a 24 hour exposure via semiocclusive application and observed for up to 14 days. The chemical was corrosive with a mean overall irritation score of 6.6 (out of a maximum irritation score of 8) with necrosis, severe oedema, severe defatting effects seen at 24 hours and skin sloughing at 10 to 14 days post-application. These effects were not reversible within 14 days (REACHb).

In an eye irritation study, 100 µL of NaMBT (purity not specified) applied to the conjunctival sac of New Zealand White rabbits (2 animals/dose) resulted in strong irritation and corrosion of the cornea (REACHb). No other details were provided.

In another eye irritation study in rabbits, application of NaMBT (50 % purity) to the conjunctival sac of New Zealand White rabbits (6 animals) resulted in immediate discomfort with pawing, squealing, thrashing of the stocks and tightly closed eyes. Corneal opacity, severe erythema, slight oedema and corrosion were reported at 1 to 24 hours. The effects were not reversible (REACHb).

Human studies

In a case study in humans, 43 volunteers were treated with NaMBT at concentrations of 0.1, 0.2 or 0.4 mg/mL. Six of the 43 volunteers showed slight primary irritant reactions to 0.4 mg/mL of NaMBT (REACHb).

Skin Irritation

Corrosive effects associated with the alkaline NaMBT are not applicable to MBT and ZnMBT due to the different pH. Based on the available data, the chemicals MBT and ZnMBT are not irritating to the skin.

In a study, MBT (97.4 % purity) was applied to clipped intact and abraded skin of New Zealand White rabbits (6 animals) for a 24 hour exposure, under a semiocclusive condition with observation up to 7 days. The chemical was not irritating to the rabbit skin (REACHa).

In another study, ZnMBT was applied to intact and abraded skin of New Zealand White rabbits (6 animals) for a 24 hour exposure under a semiocclusive condition. No irritation reactions were seen at 24 and 72 hour observations (REACHc).

Eye Irritation

Corrosive effects associated with the alkaline NaMBT are not applicable to MBT and ZnMBT due to the differing pH. Based on the available data, the chemicals MBT and ZnMBT are only slightly irritating to the eye.

In a study conducted in New Zealand White rabbits (6 animals), application of MBT (97.4 % purity) to the cornea resulted in slight to moderate erythema at 24 hours. The effects were fully reversed within 72 hours (REACHa).

In another study, application of 100 mg of ZnMBT (purity not specified) to the conjunctival sac of New Zealand White rabbits (6 animals) resulted in slight erythema and slight discharge. All the effects were fully reversed within 48 hours of treatment (REACHc).

Sensitisation

Skin Sensitisation

MBT is classified as hazardous with the risk phrase ‘May cause sensitisation by skin contact’ (R43) in the HSIS (Safe Work Australia). The positive results reported in several skin sensitisation tests for MBT support this classification. Positive results were also reported for the skin sensitisation potential of ZnMBT whilst no data are available for NaMBT. Hazard classification is warranted for ZnMBT and NaMBT.

In a guinea pig maximisation test (GPMT) conducted according to the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 406, female guinea pigs (10 animals/dose) were treated with 0.1 mL of 5 % MBT solution intradermally and 0.1 mL of 25 % solution epicutaneously in the induction phase. In the challenge phase, the animals were treated with 12 % MBT epicutaneously and observations were made at 48 and 72 hours. The vehicle used was physiological saline. A positive response was seen in seven and six guinea pigs after 48 and 72 hours, respectively (REACHa; REACHb).

In another GPMT, male guinea pigs (20 animals/dose) were treated with 2.5 % MBT solution intradermally and 40 % solution epicutaneously in the induction phase. For the first challenge, the animals were treated with 12 % or 40 % MBT. In a second challenge, animals were treated with 1 % or 3 % MBT. The vehicle used was physiological saline. Observations were made at 48 and 72 hours. Around 80 % of the animals treated in the first challenge showed positive skin reactions and 15 % of animals treated in the second challenge showed positive skin effects (REACHa).

In a local lymph node assay (LLNA) study in female Balb/c mice (three animals/dose), MBT was found to be sensitising at concentrations of 2.5 %, 5 % and 10 %; the stimulation indices were 1.33, 2.33 and 2.51, respectively (REACHa).

In a Buehler test, male Pirbright Dunkin-Hartley guinea pigs (10 animals/dose) were treated with 0.1 g of 5 % MBT in petrolatum (induction) and 0.1 %, 0.5 % or 2 % MBT (challenge). The chemical was positive for skin sensitisation reactions in two and seven animals in the 0.5 and 2 % doses, respectively (REACHa).

Ten percent MBT was found to induce skin sensitisation reactions from GPMT induction tests and LLNA from a comparison of several GPMT and LLNA studies (SCCP, 2005).

In another LLNA study in female Balb/c mice (three animals/dose), ZnMBT was found to be sensitising at concentrations of 1.25, 2.5, 5.0, 10 or 20 % with extrapolated EC3 value of 30.3 % (De Jong et al, 2001; REACHc).

Observation in humans

The positive data in animal studies are supported by the human case reports detailed below.

In a maximisation test in 24 humans volunteers, MBT was tested for sensitisation at an induction dose of 25 % and a challenge dose of 10 %. Positive responses were reported in 9/24 subjects (SCCP, 2005).

Various other case studies mentioned that patch tests on dermatological patients from North America (5 % sensitised population) and Scandinavia (2% response rate) reported positive sensitisation responses to MBT (SCCP, 2005).

Repeated Dose Toxicity

Oral

Based on the available information, hazard classification for repeated dose oral toxicity is not recommended.

B6C3F1 mice (five animals/sex/dose) were administered twelve daily doses of MBT at 0, 188, 375, 750, 1500 or 3000 mg/kg bw/day by gavage over a period of sixteen days. All animals in the 3000 mg/kg bw/day group and 4/5 females in the 1500 mg/kg bw/day group died before the end of the study. Gross examination and pathological examination showed no treatment-related effects. All animals in 375 and 750 mg/kg bw/day groups showed clinical symptoms of lethargy and rough coats. A lowest observed adverse effect level (LOAEL) of 375 mg/kg bw/day was established (NTP, 1988; REACHa; REACHb; REACHc).

In a 13-week study in Fischer 344 (F344/N) rats (groups of 10 animals/sex/dose) and B6C3F1 mice (groups of 10 animals/sex/dose), MBT in corn oil was administered by gavage at 0, 188, 375, 750 or 1500 mg/kg bw/day in rats and 0, 94, 188, 375, 750 or 1500 mg/kg bw /day in mice, five days per week for 13 weeks. No mortality was reported in rats while a dose dependent reduction in the body weight gain was observed. Increased liver weight to body weight ratios were noted at the 750 and 1500 mg/kg bw/day groups. No other gross or microscopic treatment-related effects were seen in rats. Five of ten males and seven of ten females in the 1500 mg/kg bw/day group died before 13 weeks. Males and females in the 375 and 750 mg/kg bw/day dose groups showed lethargy and rough coats, while animals in the 750 and 1500 mg/kg bw/day dose groups showed clonic seizures, lacrimation and salivation. A LOAEL of 187 mg/kg bw/day was reported (NTP, 1988; REACHa; REACHb; REACHc).

In a 103-week carcinogenicity study conducted in F344/N rats administered MBT in corn oil by gavage at doses of 0, 375 or 750 mg/kg bw/day for males and 0, 188 or 375 mg/kg bw/day for females (refer to **Carcinogenicity**), ulcers and inflammation of the forestomach were observed in all the treatment groups. Males at all treatment doses and the females at 188 mg/kg bw/day were reported to have increased incidences of epithelial hyperplasia and hyperkeratosis. Increased incidences of retinopathy and cataracts were observed in the 375 mg/kg bw/day group in both male and female rats. The LOAELs of 375 mg/kg bw/day for males and 188 mg/kg bw/day for females were reported (NTP, 1988; REACHa; REACHb; REACHc).

The groups of B6C3F1 mice (50 animals/sex/dose) were fed MBT in corn oil by gavage at doses of 0, 375 or 750 mg/kg bw/day, five days/week for 103 weeks. Mortality in male mice was 17/50 in the 375 mg/kg bw/day group and 14/50 in the 750 mg/kg bw/day group. In female mice, 10/50 died in the 188 mg/kg bw/day group and 24/50 died in the 375 mg/kg bw/day group. Minimal to mild severity of lung lesions and varied incidences of bronchopneumonia were observed in all treated mice. Minimal treatment-related changes were seen in both the sexes (NTP, 1988; REACHa; REACHb; REACHc).

Dermal

No data are available.

Inhalation

Limited information is available.

In an inhalation toxicity study, MBT was administered to rats (number and strain not reported) by inhalation (dust) at concentrations of 300 or 400 mg/m^3 for 2 hours/day for 15 days. Significant reduction in the body weights was noted in all treated groups. No treatment-related effects on oxygen consumption, neurological response or alveolar septum were observed (REACH a).

Genotoxicity

Based on the available in vitro and in vivo genotoxicity studies, the chemicals are not considered to be genotoxic.

In vitro studies

In a bacterial gene mutation test, MBT was tested in *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 up to a maximum concentration of 300 µg/plate with negative responses in all strains with and without metabolic activation (REACHa).

In another bacterial gene mutation test, NaMBT was negative in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 at concentrations up to 5 µL/plate in the presence and absence of metabolic activation (REACHb).

In a mammalian chromosomal aberration test in Chinese hamster ovary (CHO) cells, MBT was tested at concentrations of up to 0.6 µg/mL. The chemical, MBT, caused a negative response without metabolic activation and inconclusive results with metabolic activation were reported (REACHa & c).

In a mouse lymphoma assay, MBT in concentrations up to 100 µg/mL was tested in mouse lymphoma L5178Y cells. No significant increases in mutant frequency were observed at any tested concentration, either in presence or absence of metabolic activation (REACHa).

In vivo studies

In a micronucleus assay, MBT was tested in CD-1 mice (4 animals/sex/dose) at 300 mg/kg bw/day once or twice by intraperitoneal (i.p.) administration. No increase in the number of micronuclei was reported (REACHa & b).

In a chromosome aberration assay, Swiss albino mice (4 animals/sex/dose) were administered ZnMBT at 0, 24, 43 or 96 mg/kg bw/day by a single i.p. injection. Chromosome preparations were made from the bone marrow (femur) of the mice. The chemical, ZnMBT, had no effect on structural chromosomal aberration in the treatment groups (REACHc).

Carcinogenicity

Based on the available data from the rat and mouse studies on MBT, there is insufficient evidence to determine the carcinogenic potential of the chemicals in this group.

A group of F344/N rats (50 animals/sex/dose) was fed MBT at doses of 0, 375 or 750 mg/kg bw/day for males and 0, 188 or 375 mg/kg bw/day for females for five days/week for 103 weeks. The survival rates for male rats were lower in the 375 mg/kg bw/day group after week 85 and in the 750 mg/kg bw/day group after week 83. Mortality in males was 28/50 in the 375 mg/kg bw/day group and 29/50 in the 750 mg/kg bw/day group. Mortalities were significantly greater than the controls. In females, 18/50 died in the 188 mg/kg bw/day group and 25/50 died in the 375 mg/kg bw/day group. Significantly greater incidence of leukaemia was reported in 375 mg/kg bw/day males. Female rats showed a significant positive trend in the occurrence of adenocarcinomas; and significantly greater incidence of adenocarcinomas was reported in males in the 375 mg/kg bw/day dose group. The male rats in the 375 mg/kg bw/day group had slightly increased incidence of hyperplasia of the anterior pituitary and pancreatic acinar cell adenomas. Nephropathy with tubular degeneration and regeneration was seen in all treated male rats and in more than 75 % female rats. Pelvic epithelial hyperplasia, transitional cell papillomas, tubular cell hyperplasia and tubular cell adenomas were also observed in all treated male rats (NTP, 1988; REACHa; REACHb; REACHc).

In a study conducted on B6C3F1 and B6AKF1 mice (18 animals/sex/dose), MBT was administered once by subcutaneous injection at 1000 mg/kg. No increase in the tumour incidence was reported and no adverse treatment-related effect was observed (REACHa).

In an 18-month study, ZnMBT was administered to B6C3F1 and B6AKF1 mice (18 animals/dose/sex/strain) by gavage at 1000 mg/kg bw/day on days 7-28 of age and in the diet at 508 mg/kg bw/day (3385 ppm) after 28 days of age. No gross or histopathological effects were observed in any animals at any dose. There was no significant increase in tumours reported (REACHc).

The International Agency for Research on Cancer (IARC) has listed MBT in the recommended priorities for evaluation of carcinogenic risks to humans based on the available data from various occupational cohort studies, epidemiological studies and increased occurrence of large intestine and bladder cancers and multiple myeloma in workers exposed to MBT in industrial settings (IARC, 2014).

Reproductive and Developmental Toxicity

The chemicals do not show specific reproductive or developmental toxicity. Any reproductive and developmental effects were only observed secondary to maternal toxicity.

In a two-generation study conducted according to OECD TG 416, Sprague Dawley rats (28 animals/sex/dose) were administered MBT (98.5 %) in the diet at 0, 2500, 8750 or 15000 ppm (calculated to 778 to 1238 mg/kg bw/day for F0 (parent) males; 779 to 2633 mg/kg bw/day for F1 (first generation) males; 745 to 1760 mg/kg bw/day for F0 females and 980 to 1770 mg/kg bw/day for F1 females). The exposure period was for 10 weeks before mating, through gestation and lactation until sacrifice. Males and females were exposed to the chemical for 10 weeks (70 days) during the premating period. The approximate duration of the treatment was approximately 88 days post weaning. No treatment-related clinical signs were observed in the treated F0 generation. Slight reduction in the mean body weight and food consumption in both sexes in the 15000 ppm group was noted. Pathology examination revealed no treatment-related gross lesion in any treatment group. Increased incidence of basophilic tubules and alpha-2μ-globulin inclusions in the proximal convoluted tubules were seen in males in all treatment groups. Significantly increased absolute testes weights were observed in male rats in the 2500 and 8750 ppm groups but not in the 15000 ppm group. However, the changes in absolute testes weight were within historical controls and were not seen in the males of F1 generation. No treatment-related effects were noted in F1 generation pups and adults and F2 generation pups. Gross lesions observed in F1 generation parental animals from all treated groups included small epididymides, pitted kidneys, dilated renal pelvis, enlarged lymph nodes, corneal opacity, ovarian cyst, white splenic loci and enlarged thyroid. The gross lesions and the alpha-2μ-globulin inclusions observed in the male rats are likely to be species-specific and not toxicologically relevant to humans (REACHa; REACHb; REACHc).

In a developmental toxicity study conducted according to OECD TG 414, New Zealand White rabbits (20 animals/sex/dose) were treated with MBT in 1 % aqueous carboxymethyl cellulose) by gavage once daily at doses of 0, 50, 150 or 300 mg/kg bw/day on days 6 to 18 of gestation. No treatment-related mortality or clinical signs were noted. A few treated animals had soft stools, reduced faeces, urine or faecal staining and hair loss. No significant body weight changes were observed. Necropsy examination showed slightly increased absolute and relative liver weights in females in the 300 mg/kg bw/day group. No developmental effects were observed at any dose (REACHa; REACHb; REACHc).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include skin sensitisation for all the chemicals and corrosivity for NaMBT only.

Public Risk Characterisation

NaMBT is reportedly used in domestic products overseas at concentrations up to 1.5 %. Currently, there are no restrictions in Australia on using NaMBT in domestic products. However, the reported overseas use of the chemical in auto (car) products

(radiator cleaner) does not lead to widespread exposure and, thus, NaMBT is not expected to pose an unreasonable risk to the public.

Occupational Risk Characterisation

During product formulation, dermal and ocular exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory. NICNAS will continue to monitor the high quality assessment work that may be conducted by IARC on MBT and further assessment of the chemicals may be required.

Regulatory Control

Work Health and Safety

The chemicals are recommended for classification and labelling under the current approved criteria and adopted GHS as below. No change in classification has been recommended for MBT (CAS No. 149-30-4) and classification for corrosivity (C; R34) only applies to NaMBT (CAS No. 2492-26-4). This assessment does not consider classification of physical and environmental hazards.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Irritation / Corrosivity	Causes burns (C; R34)	Causes severe skin burns and eye damage - Cat. 1C (H314)
Sensitisation	May cause sensitisation by skin contact (Xi; R43)	May cause an allergic skin reaction - Cat. 1 (H317)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from dermal and ocular exposure to the chemicals should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- using local exhaust ventilation to prevent the chemicals from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemicals, if valid techniques are available to monitor the effect on the worker's health;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemicals.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemicals are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

References

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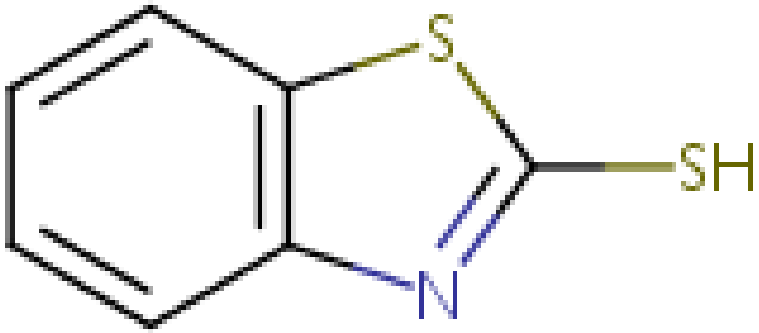
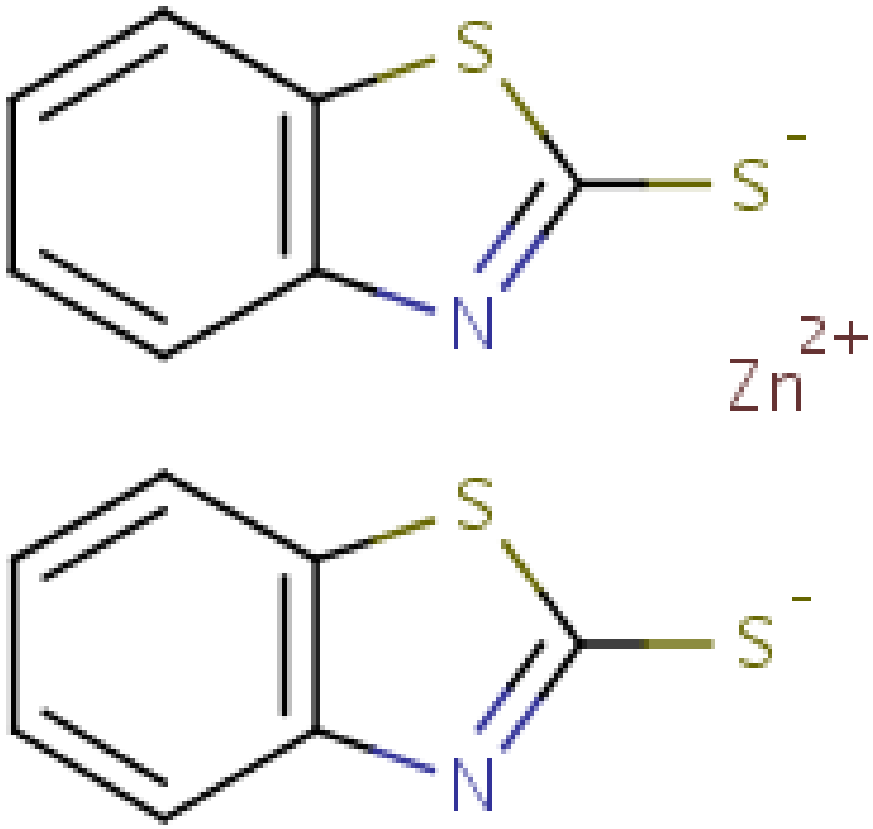
Last Update 05 February 2016

Chemical Identities

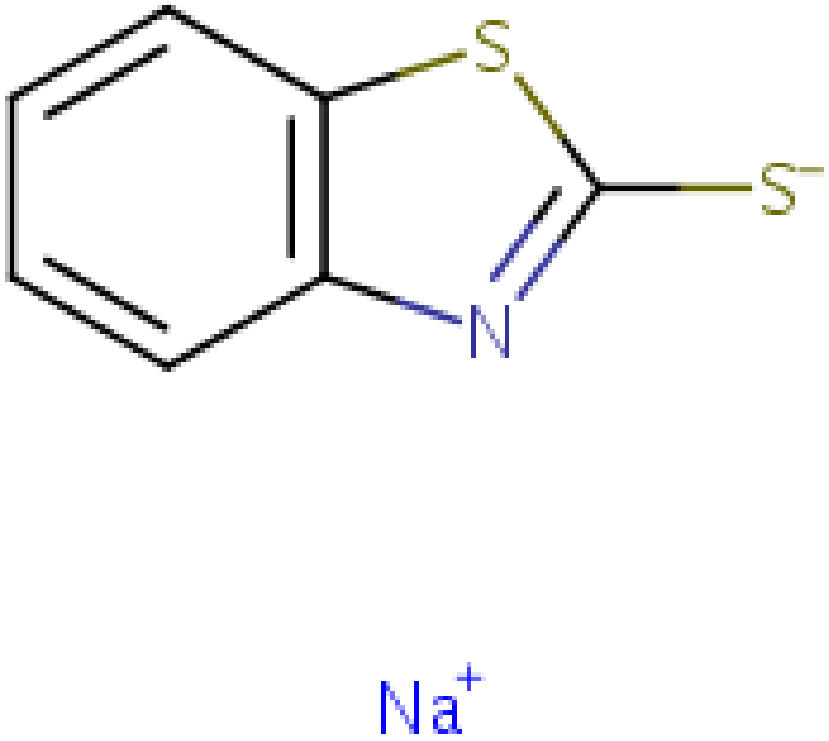
Chemical Name in the Inventory and Synonyms	**2(3H)-Benzothiazolethione** mercaptobenzothiazole 2-benzothiazolethiol 2-MBT Kaptax Accelerator M
CAS Number	149-30-4

Structural Formula	
Molecular Formula	C7H5NS2
Molecular Weight	167.26

Chemical Name in the Inventory and Synonyms	**2(3H)-Benzothiazolethione, zinc salt** zinc 2-mercaptobenzothiazole (ZnMBT) 2-benzothiazolethiol zinc salt zinc di(benzothiazol-2-yl) disulphide mercaptobenzothiazole zinc salt
CAS Number	155-04-4
Structural Formula	

	
Molecular Formula	C7H5NS2.1/2Zn
Molecular Weight	397.89

Chemical Name in the Inventory and Synonyms	**2(3H)-Benzothiazolethione, sodium salt** 2-mercaptobenzothiazole, sodium salt 2-benzothiazolethiol, sodium salt Nacap sodium MBT NaMBT
CAS Number	2492-26-4
Structural Formula	

	
Molecular Formula	C7H5NS2.Na
Molecular Weight	189.24

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