



**German Chemical Society
Gesellschaft Deutscher Chemiker**

GDCh-Advisory Committee
on Existing Chemicals of
Environmental Relevance (BUA)

2-Mercaptobenzothiazole

BUA Report 74

(June 1991)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1997

GDCh-Advisory Committee on Existing Chemicals of Environmental Relevance (BUA)

Chairman:

Prof. Dr. E. Bayer, Institut für Organische Chemie der Universität Tübingen

Members:

Dr. G. Alfke, Mineralölwirtschaftsverband e. V., Hamburg
Prof. Dr. K. Ballschmiter, Abteilung Analytische Chemie und Umweltchemie der Universität Ulm
Dr. B. Broecker, HOECHST AG, Abteilung Umweltchemikalien/Verbrauchersicherheit, Frankfurt am Main
Prof. Dr. O. Fränze, Geographisches Institut der Universität Kiel
Prof. Dr. F. H. Frimmel, DVGW-Forschungsstelle am Engler-Bunte-Institut der Universität Karlsruhe
Prof. Dr. H.-P. Gelbke, BASF AG, Toxikologie, Ludwigshafen a. Rh.
Prof. Dr. H. Greim, GSF - Institut für Toxikologie, Neuherberg (Vice Chairman)
Dr. W. G. Haltrich, BASF AG, Emissionsüberwachung und Ökologie, Ludwigshafen
Dr. H. Jungen, Deutsche Wissenschaftliche Gesellschaft für Erdöl, Erdgas und Kohle e. V., Hamburg
Prof. Dr. D. Kayser, Bundesgesundheitsamt, Berlin
Prof. Dr. W. Mücke, Institut für Toxikologie und Umwelthygiene der TU München
Prof. Dr. P. Müller, Institut für Biogeographie, Universität des Saarlandes, Saarbrücken
Prof. Dr. E. Offhaus, Umweltbundesamt, Berlin
Dr. R. Ott, Deutsche Shell Chemie GmbH, Eschborn/Ts.
Prof. Dr. U. Schlottmann, Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit, Bonn
Dr. N. Schön, BAYER AG, LE Umweltschutz/AWALU, Leverkusen
Dr. A. Troge, Umweltbundesamt, Berlin

Guests:

Dr. H. W. Kraus, Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit, Bonn
Prof. Dr. R. Kümmel, Technische Hochschule Leuna-Merseburg
Dr. J. Oberhansberg, BG Chemie, Heidelberg
Dr. H. K. Schäfer, Initiative umweltrelevante Altstoffe, Frankfurt am Main

In collaboration with:

Priv.-Doz. Dr. J. Ahlers, Umweltbundesamt, Berlin
Dr. D. Cohors-Fresenborg, Umweltbundesamt, Berlin
Dr. S. Ettel, Institut für Organische Chemie der Universität Tübingen
Dr. H. Lindemann, Bayer AG, Toxikologie, Wuppertal
Frau Dr. I. Mangelsdorf, GSF - Institut für Toxikologie, Neuherberg
Frau Dr. A. Marschner, Umweltbundesamt, Berlin
Frau Dr. B. Richter, Bayer AG, Umweltschutz, Leverkusen
Frau Dr. H. Sterzl-Eckert, GSF - Institut für Toxikologie, Neuherberg
Dr. D. Vogel, Institut für Organische Chemie der Universität Tübingen
Frau Dipl.-Biol. L. Weis, Institut für Organische Chemie der Universität Tübingen
Frau Dr. K. Widmann, Institut für Organische Chemie der Universität Tübingen

GDCh Office:

Dr. H. Behret, GDCh, Frankfurt am Main

2-Mercaptobenzothiazole

BUA Report 74

(June 1991)

edited by the GDCh-Advisory
Committee on Existing Chemicals
of Environmental Relevance

Beratergremium für
Umweltrelevante Altstoffe (BUA)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1997

Dr. H. Behret
Gesellschaft Deutscher Chemiker
Postfach 90 04 40
D-60444 Frankfurt am Main

Translated by P. Arend

This book was carefully produced. Nevertheless, authors, editors and publisher do not warrant the information contained therein to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

The use of general descriptive names, trade names, trademarks, etc. in a publication, even if not specifically identified, does not imply that these names are not protected by the relevant law and regulations.

Die Deutsche Bibliothek — CIP-Einheitsaufnahme

2-Mercaptobenzothiazole / ed. by the GDCh Advisory
Committee on Existing Chemicals of Environmental Relevance
(BUA) - (June 1991) - Stuttgart: Hirzel ; Stuttgart : Wiss.
Verl.-Ges., 1997
 (BUA report; 74)
 Dt. Ausg. u.d.T.: 2-Mercaptobenzothiazol
 ISBN 3-7776-0752-5
NE: Gesellschaft Deutscher Chemiker / Beratergremium für
 Umweltrelevante Altstoffe: BUA report

All rights reserved. No part of this publication may be translated, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without permission in writing from the publisher.

© 1997 S. Hirzel Verlag, Birkenwaldstraße 44, 70191 Stuttgart

Printed in acid-free and low-chlorine paper.

Printing and binding: Druckhaus Beltz, Hemsbach
Printed in F.R. Germany

Foreword

The German Chemicals Act (Chemikaliengesetz - ChemG) of 1980 stipulates that certain existing chemicals must be reported to the competent authority, if they exhibit properties which indicate that they may be hazardous, either alone or in combination with other substances.

In the summer of 1982, an Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) was set up by the German Chemical Society (Gesellschaft Deutscher Chemiker - GDCh). It brings together representatives from the scientific community, the chemical industry and the governmental authorities. This Advisory Committee is responsible for elaborating appropriate solutions for substances of relevance for health and the environment on the basis of voluntary measures. It selects and examines existing chemicals from the aforementioned angles. The testing and evaluation are based on scientific criteria alone.

It was, therefore, necessary to develop priority setting procedures. In a first phase reports were only prepared for priority chemicals. Within the framework of a first priority setting procedure, chemicals were compiled from several priority lists and 135 chemicals were selected for detailed substance reports.

In a second priority setting procedure the survey of the German Chemical Industry Association (VCI) on all substances with a production volume of more than 10 tons per year was used as a starting list. Since this survey covered 4,600 chemicals, BUA decided to process the corresponding list in several stages. The first stage included approx. 1,050 substances with a production volume of more than 1,000 tons per year.

Detailed reports are drawn up on chemicals suspected of having a hazard potential and abridged reports on those presenting only a minor hazard potential, according to the current state of knowledge.

The detailed BUA reports take in both the published literature and data from industry. If data for the evaluation of the chemicals are not available, additional studies are recommended and the results are published as updates to the reports. The reports serve as a basis for the instigation of administrative measures, when there are indications of risks to health or the environment.

Tübingen, May 1993

Ernst Bayer
Chairman of the Advisory Committee
on Existing Chemicals
of Environmental Relevance

Contents

Summary and Conclusions XI

Recommendations XXIII

2-Mercaptobenzothiazole

(2-(3H)-Benzothiazolethione) and its salts

1.	Chemistry of the substance	1
1.1	Chemical identity	1
1.1.1	MBT, free acids	1
1.1.2	MBT, sodium salts	2
1.1.3	MBT, zinc salt	2
1.1.4	MBT, other salts	3
1.2	Composition of the technical product	3
1.3	Chemical properties	4
1.3.1	MBT, free acids	4
1.3.2	MBT, sodium and zinc salt	5
2.	Physical properties	6
2.1	MBT, free acids	7
2.2	MBT, sodium salt (50 % aqueous solution)	9
2.3	MBT, zinc salt	9
3.	Analysis	10
3.1	Determination in air	10
3.2	Determination in water	11
3.3	Determination in soil, sediment and biological material	14
4.	Discharge into the environment during manufacture, processing, use and waste disposal	16
4.1	Manufacturing processes for MBT, 50% Na-MBT solution, ZMBT, MBTS and benzothiazolesulphenamides	16
4.2	Manufacturers and processors, production volume, exports imports, total consumption	18
4.2.1	Manufacturers and production volumes	18
4.2.2	Processors, exports, imports, demand	19
4.2.3	Total consumption in the Federal Republic of Germany	23

4.3	Processing, uses, consumption.....	23
4.3.1	Processing.....	23
4.3.1.1	Processing as vulcanisation accelerators.....	23
4.3.1.2	Fields of application for thiazole and sulphenamide accelerators in the Federal Republic of Germany.....	29
4.3.1.3	Processing as an intermediate	31
4.3.2	Use	33
4.4	Discharge into the atmosphere	35
4.4.1	Discharge during manufacture and processing.....	35
4.4.2	Discharge during use	36
4.5	Discharge into the hydrosphere	36
4.5.1	Discharge during manufacture and processing	36
4.5.1.1	Discharge during manufacture	36
4.5.1.2	Discharge during processing.....	36
4.5.2	Discharge during use	37
4.5.3	Discharge during the use of secondary products	38
4.5.4	Discharge during the use of tyres and rubber articles.....	38
4.6	Discharge by way of tyre abrasion	39
4.7	Discharge into the geo- and biosphere.....	40
4.8	Discharge from waste and waste treatment	41
4.9	Summary of environmental discharge.....	43
5	Occurrence in the environment	45
5.1	Atmosphere	45
5.2	Hydrosphere.....	46
5.3	Migrates out of commodities and tyres.....	48
5.4	Geosphere.....	51
5.5	Biosphere	51
5.6	Natural sources	51
6.	Behaviour in the environment.....	52
6.1	Transformation and degradation, degradation products.....	52
6.1.1	Biodegradation	52
6.1.2	Hydrolytic degradation.....	54
6.1.3	Photochemical decomposition.....	54
6.1.3.1	Photochemical decomposition in the atmosphere.....	54
6.1.3.2	Photochemical decomposition in the hydrosphere	65
6.1.4	Treatment of MBT-containing waste water.....	56
6.2	Accumulation	57
6.2.1	Bioaccumulation	57
6.2.2	Geoaccumulation	58
6.3	Distribution behaviour and transport in and between environmental compartments	58
6.3.1	Henry's constant.....	58
6.3.2	n-octanol/water partition coefficient.....	59

6.3.3	Soil sorption coefficients	59
6.4	Fate in the environment.....	60
7.	Ecotoxicology	64
7.1	Effects on aquatic organisms	64
7.1.1	Microorganisms	64
7.1.2	Protozoa	67
7.1.3	Plants	68
7.1.4	Invertebrates	68
7.1.5	Vertebrates	71
7.2	Effects on terrestrial organisms.....	77
7.2.1	Microorganisms	77
7.2.2	Plants	79
7.2.3	Invertebrates	80
7.2.4	Vertebrates	80
7.3	Effects on ecosystems	81
8.	Toxicity in warm-blooded organisms	82
9.	Substance-specific statutory regulations	83
9.1	MBT, free acids	83
9.2	MBT, sodium salt.....	84
9.3	MBT, zinc salt.....	86
10.	Literature	

Appendix:

Toxicological evaluation No. 70 "2-Mercaptobenzothiazole". Berufsgenossenschaft der chemischen Industrie, Heidelberg (1980)

BUA Report on 2-Mercaptobenzothiazole

(2-(3H)-Benzothiazolthione) and Salts

Summary and conclusions

Ecological aspects

Occurrence and distribution in the compartments

MBT and its salts, 2,2'-dithiobisbenzothiazole (MBTS) and the 2-benzothiazole sulphenamides that form MBT during their use are not manufactured in the Federal Republic of Germany.

The total consumption in 1990 of MBT and its salts is estimated to have been 870 - 1,150 tonnes, that of MBTS 700 - 900 tonnes and that of benzothiazole sulphenamides 3,500 - 4,600 tonnes (corresponding to about 2,200 - 2,820 tonnes of MBT).

In addition, unknown quantities of these substances are imported and exported into and from the Federal Republic of Germany in, e.g., rubber articles and preparations.

In the Federal Republic of Germany MBT and its zinc salt (ZMBT) are used almost exclusively as non-volatile vulcanization accelerators in the rubber industry. Small amounts of MBT are used also to stabilize film emulsions, to precipitate heavy metals in quantitative analysis and as auxiliaries in the electrochemical plating of metal surfaces. Further applications of ZMBT are not known.

About 47 % of the 106 tonnes of the sodium salt of MBT (NaMBT) consumed annually is used as an intermediate in the manufacture of 2-thiocyanatomethylthiobenzothiazole (TCMTB). NaMBT is also used as a corrosion inhibitor for drilling and cutting oils (lubricoolants) and, in small quantities, as a corrosion inhibitor in cooling water circuits and in metal-working fluids (pickling acids). The demand accounted for by these three fields of application

in 1989 is estimated to have been 40 tonnes (approx. 38 %). About 15 % of the quantity of NaMBT consumed is used as an auxiliary in formulations for slime control in paper production.

In the Federal Republic of Germany, in contrast to the USA, the use of NaMBT in glycol-based antifreezes for motor vehicles is insignificant.

The quantities of MBT and its salts and also of MBTS and the sulphenamides (which are used entirely in the rubber industry) that enter the environment during their industrial use are believed to be emitted mainly with waste water and to only a smaller extent with waste air or as components of industrial waste. Owing to the lack of data these emissions are not quantifiable.

Direct emissions of MBT or its salts into the geosphere and subsequently into the hydro- and biosphere occur via the residual MBT content of the registered pesticide metha-benzthiazuron. The sum of these emissions is estimated to be about 150 kg MBT/a.

In the processing of NaMBT to TCMTB not more than 250 kg/a enter the hydrosphere. It is not known whether MBT enters the environment for example via metabolization during the use of TCMTB.

MBT and its salts are emitted indirectly by tyres during use, storage (e.g. in the open) and with debris lost through abrasion. MBT can migrate to the surfaces of tyres or of the tyre wear debris and enter surface waters and soil via condensed water and rain. In the Federal Republic of Germany approximately 3,700 - 4,800 tonnes of MBT are used annually in rubber manufacture (as MBT and ZMBT themselves or as a decomposition product of MBTS and sulphenamides). The proportion of this amount used to

produce the rubber of the tyre wear debris is about 300 - 400 tonnes. The actual amount of free MBT in tyre rubber after the process of vulcanization cannot be quantified.

Only isolated extraction studies have been conducted to determine the proportions in which thiazole accelerators are converted chemically during vulcanization. Neither the amount of MBT decomposed in vulcanization nor the amount bound to the polymer matrix as a pending group is known. The extent to which MBT is transformed during the technical use of tyres and in consequence of their abrasion is not known either. Therefore, and also because the migration behaviour of MBT during tyre use and subsequently in abraded tyre particles is not known and because details concerning the different decomposition times of the abraded particles are lacking, it is not possible to quantify the amount of MBT that enters the environment through tyre use and tyre wear.

The quantities of waste rubber formed in 1988 from tyres and other rubber articles are estimated to have been 455,000 tonnes (with 135,000 tonnes deposited on waste dumps) and 445,000 tonnes respectively.

It is likely that MBT is additionally emitted indirectly through the migration of MBT and its salts from rubber articles during their use and subsequent existence on waste dumps. These emissions cannot be quantified either.

MBT enters the human and animal organism through the use of contaminated injection solutions and X-ray contrast media. Intake through direct contact with rubber goods containing MBT is also possible.

MBT has been detected in dust of the workplace air at rubber-processing factories in the USA and Bulgaria.

XIV

Although in the USA and respectively Japan the occurrence of MBT in work-place air (unquantified) in surface waters ($< 0.001 \mu\text{g/l} - 30 \mu\text{g/l}$) and sediments ($2.1 \mu\text{g/kg} - 58 \mu\text{g/kg}$) has been reported, no measurements have been published for the Federal Republic of Germany.

In the Federal Republic of Germany aqueous extracts from rubber articles (babies' dummies) have been found to contain up to 30 mg NBT/l (average value 3 mg MBT/l). In other countries MBT has been measured in extracts from parts consisting of rubber in medicine packages and from disposable syringes (the extracts in this case being injection solutions, for example) at concentrations of 0.7 - 53 mg/l. In extracts prepared from 100 g ground tyre tread scrap from used tyres and having a pH value of 7, MBT was measured after 7 days at concentrations of 46 and 54 mg/l.

Articles intended for contact with food were found in Japan to contain up to 85.6 mg MBT/kg.

In a Japanese study MBT was found in the human liver.

Degradation

Calculations according to the method of Atkinson, which are possible for one tautomer only (benzothiazolinthione), showed photochemical oxidation to be a possible degradation route for MBT which has entered the atmosphere. The half life has been estimated at < 1 day.

The UV spectrum shows that photochemical degradation is possible in the case of MBT emitted into the hydrosphere. Accordingly the half life under the experimental conditions for direct photodegradation (primary step) is about 68 minutes or, if humic substances are present, about 59 minutes. Under environmental conditions, though, somewhat lon

ger half lives must be expected. As, however, no quantum yield or metabolites were determined, the reported findings do not permit a reliable assessment of photochemical degradation in the hydrosphere.

According to several mutually independent investigations MBT is not biologically degradable, even after adaptation of the microorganisms.

On the other hand aerobic biological degradation by adapted activated sludge of 35 % and 10 % was measured in one study. In another investigation, in which MBT was present in the waste water at a concentration of < 10 mg/l in addition to benzothiazole (< 300 mg/l) as an inductor, a degradation of both compounds of 91 % was reported.

As those investigations were done under particular laboratory conditions, the assessment of the environmental significance of the results is not quite clear.

A study of the anaerobic degradability of MBT by adapted sulphur bacteria has been discussed also. With MBT as sole source of carbon, and after an incubation time of 5 weeks, primary degradation rates of 74 % and 44 % were determined at MBT inputs of 5 and 10 mg/l. An addition of glucose, which is readily degradable, reduced the degradation rates markedly to 13 % and 9 %.

In the case that MBT is emitted into the soil or via the soil into the hydrosphere and via deep layers of surface waters into ground water layers an anaerobic biotic degradation seems possible.

Bioaccumulation

In a study according to OECD Guideline 305C performed by

CITI in Japan a log BCF of < 1 was determined for the orange-red killifish (family: *Cyprinodontidae*). The MITI list ranks MBT among compounds with little to no bioaccumulation.

In a study on the intake, distribution and excretion of MBT in carps it was found that MBT is metabolized and eliminated very rapidly (< 72 hours) if the fish are fed after the MBT has been administered.

The available test results, together with the experimentally determined values for log P_{OW} of 1.61 - 2.42, lead to the conclusion that the bioaccumulation potential of MBT is low.

Geoaccumulation

No data on geoaccumulation are available. The available results of studies to determine the soil sorption of MBT show that the nobility of MBT in soils and in sediments is slight

Ecotoxicology

Several studies of the effects of MBT and its salts on aquatic organisms have been published. During valuation of the following investigations one has to keep in mind, that some of the studies were done in a concentration range which was above the water solubility of the chemicals tested.

In investigations (direct weighing in, nominal concentrations) of the effect of MBT on bacteria the EC_0 (growth) for *Pseudomonas putida* was found to be $> 1,000$ mg/l. For *S. aureus* and *E. coli* and several strains of *mycobacteriaceae*

an EC₁₀₀ (growth) of ≤ 50 mg/l to $> 1,000$ mg was measured. In a respiratory inhibition test with activated sludge (OECD-Guideline 8192, direct weighing in, nominal concentration, high bacteria density) an EC₅₀ of 3,301 mg/l was measured. 75 % inhibition of the nitrification rate was observed in two model waste water treatment plants, one of them unadapted and charged with approximately 2.5 mg MBT/l and the other adapted and charged with 44 mg MBT/l.

50 % inhibition of the respiration rate of activated sludge (EC₅₀; OECD-Guideline 8192, direct weighing, nominal concentration, high bacteria density) was observed at 857 mg/l for NaMBT (50 % solution) and at 1,220 mg/l for ZMBT.

A cell multiplication inhibition test with the ciliate *Tetrahymena pyriformis* gave an EC₅₀ (24 h) of 10 mg/l for MBT.

In the case of a fresh water alga species the EC₅₀ (96 h) of MBT was found to be 0.23 mg/l for chlorophyll formation and 0.25 mg/l for growth. In analogous investigations with the 50 % aqueous solution of NaMBT the EC₅₀ (96 h) was 0.4 mg/l for chlorophyll formation and 0.3 mg/l for growth.

In acute toxicity tests on *Daphnia magna* the EC₅₀ (48 h) was 4.1 mg/l for MBT and 19.0 mg/l for NaMBT (50 %), while the NOEC (48 h) was 1.8 mg/l for MBT and 10.0 mg/l for NaMBT (50 %).

In an investigation conducted in 1989 within the framework of a Final Test Rule for the United States Environmental Protection Agency to ascertain the chronic toxicity of MBT to *Daphnia magna* (under flow-through conditions) an EC₅₀ (21 days) of > 0.47 mg/l was measured. The toxic concentration limit (based on mortality as the criterion of effect) is ≥ 0.24 mg/l (NOEC) and ≤ 0.47 mg (LOEC). The geometrical mean is 0.34 mg/l (MATC).

XVIII

A reproduction test according to a procedure based on OECD-Guideline 202 and performed at a concentration of 2.22 mg/l gave a reproduction rate of 48.3 % after 21 days. On the basis of the reproduction the NOEC value was estimated at ≤ 0.22 mg/l.

In an early life stage test performed for the US EPA and lasting 89 days the effect of MBT on rainbow trout larvae under flow-through conditions was investigated. The toxic concentration limit (with the length of the larvae as criterion) was found to be 0.057 mg MBT/l and the NOEC ≥ 0.041 mg/l.

In static tests to determine the acute toxicity of MBT to fish, LC₅₀ (96 h) values of between 0.75 mg/l (rainbow trout) and 1.6 mg/l (zebra fish) were found. The corresponding values for the 50 % aqueous solution of NaMBT were 1.8 mg/l (rainbow trout) and 3.8 mg/l (bluegill sunfish). In a screening test to find the harmful effect of NaMBT on the golden orfe a 48 h LC₀ of > 5.0 mg/l was determined.

A study of the effects of MBT and its salts on terrestrial organisms gave the following results:

50 % growth inhibition of fungi (*Drechslera ramera*, *Alternaria alternata* and *Fusarium oxisporum*) was noted at an MBT concentration of approx. 100 mg/kg agar and approx. 50 % inhibition of the spore germination (18 h) was noted at 0.061 mg MBT/l in the case of *Memnoniella echinata* and at 0.604 mg/l (gelatin medium) in the case of *Aspergillus niger*.

In greenhouse tests to find the effect of MBT on the growth of the useful plants rice (*Oryza sativa*), turnip (*Brassica rapa*) and soya bean (*Glycine max*) a concentration of 100 mg MBT/l inhibited the growth of all three species, that of the shoots by 11 - 23 % and that of the roots by

38 - 58 %; the controls were grown with 3 % gum arabic solution. At MBT concentrations of 10 and 1 mg/l, rice and the soya bean were affected less (effect on root growth 0 to - 28 %; epigeous parts + 4 to - 18 %). In contrast, the growth of the investigated parts of *Brassica rapa* at these concentrations was increased by 11 to 28 %. In general the roots were affected more than the epigeous parts.

In a study to find the harmful effect of MBT on chicken embryos (incubated at 37.7 °C) the compound was injected at various concentrations into the heart of 3-day old embryos. At the highest concentration (334.5 µg per embryo) 13 % of the embryos died within the two following days; after 14 days externally visible deformities of the eyes, wings and abdominal cavity (coelom) were found in 30 % of the surviving embryos.

Toxicological aspect*

After oral, dermal and parenteral administration, 2-mercaptobenzothiazole (MBT) is rapidly absorbed, is metabolised within 96 hours and is almost completely eliminated, primarily in the urine. Also present in the urine, in addition to the unchanged substance, are the following metabolites: a glucuronide, a mercapturic acid derivative, 2-mercapturic acid benzothiazole sulphate, and the dimer dibenzothiazole disulphide.

MBT is of low acute toxicity and can penetrate the skin (LD₅₀ oral rat, mouse, rabbit, guinea pig 1680 - 3800 mg/kg; LD₅₀ dermal rabbit > 7940 mg/kg; LC₅₀ 4 hours,

** With permission of BC Chemie taken from:

Toxikologische Bewertung Nr. 70 '2-Mercaptobenzothiazol'. Berufsgenossenschaft der chemischen Industrie, Heidelberg (1990), Kap. 1: Summary and assessment

XX

rat > 1270 mg/m³). The symptoms of poisoning in animals include peripheral vasodilation, salivation, lacrimation and tonic/clonic spasms.

The results of animal tests for the irritant activity of MBT on the skin and eyes are contradictory, but in all cases the irritant activity is weak.

In subacute and subchronic tests on rodents, body weight reduction and microscopically visible changes in the liver and kidneys are observed; with repeated inhalation exposure body weight is reduced but no effects are observed on the lung and nervous system. In dogs, the oral administration of about 3 mg/kg per day for 1 year does not result in any adverse effects.

MBT is not mutagenic either in the Salmonella/microsome test (with and without S9 mix) or on *Escherichia coli*. Tests on mammalian cells (CHO, HGPRT and in mouse lymphoma cells) provide contradictory results. In cytogenetic tests on CHO cells, an increased incidence of chromosomal aberrations **but no increased sister chromatid exchange rate**** have been observed at a high concentration, in the presence of a metabolising system (S9 mix). MBT is negative in the mouse micronucleus test, and slightly positive in the rat dominant lethal test. In the DNA covalent binding test, only slight DNA-binding has been observed.

Early long-term oral studies in rats given a low dose of MBT (approx. 6 mg/kg daily) provide no indication of carcinogenic activity, whilst oral administration to mice (50 to 100 mg/kg per day) gives rise to the suspicion of a dose-dependent increase in reticulocarcinomas; after a

** Change by BG Chemie (1992)

single subcutaneous injection in mice, followed by observation for 17 months, an increase in reticulocarcinomas is again observed. In neither case is the increased incidence of reticulocarcinomas significant.

In more recent tests involving oral administration of much higher doses (188 to 750 mg/kg per day) by stomach tube for 2 years, increased tumour incidence has been observed in rats of both sex (male: adrenal gland pheochromocytoma, preputial gland adenomas or carcinomas, glandular cell adenomas in the pancreas, monocytic leukaemia; female: adrenal gland pheochromocytoma, hypophysis adenomas). In female mice, the increased incidence of hepatocellular adenomas or carcinomas in the low-dose group is of questionable significance.

In the cell transformation test in mice, MBT is negative.

In tests on pregnant rats and rabbits MBT is not maternally toxic, foetotoxic or teratogenic. After subcutaneous injection of maternally toxic doses, foetal abnormalities are observed in mice. A three-generation study in rats shows no effect on reproduction or lactation.

Both *in vitro* and *in vivo*, MBT inhibits dopamine- β -hydroxylase activity, and hence the conversion from dopamine to noradrenaline. **MET seems to have a radio-protective effect in mice after intraperitoneal application.****

In man, MBT is a skin irritant and a skin sensitizer.

** Change by EG Chemie (1992)

On the basis of the results obtained in long-term studies, the possibility of MBT being carcinogenic cannot be ruled out.

A reproduction toxicity study (2 generations) in rats is currently in progress.

Recommendations

Ecotoxicology

Pilot studies should first be carried out to ascertain the occurrence and entry of mercaptobenzothiazole (MBT) in the environment. The lack of data currently makes assessment of its environmental relevance impossible.

1. Determination of the chemical behaviour of MBT in the environment, i.e. possible chemical reactions such as oxidation, formation of poorly soluble salts following release into the environment.
2. Analysis of surface water in places very likely to be exposed (transport routes).
3. Identification of major sources of emission such as migration from rubber articles, abrasion loss from tyres, oxidative degradation and migration.

The next course of action cannot be decided until major sources of exposure have been identified.

The problem could be approached as follows:

- A balance of the entry of MBT and its transformation products from tyres and important rubber articles throughout their life cycle;
- Determination of the quantum yield of MBT photodegradation in water, taking known metabolites into account, to provide a reliable evaluation of photodegradation;

- Systematic measurement of occurrence in the environment;
- Scrutiny of data on toxicity of MBT to plants and on migration behaviour (Japanese Progress Report), and, where necessary, studies in the geosphere.

Toxicology

Data are available for all significant toxicological end points, and it is thus possible to assess the activity profile of MBT. The reproductive toxicity study mentioned above (two-generation feeding study) meanwhile has been completed and the final report will be available soon.

In the USA additional toxicity studies have been carried out in compliance with a 1988 Test Rule introduced by the EPA. The following studies have now been completed and the final reports will be available in the near future.

- Range-finding study with acute oral administration (by gavage) to rats to investigate the effect of MBT on motor activity;
- Neurotoxicity study with acute oral administration of MBT to rats (by gavage);
- Three-months feeding study in rats to investigate the effect of MBT on behaviour and neuromorphology.

At the moment further toxicological studies are not considered necessary.