
Benzothiazole- and Morpholine-Based Thiazoles Category Justification and Testing Rationale

CAS Nos.: **95-32-9 and 103-34-4**
(+CAS Nos. 95-16-9, 102-77-2, 110-91-8, 149-30-4 and 120-78-5 for data purposes)

Rubber and Plastic Additives Panel
American Chemistry Council
December 2003

List of Member Companies in the Rubber and Plastic Additives Panel

The Rubber and Plastic Additives Panel of the American Chemistry Council includes the following member companies: Alco Chemicals; Bayer Polymers LLC.; Ciba Specialty Chemicals Corporation; Crompton Corporation; Eliokem, Inc.; Flexsys America L.P.; The Goodyear Tire & Rubber Company; The Lubrizol Corporation; Noveon, Inc.; and, R.T. Vanderbilt Company, Inc.

Executive Summary

The American Chemistry Council's Rubber and Plastic Additives (RAPA) Panel hereby submits for review and public comment their revised test plan for the Benzothiazole- and Morpholine-based Thiazoles (BMBT) category of chemicals under the High Production Volume (HPV) Chemical Challenge Program. Based on EPA's comments (dated September 6, 2002) on the Benzothiazole-based Thiazole category as originally conceived, RAPA has created two separate categories from the original Benzothiazole-based Thiazoles category. The new categories are the BMBT category, which is the subject of this submission and the Benzothiazole-based Thiazole category, which is the subject of a separate submission (dated July 17, 2003) and which no longer includes chemicals containing morpholine. While some characteristics of many of these chemicals overlap, RAPA has made this category revision to more clearly explain and substantiate the category justifications. RAPA also is providing supporting information for benzothiazole and additional supporting information for three new surrogate chemicals. Furthermore, RAPA is providing a tabular summary of data on morpholine (CAS No. 110-91-8) that is available in the current IUCLID Data Set and is referencing information provided to EPA in the ACC Amines Panel's test plan and robust summary for morpholine under the International Council of Chemical Associations (ICCA) HPV program. The robust summary for morpholine has already been submitted to EPA by the Amines Panel and, therefore, is publicly available for review. In addition, 4,4'-dithiodimorpholine (CAS No. 103-34-4), a chemical volunteered for data submission in 2003, is now included in the BMBT category.

As discussed in the report that follows, chemicals in the BMBT category, which are used primarily as cure-rate accelerators or sulfur donors in natural and synthetic rubbers or as chemical intermediates in the manufacture of rubber accelerators, are described as possessing a morpholine group attached to a

Benzothiazole- and Morpholine-Based Thiazole Category

benzothiazole group [benzene ring + thiazole ring] or another morpholine group via a sulfur or sulfur-sulfur bond. Their use in the rubber vulcanization process requires stability at high temperatures, low biodegradation, negligible water solubility and low vapor pressure. Non-rubber applications for this category include metal chelation, ore flotation, corrosion inhibition, veterinary drugs and industrial biocide/water treatment for 2-mercapto-benzothiazole and sodium 2-mercaptobenzothiazole.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the Panel has conducted an extensive literature search for all available data, published and unpublished. The Panel has also performed an analysis of the adequacy of the existing data and developed a scientifically supportable category of related chemicals and used structure-activity relationship information to address HPV requirements.

Existing data for members of this category indicate that they are of moderate concern for aquatic toxicity, low concern as Persistent Organic Pollutants (POPs), moderate concern for skin irritation/allergic skin reaction, and low concern for mammalian toxicity and carcinogenicity. In addition, the Food and Drug Administration has approved several food-contact uses for this category of chemicals. The RAPA Panel concludes that there is sufficient data on the members of this category and no additional testing is recommended for purposes of the HPV Program.

Benzothiazole- and Morpholine-Based Thiazoles Category

According to guidelines for the HPV Chemical Program, a chemical category is “a group of chemicals whose physico-chemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity.” The similarities should be based on a common functional group, common precursors or breakdown products (resulting in structurally similar chemicals) and an incremental and constant change across the category. The goal of developing a chemical category is to use interpolation and/or extrapolation to assess chemicals rather than conducting additional testing with specific consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals.

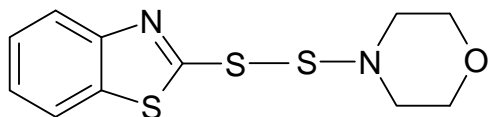
Relying on several factors specified in “Development of Chemical Categories in the HPV Challenge Program,”¹ in which use of chemical categories is encouraged, the following closely related chemicals described in Figure 1 constitute a chemical category.

Structural Similarity

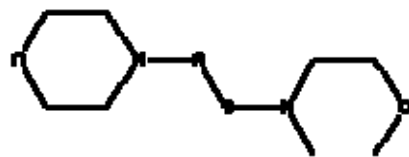
A key factor supporting the classification of these chemicals as a category is their structural similarity (See Figure 1). All materials in this category contain a morpholine group attached to a benzothiazole group [benzene ring + thiazole ring] or to another morpholine group via a sulfur or sulfur-sulfur bond.

¹ US EPA, Office of Pollution Prevention and Toxics. Development of Chemical Categories, Chemical Right-to-Know Initiative. <http://www.epa.gov/opptintr/chemrtk/categuid.htm>.

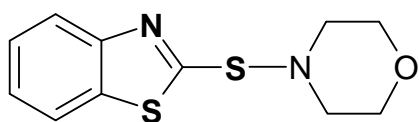
Benzothiazole- and Morpholine-Based Thiazole Category



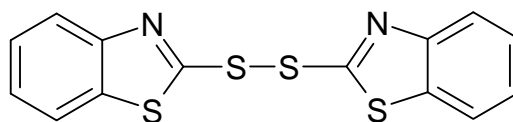
95-32-9
Benzothiazole, 2-(4-morpholinyldithio)-
(Morfax)



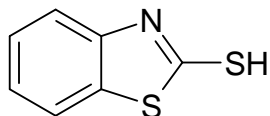
103-34-4
4,4'-Dithiodimorpholine
(DTDM)



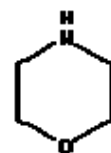
102-77-2
N-oxydiethylenebenzothiazole-2-sulfenamide
(MBS)



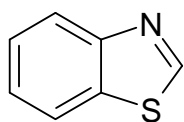
120-78-5
(MBTS)



149-30-4
2-Mercaptobenzothiazole
(MBT)



110-91-8
Morpholine



95-16-9
Benzothiazole
(BTH)

Figure 1. Chemical Structures for Members of the BMBT Category

Benzothiazole- and Morpholine-Based Thiazole Category

Morfax and DTDM are the HPV chemicals of interest in this category. N-oxydiethylene benzothiazole 2- sulfenamide (OBTS) and 4,4'-dithiodimorpholine (DTDM) are structurally similar to Morfax. OBTS is composed of the same basic components, mercaptobenzothiazole and morpholine joined by a sulfur atom, while DTDM contains the sulfur-sulfur-morpholine configuration found in Morfax. The similar molecular weights also indicate that OBTS and DTDM are good surrogates for Morfax (see Table 1). However, because Morfax has been shown to hydrolyze to MBTS and morpholine (Luecken and Sullivan, 1981; Lawrence, 1976), data on morpholine that were obtained from the ACC Amines Panel's robust summaries and test plan also are referenced as surrogate data in support of Morfax. MBTS has been shown to be metabolized to MBT as reported to EPA under TSCA Section 4 testing for MBT. EPA also considered Morfax for TSCA Section 4 testing and determined that further testing was not needed. The Panel believes that these data fully brackets the chemistry of Morfax and DTDM and provide adequate data to predict the physical properties, environmental fate, and hazards of this chemical.

Common Precursors

All category members are formed by the reaction of morpholine with benzothiazole or another molecule of morpholine in the presence of a sulfur donator.

Common Breakdown Products

2-Mercaptobenzothiazole and/or morpholine are the ultimate chemicals formed when these compounds undergo hydrolysis and/or metabolism.

Similarity of Physical Chemical Properties


The physical chemical properties of Morfax, DTDM and the other structural analogs parallel their structural similarity. All have molecular weights that are close to each other and exhibit limited water solubilities, low vapor pressures, high flash points, high boiling/decomposition points, excellent thermal stability, lack of reactivity, and Log P values at or below 5. Not unexpectedly, a few of the physical chemical properties for the hydrolysis products/metabolites are different than the parent compounds. For purposes of the HPV program, the existing data are adequate to describe the physical chemical properties of the category and/or for extrapolation (read-across) to members.

Fate and Transport Characteristics

The members of this category (parent compounds) are expected to distribute primarily in soil and water (Table 2) and have been shown to rapidly hydrolyze to their starting materials, especially under acidic conditions. These parent compounds are not readily biodegradable when measured by CO₂ evolution, mineralization or hydrolysis, and marginal by indirect photolysis. Testing and published literature has shown that, if hydrolysis occurs, the primary hydrolysis product will be MBTS, ultimately MBT, and morpholine. Morpholine is readily biodegradable, while MBT is not. Photodegradation is expected to have minimal impact on overall degradation. For purposes of the HPV program, the existing data is adequate to describe the environmental fate and transport of the category and/or for extrapolation (read-across) to members.

Table 1. Physico-chemical Properties of Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpholinylidithio)-	4,4'-Dithio dimorpholine	N-Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (ICCA)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS No.	95-32-9	103-34-4	102-77-2	120-78-5	110-91-8	149-30-4	95-16-9
Molecular Weight	284.42	236	252.4	332.38	87.12	167.24	135.18
Melting Point	128.6°C	130°C	75-90°C 150.7°C (EPI)	180°C	-5° C	181°C	2°C
Boiling Point	Decomp. 207.5°C	334.98°C	Decomp. 385° C (EPI)	Decomp.	128-130° C	Decomp. above 260°C	231°C
Relative Density	1.51g/cm3	1.36g/cm3 @25°C	1.35g/cm3 @20°C	1.54g/cm3 @25°C	1 g/cm ³ @ 20° C	1.42g/cm3 @20°C	1.246g/cm3 @20°C
Vapour Pressure	1.16 x10(-7) hPa @25°C (EPI)	3.55 x10(-5) hPa @25°C (EPI)	1.34 x10(-6) hPa @25°C	5.97 x10(-10) hPa @20°C	10 hPa @20° C	3.0 x10(-6) hPa @25°C	0.018 hPa @20°C
Partition Coefficient	1.59 (EPI)	2.49 @ 25°C	3.49 1.025 (EPI)	4.5 (4.66 EPI)	-2.55 @ 25° C	2.4 (2.86 EPI)	1.94 (2.01 EPI)
Water Solubility	657.6 mg/l @25°C (EPI)	237 ppm @25°C	32ppm 3 gm/l @ 25°C (EPI)	80 – 96 mg/l @22°C pH 5.0	5 g/l @ 25° C pH 10.6 miscible	118mg/l @25°C pH 7.0	3.5g/l @20°C

 = Non-sponsored chemicals used for data purposes only

EPI = EPIWin Modeling Program. Meylan W. and Howard P. (1999) Syracuse Research Corporation.

Table 2. Environmental Fate of the Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpholinylidithio)-	4,4'-Dithio dimorpholine	N-Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (ICCA)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS No.	95-32-9	103-34-4	102-77-2	120-78-5	110-91-8	149-30-4	95-16-9 (SIDS)
Hydrolysis	Hydrolyzes	T _{1/2} = 168 hr @ 23°C pH 7.0	T _{1/2} = 1.1 hr (AOP) T _{1/2} = 1 hr (water)	37% (7 days)	Addressed by Amines Panel ICCA	0-15 % (7 days)	No adequate data were located
Biodegradation	No adequate data were located	76% (49 days, 20.1 mg/l)	0% (28 days)	0-2 % (28 days)	91% (21 days) Readily Biodegradable	< 1 % (28 days)	0% (28 days, 100 mg/l) >65% (21 days, 0.8mg/l)
Photodegradation (T _{1/2})	0.37 hr (air; EPI)	0.34 hr (air; EPI)	1.1 hr (air; EPI) 1 hr (water; EPI)	0.4 hr (air; EPI) 3 hr (water)	< 1 day	2.4-4.8 hr (air) 31 min (water)	0.76 hr (air; EPI) 110 days (water)
Fugacity Level III (distribution)	(EPI)	(EPI)	(EPI)	(Calculated)		(EPI)	(EPI)
Air	< 0.1 %	0.00389%	<0.01%	< 0.1 %	0.0955%	0.507 %	23.3 %
Water	36.6 %	24.8%	44.6%	17.2 %	56.1%	35.9 %	56.4 %
Soil	63.3 %	75%	55.3%	72.7 %	43.8%	63.4 %	20.1 %
Sediment	0.09 %	0.175%	0.0904%	10.2%	0.0934%	0.172 %	0.16 %

 = Non-sponsored chemicals used for data purposes only

Toxicological Similarity

Review of existing published and unpublished test data for chemicals in the BMBT category shows that aquatic and mammalian toxicity among category materials are similar. Morfax, DTDM, and MBS are expected to hydrolyze and/or metabolize ultimately to MBT and morpholine.

Aquatic Toxicology - Acute

Ecotoxicity data indicate these chemicals exhibit a low to moderate toxicity to aquatic organisms (See Table 3). The calculated ECOSAR value of 512 mg/l for the 96-hr LC₅₀ with fish for Morfax is consistent with the observed results: 3.5 mg/l to >1000 mg/l in *P. promelas* and 1.6 mg/l to 350 mg/l for *L. macrochirus*. However, other limited data indicates that the 96-hr LC₅₀ value will be lower (moderate toxicity) for some species of fish. The calculated ECOSAR value of 533 mg/l for the 48-hr LC₅₀ with *daphnia* for Morfax also is close to the observed results which ranged from around 4 mg/l to 100 mg/l. The calculated ECOSAR value of 325 mg/l for the 96-hr EC₅₀ with algae for Morfax also is close to the observed results which ranged from around 4 mg/l to > solubility (80-96 mg/l; MBTS). Based on the robust data sets that are available for most chemicals in this category and ECOSAR modeling data, the data is adequate to evaluate the toxicity to aquatic organisms for the purposes of the HPV Program. Therefore, no additional ecotoxicity toxicity testing is proposed.

Mammalian Toxicology - Acute

The data on acute mammalian toxicity indicate that the members of this category pose a low concern for acute toxicity. Data are available for most members of the category by the oral and dermal routes of exposure, and inhalation exposure testing has been done on three members of the category, indicating that the category has been well tested for acute mammalian effects. Therefore, for purposes of the HPV Program, no additional acute mammalian toxicity testing is proposed. (See Table 4)

Mammalian Toxicology - Mutagenicity

Data from bacterial reverse mutation assays, *in vitro* and *in vivo* chromosome aberration studies, as well as additional supporting *in vitro* and *in vivo* genetic toxicity studies were reviewed, and the findings indicate a low concern for mutagenicity (See Table 4). Data are available for all members of the category in the Ames assay. Data are available for all but one chemical for chromosome aberration studies, and these data can be bridged to Morfax and DTDM, the HPV chemicals in this category. There are also carcinogenicity studies available and summarized in the IUCLID documents. Therefore, the category has been adequately tested for mutagenicity for purposes of the HPV Program and no additional mutagenicity testing is proposed.

Mammalian Toxicology – Repeated Dose Toxicity

Data from repeated-dose toxicity studies were reviewed. Repeat dose studies are available for five of the seven members in the category (See Table 4). The repeat dose testing consists of 28-day, 90-day and chronic studies. These data are adequate to characterize the repeated dose toxicity of this category and to characterize the toxicity of Morfax for purposes of the HPV Program. Therefore, no additional

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
testing is proposed for these materials.

Mammalian Toxicology - Reproductive and Developmental Toxicity

There are several adequate reproductive/developmental studies for members of this category (See Table 4). These studies provide sufficient data to adequately characterize the reproductive and developmental toxicity of this category and to bridge to Morfax and DTDM for HPV program purposes. Therefore, no additional testing is proposed.

Table 3. Ecotoxicity of the Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpholinyl)dithio-	4,4'-dithio dimorpholine	N-Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (ICCA)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS No.	95-32-9	103-34-4	102-77-2	120-78-5	110-91-8	149-30-4	95-16-9
Acute Fish Toxicity (96-hr LC ₅₀)	512 mg/l (ECOSAR)	1.6 mg/l to 3.6 mg/l (3 species)	1-5 mg/l to 11.5 mg/l (3 species)	66 mg/l to > 1000 mg/l (2 species)	180 to >1000 mg/l (7 species)	0.8 to 3.2 mg/l to 11 mg/l (2 species)	18 to 87 mg/l (5 species)
Acute Invertebrate Toxicity (48-hr EC ₅₀)	533 mg/l (ECOSAR)	4.5 mg/l <i>Daphnia</i>	4 – 4.5 mg/l <i>Daphnia</i>	> solubility <i>Daphnia</i>	119 mg/l <i>Daphnia</i>	2.9 - 4.1 mg/l <i>Daphnia</i>	20 mg/l <i>Daphnia</i>
Algal Toxicity (96-hr EC ₅₀)	325 mg/l (ECOSAR)	29 mg/l Algae	2 mg/l (other) 923 mg/l (Green algae; ECOSAR)	> solubility <i>S. subspicatus</i>	28 mg/l <i>S. capricornutum</i>	0.25 mg/l <i>S. capricornutum</i>	64 mg/l Algae

 = Non-sponsored chemicals used for data purposes only

ECOSAR = Modeling Program - version 0.99e. Meylan W. and Howard P. (1999) Syracuse Research Corporation.

Table 4. Mammalian Toxicity of the Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpholinylthio)-	4,4'-Dithio dimorpholine	N-Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (Amines Panel)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS No.	95-32-9	103-34-4	102-77-2	120-78-5	110-91-8	149-30-4	95-16-9
Acute Oral LD ₅₀	No adequate data were located	5600 mg/kg (rat)	12,560 mg/kg (rat)	> 7940 mg/kg (rat)	1450 mg/kg (rat)	2830 – 3800 mg/kg (rat)	380-492 mg/kg (rat)
Acute Dermal LD ₅₀	No adequate data were located	> 5010 mg/kg (rabbit)	>3000 mg/kg (rabbit)	> 7940 mg/kg (rabbit)	300-1200 mg/kg (rabbit)	> 7940 mg/kg (rabbit)	>126-<1000 mg/kg (rabbit)
Acute Inhalation LC ₅₀	No adequate data were located	1624 mg/m ³ (mice, no time given)	> 151 mg/l (1 hr) 0.09 mg/ l (4-hr) (rat)	No adequate data were located	>260 mg/l (4 hr, rat)	> 1.27 mg/l (4 hrs, rat)	~5 mg/l (4-hr, rat) >1400 mg/m ³ (6-hrs, rat)
Mutagenicity/ Gene Mutation	Negative Ames	Negative Ames Negative Mitotic Recomb.	Negative Ames Negative CHO gene mutation	Negative Ames Negative <i>E. coli</i>	Negative Ames Positive <i>E. coli</i>	Negative Ames Negative Yeast Negative <i>E. coli</i>	Negative Ames Negative Yeast
Mutagenicity/ Chromosome Aberration	No adequate data were located	Negative MLA Negative <i>in vivo</i> cytogenetics (rat)	Positive MLA Negative SCE Negative CHO cytogenic assay Negative Dom. Lethal	Negative MLA	Ambiguous MLA Negative SCE Negative Cytogenic assay (hamster)	Negative MLA Negative Dominant Lethal Negative MNT	No adequate data were located

Table 4 (Continued). Mammalian Toxicity of the Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpholinyl)dithio-	4,4'-Dithio dimorpholine	N-Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (Amines Panel)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS No.	95-32-9			120-78-5	110-91-8	149-30-4	95-16-9
Mutagenicity/ Other	Negative Balb3T3 Positive <i>E. coli</i> Pol A ⁻ DNA Damage	Negative UDS	Negative <i>E. coli</i> DNA Damage & Repair	No adequate data were located	Negative DNA Damage Ambiguous Balb3T3	No adequate data were located	No adequate data were located
Repeated Dose (NOEL/NOAEL)	No adequate data were located	100 mg/kg (10 day, oral, rats) 1.1 mg/m ³ (28 day dust inhalation, rats)	200 mg/kg (28 day, oral, rats) 5 mg/kg (113 wk, oral, rats) 9.8 mg/m ³ (28 day inhalation, rats)	237 – 464 mg/kg (17 month, gavage & diet, mouse) 100 mg/kg bw (90 day, gavage, rats)	10 ppm (104 Week, inhalation, rats, LOAEL)	375 mg/kg (90 day, rat) 714 mg/kg (28 day, rat)	No adequate data were located
Reproductive Toxicity (NOAEL)	No adequate data were located	No adequate data were located	500 mg/kg (gavage, rats)	200 mg/kg (gavage, rats, LOAEL)	No gonad histopath changes (13 wk study) Multigen. Neg.	< 179 mg/kg (diet, rats) 1071 mg/kg (diet, rats)	No adequate data were located
Developmental Toxicity (NOAEL)	No adequate data were located	500 mg/kg (rats)	1000 mg/kg (oral, rats)	596 mg/kg (diet, rats)	Addressed by Amines Panel ICCA	1800 – 2200 mg/kg (rat)	No adequate data were located


 = Non-sponsored chemicals used for data purposes only


Table 5. Test Plan for the Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpho linyldithio)-	4,4'-Dithio dimorpholine	N- Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (ICCA)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS#	95-32-9	103-34-4	102-77-2	120-78-5	110-91-8	149-30-4	95-16-9
Environmental Fate							
Hydrolysis	C	A	A	A	(ICCA)	A	N
Bio- degradation	C	A	A	A	A	A	A
Photo- degradation	A	A	A,C	A	A	A	A
Fugacity	A	A	C	A	A	A	A
Ecotoxicology							
Acute Fish Toxicity	S	A	A	A	A	A	A
Acute Invertebrate	S	A	A	A	A	A	A
Alga Toxicity	S	A	A,C	A	A	A	A
Mammalian Toxicology							
Acute Toxicity	C	A	A	A	A	A	A
Mutagenicity gene mutation	A	A	A	A	A	A	A

Table 5 (continued). Test Plan for the Benzothiazole- and Morpholine-based Thiazoles Category

Chemical	Benzothiazole 2-(4-morpho linylidithio)-	4,4'-Dithio dimorpholine	N- Oxydiethylene Benzothiazole 2-sulfenamide	Benzothiazole Disulfide (SIDS)	Morpholine (ICCA)	2-Mercapto benzothiazole	Benzothiazole (SIDS)
CAS#	95-32-9	103-34-4	102-77-2	120-78-5	110-91-8	149-30-4	95-16-9

Mammalian Toxicology (continued)							
Mutagenicity chromosome aberration	C	A	A	A	A	A	N
Repeated Dose	C	A	A	A	A	A	N
Reproductive Toxicity	C	C	A	A	A	A	N
Develop- mental Toxicity	C	A	A	A	(ICCA)	A	N

 = Non-sponsored chemicals used for data purposes only

Key for symbols in table:

A = Adequate data available

C = Use of Category Approach

T = Testing to be done

S = Structure activity relationship

N = No testing; SIDS chemical

Benzothiazole- and Morpholine-Based Thiazole Category

Background Information: Manufacturing and Commercial Applications

Manufacturing

Chemicals in the BMBT category are all made in batch processes using carbon disulfide, aniline and sulfur as starting materials. That reaction produces crude MBT (90%) and BTH (5%). MBT is treated with aqueous sodium hydroxide to produce sodium MBT (NaMBT). The NaMBT solution is reacted with sulfuric acid to produce purified MBT, and with chlorine to produce MBTS. MBTS is reacted with morpholine and additional sulfur to produce Morfax.

Commercial Applications

BMBT category chemicals have been manufactured for use in the rubber industry in the United States since the late 1920s, and are widely used throughout the industry due to their excellent stability, functionality and low cost. Over 90% of all usage is as cure-rate accelerators in the manufacture of tires (sidewall, tread and retread, carcass, belt skim, liner, bead filler/chafer, and base tread) and industrial rubber products (automotive extruded sponge, latex and foam, insulated wire, insulation jackets, molded and mechanical goods). Latex applications include shoe soles, elastic, carpet backing, gloves and tubing. The typical usage for a cure-rate accelerator application ranges from 0.5 to 5 parts accelerator per 100 parts of rubber (phr). Specialty chemical (non-rubber) applications for BMBT category chemicals include chemical intermediates for rubber additives, herbicides and pharmaceuticals, as industrial water treatment additives, for ore chelation/flotation/separation, lubrication additives, as a corrosion inhibitor in ethylene glycol-based automotive antifreeze and as topical veterinary drugs.

Compounds in the BMBT category are sold to large industrial users as ingredients or reagents for their products or processes. There are no known direct consumer applications for this class of compounds, and on this basis no direct sales to the general public.

The Food and Drug Administration has approved several of these compounds for use in various food-contact applications:

CFR² Reference	Application	Chemical
173.310	Boiler Water Additives	Morpholine
175.105	Components of Adhesives	MBT, MBTS, DTDM, Morpholine
176.180	Components of Paper/Paperboard	Morpholine
176.210	Defoaming Agents – Coatings	Morpholine
176.300	Slimicides	MBT
177.2600	Rubber Articles	MBT, MBTS, DTDM, MBS
178.3300	Corrosion Inhibitors – Steel	Morpholine

Worker/Consumer Exposure

The rubber and plastics additives industry has a long safety record and sophisticated industrial users handle these materials. Exposure of workers handling BMBT materials is likely to be the highest in the

² Code of Federal Regulations

Benzothiazole- and Morpholine-Based Thiazole Category

area of material packaging rather than from chemical manufacturing. These materials are made as pastilles (pellets), powders, flakes, solids and liquids. Product forms that minimize dust generation, coupled with the mechanized materials handling systems of the large industrial users, combine to help keep exposures to minimum levels. Occupational exposures are controlled through the use of personal protective equipment during material packout at the manufacturing site and during weigh-up activities at the customer site, to minimize potential for skin and inhalation exposure (nuisance dust is the primary route of worker exposure) as well as dermal contact with liquid forms.

Consumer exposure is considered minimal. Only very small amounts are used in rubber processing, and the materials themselves become bound in the rubber matrix during the vulcanization process. The most likely route of consumer exposure is skin contact from rubber or latex articles. Skin irritation, or possibly an allergic skin reaction may occur, but only in sensitive individuals subjected to prolonged and repeated exposure, especially under moist conditions. In the specialty application of additives to antifreeze, the amount used is less than 3%.