Addendum to SIDS Initial Assessment Report

For

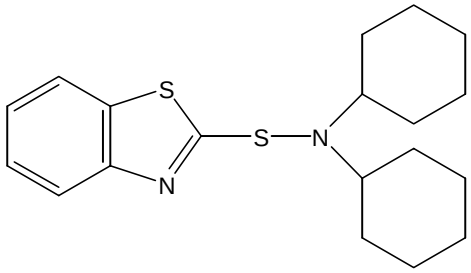
SIAM 18

Paris, France, 20-23 April 2004

1. Chemical Name:	N, N-Dicyclohexyl-2-benzothiazolesulfenamide
2. CAS Number:	4979-32-2
3. Sponsor Country:	Japan Contact Point: Mr. Motohiko Katho Director Second International Organizations Division Ministry of Foreign Affairs, Japan
4. Shared Partnership with:	
5. Roles/Responsibilities of the Partners: Name of industry sponsor /consortium Process used	
6. Sponsorship History How was the chemical or category brought into the OECD HPV Chemicals Programme?	
7. Review Process Prior to the SIAM:	Expert committee performed spot checks on randomly selected endpoints and compared original studies with data in SIDS dossier.
8. Quality check process:	
9. Date of Submission:	January 15, 2004
Date of last update	February 9, 2007
10. Comments:	The SIDS documents for N,N-dicyclohexyl-2-benzothiazolesulfenamide were discussed at SIAM 11 and the conclusion and recommendation on the human health part were agreed. With regard to the environment part SIAM 11 recommended that some additional studies (e.g. water solubility and identification of major metabolites as a result of hydrolysis) should be preformed. The original assessment documents are published by UNEP Chemicals as a SIDS Publication in August 2006. Additional information on bioaccumulation was reviewed by member

countries in in 2007. The current documents include an update of the SIDS Profile as well as addenda to the SIDS Initial Assessment Report and the SIDS Dossier, based on the results of post-SIDS testing.

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	4979-32-2
Chemical Name	N,N-Dicyclohexyl-2-benzothiazolesulfenamide
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The acute toxicity of N,N-dicyclohexyl-2-benzotazothiazolesulfenamide (DCBS) is low. The oral LD_{50} in rats is greater than 1,000 mg/kg and the dermal LD_{50} in rabbits is more than 2,000 mg/kg. This chemical is moderately irritating to skin and slightly irritating to eyes but no sensitizing to skin.

In an oral study with rats according to the OECD combined repeated dose and reproductive/developmental toxicity screening test [TG 422], the major toxicities were found in clinical observation and histopathological examination in kidneys. Salivation in males at 400 mg/kg bw/day and decreased locomotor activity in females at 100 and 400 mg/kg bw/day were noted. Histopathological examination revealed hyaline droplets in the renal tubular epithelia in males and fatty degeneration of the renal tubular epithelia in females at 100 and 400 mg/kg bw/day. In addition, adrenal enlargement with vacuolation of the adrenocortical cells and atrophy of spleen in females at 100 and 400 mg/kg bw/day were observed. A NOAEL for repeat dose toxicity was established at 25 mg/kg bw/day for both sexes.

In the above screening test [OECD TG 422], the toxic effects were revealed in females and pups at the dose of 400 mg/kg bw/day. There was a decreased number of corpus lutea accompanied with decreases in the number of implantation sites and litter size. Three dams died on the expected delivery day or on the following day. All dams at 400 mg/kg bw/day lost their litters at delivery or by day 4 of lactation. There were no effects on the mating and fertility, and morphogenesis in pups at and below 100 mg/kg bw/day. A NOAEL for reproductive/developmental toxicity was established at 100 mg/kg bw/day.

The genotoxic potential of this chemical was mostly negative with and without an exogenous metabolic activation system in bacteria as well as mammalian cells, while the cytogenetic effect was judged to be positive in *in vitro* tests without an exogenous metabolic activation because of a slight increase of polyploid cells and induction of micronucleus cells. However, this chemical did not induce cytogenetic effects in an *in vivo* bone marrow chromosome test although a standard method was not used. The weight of evidence suggests this chemical may not be genotoxic *in vivo*.

Environment

DCBS is a white powder with a water solubility of 1.9×10^{-3} mg/L at 25 °C, a melting point of 99 °C at 1013 hPa and a vapour pressure of $< 7.0 \times 10^{-5}$ Pa at 100 °C. A measured log Kow value is of > 4.8 suggests that this chemical is suspected to have a high bioaccumulation potential. DCBS has a high bio-concentration potential (steady-state BCF is 6,000 with Japanese carp). This chemical is hydrolysed in water and its half-lives at 25 °C have been measured as 4.92 day at pH 4.0, 18.6 days at pH 7.0 and 112 days at pH 9, producing two major metabolites (dicyclohexylamine and 2-mercaptobenzothiazole). However actual hydrolysis rates are uncertain since the test was conducted above the water solubility limit. Environmental distribution using a Mackay level III model indicates that if the substance is released into water or soil it tends to remain its in original compartment whereas if released into

air the substance is distributed into air (42.8 %) and soil (52.9 %). This substance is not readily biodegradable. In the atmosphere the substance is indirectly photodegraded by reaction with OH radicals with a half-life of 2.26 hrs. One of the degradation products, 2-mercaptobenzothiazole is non-volatile and not readily biodegradable whereas dicyclohexylamine is non-volatile but readily biodegradable in the environment.

In acute toxicity tests with fish, daphnids and algae, no effects were observed at the limit of solubility of the substance [96 h LC50 of > 0.0344 mg/L (*Orizias latipes*, OECD TG 203); 48 h EC50 of > 0.0314 mg/L (*Daphnia magna*, OECD TG 202, Immobilisation); 72 h EC of > 0.0118 mg/L (*Selenastrum capricornutum*, OECD TG 201, both biomass method and growth rate method) were reported].
Also in chronic toxicity tests with daphnids and algae, no effects were observed at the limit of solubility of the substance. A 21 d NOEC of >= 0.0331 mg/L (*Daphnia magna*, OECD TG 211, reproduction) and a 72 h NOEC of >= 0.0118 mg/L (*Selenastrum capricornutum*, OECD TG 201) were reported.

Exposure

Annual production volume of DCBS in Japan was about 1,900 tonnes in 2000-2003, and there is no information on import and export volumes.
In Japan, DCBS is solely used as an accelerator of vulcanization and is completely reacted in the vulcanizing process. During vulcanisation processes and the use of rubber products, some degradation products (e.g. mercaptobenzothiazole: CAS No. 149-30-4 or di(benzothiazoyl-2)disulfide: CAS No. 120-78-5) may appear and they can be released into the environment. It is reported that during the vulcanization the unstable sulphur-nitrogen-bond of DCBS is split with the intermediate formation of mercaptobenzothiazol radicals. Products resulting from the process are the basic amines, benzothiazole derivatives and further reaction products. As further degradation products, benzothiazole, 2-methylbenzothiazole and 2-benzothiazolone and 2-methylthiobenzothiazole are reported.
Occupational exposures at production sites may occur by the inhalation route during bag filling operation. No actual workplace concentration data was available. Workers wear dust respirator and body-covering clothing and local exhaust ventilation system is operated during the filling process.

RECOMMENDATION

The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health
The chemical possesses a hazard for human health (repeated dose toxicity). An exposure assessment and, if necessary risk assessments for workers and consumers should be performed taking into account possible breakdown products.

Environment
The chemical did not show any adverse effects in several acute and chronic toxicity tests with aquatic organisms, but shows a high bio-concentration potential. During the use of the substance several degradation products are formed which possess properties indicating a hazard for the environment. These degradation products are present in many rubber products and a release to the environment is possible. An exposure assessment, and if necessary a risk assessment for the environment of the degradation products should be performed. The currently on-going assessment of di(benzothiazoyl-2)disulfide (CAS No. 120-78-5), of N-cyclohexylbenzothiazole-2-sulfenamide (CAS No. 95-33-0) and of the sulfenamide accelerator category should be taken into account.

SIDS Initial Assessment Report

2.2.5 Biodegradation

A ready biodegradability test was conducted according to OECD TG 301 C (MITI, 1994b). Based on the BOD and HPLC analysis, only up to 6 % (average 3 %) of biodegradation was determined.

2.2.6 Bioaccumulation

A measured log Kow value is > 4.8 (MITI, 1994b). A bio-concentration test was conducted according to OECD TG305 (METI, 2001) with a steady-state BCF of 6,000 (BCF: 2,800 - 7,700) using Japanese carp at the test concentration of 0.01 μ g/L.

4.4 Initial Assessment for the Environment

This chemical has a high bioaccumulation potential (steady-state BCF is 6,000, OECD TG305), and it is not readily biodegradable. Although no biodegradability is observed, this chemical tends to be hydrolyzed under acidic and environmental conditions.

In acute toxicity tests with fish, daphnids and algae, no effects were observed at the limit of solubility of the substance [96 h LC50 of > 0.0344 mg/L (*Orizias latipes*, OECD TG 203); 48 h EC50 of > 0.0314 mg/L (Daphnia magna, OECD TG 202, Immobilisation); 72 h EC of > 0.0118 mg/L (*Selenastrum capricornutum*, OECD TG 201, both biomass method and growth rate method) were reported].

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5 RECOMMENDATIONS

Environment

The chemical did not show any adverse effects in several acute and chronic toxicity tests with aquatic organisms, but shows a high bio-concentration potential. During the use of the substance several degradation products are formed which possess properties indicating a hazard for the environment. These degradation products are present in many rubber products and a release to the environment is possible. An exposure assessment, and if necessary a risk assessment for the environment of the degradation products should be performed. The currently on-going assessment of di(benzothiazoyl-2)disulfide (CAS No. 120-78-5), of N-cyclohexylbenzothiazole-2-sulfenamide (CAS No. 95-33-0) and of the sulfenamide accelerator category should be taken into account.

6 REFERENCES

METI, Japan (2001) Study on bio-concentration of N, N-Dicyclohexyl-2-benzothiazolesulfenamide, Report Number 51231IV. Test was performed in Chemicals Evaluation and Research Institute, Japan.

SIDS DOSSIER

N, N-Dicyclohexyl-2-Benzothiazolesulfenamide

CAS No. 4979-32-2

Sponsor Country: Japan

3.7 BIOACCUMULATION

Speies:	Cyprinus carpio (Fish, fresh water)
Exposure period:	42 day at 25 degree C
Concentration:	0.01 μg/l
BCF:	2,800 – 7,700 Steady-state BCF: 6,000
Elimination:	6.1 days (half life time for elimination)
Method:	OECD Test Guideline 305 C "Flow-through fish test"
Test substance:	Source: Ouchishinko Chemical Industry Co., Ltd. Purity: > 99 %
Remark:	Concentration of test fish and test water were determined by HPLC.
GLP:	Yes **[X]** No **[ ]** ? **[ ]**
Reference:	METI, Japan (2001)
Flag:	Critical study for SIDS endpoint
Reliability:	(1) valid without restriction

METI, Japan (2001) Study on bio-concentration of N, N-Dicyclohexyl-2-benzothiazolesulfenamide, Report Number 51231IV. Test was performed in Chemicals Evaluation and Research Institute, Japan.