UN/SCEGHS/32/INF.4/Add.1

Committee of Experts on the Transport of Dangerous Goods and on the Globally Harmonized System of Classification and Labelling of Chemicals

Sub-Committee of Experts on the Globally Harmonized System of Classification and Labelling of Chemicals
Thirty-second session
Geneva, 7– 9 (morning) December 2016
Item 4 (a) of the provisional agenda
Implementation of the GHS:
Development of a list of chemicals classified in accordance with the GHS

18 November 2016

Report on the proposal for classification and labelling of Dimethyltin Dichloride

Transmitted by the secretariat of the Organisation for Economic Cooperation and Development (OECD)

Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development

15-Nov-2016

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

REPORT ON THE PROPOSAL FOR CLASSIFICATION AND LABELLING (C&L) OF DIMETHYLTIN DICHLORIDE

Series on Testing & Assessment
No. 247

The corresponding annexe is available in the following cote : ENV/JM/MONO(2016)44/ANN1

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Unclassified

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OECD Environment, Health and Safety Publications

Series on Testing & Assessment

No. 247

REPORT ON THE PROPOSAL FOR CLASSIFICATION AND LABELLING (C&L) OF DIMETHYLTIN DICHLORIDE

Joint Pilot Project of the OECD and the UN Sub-Committee of Experts on the Globally Harmonised System of Classification and Labelling of Chemicals

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD

Environment Directorate

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Paris, 2016

ABOUT THE OECD

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This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organisations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWARD

In 2014, the OECD Task Force on Hazard Assessment (TFHA) and the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology (JM) agreed to provide a coordination role for a pilot classification project upon invitation from the UN Sub-Committee of Experts on the Globally Harmonised System of Classification and Labelling of Chemicals (UNSCEGHS). A report of the Pilot Project of the OECD and the UN Sub-Committee of Experts on the Globally Harmonised System of Classification and Labelling of Chemicals detailing the process of the pilot project and learnings is published along with this report. (Report on the Pilot Project on Assessing the Potential Development of a Global List of Classified Chemicals. ENV/JM/MONO(2016)43, Series on Testing & Assessment No. 246). It also contains a template for Proposals for Classification and Labelling (Annex 1 to ENV/JM/MONO(2016)43/ANN1/PART1 & ENV/JM/MONO(2016)43/ANN1/PART1).

Accompanying the report are three case study chemicals where non-binding agreement on their classification have been reached. The results of this pilot project will be submitted to the UNSCEGHS for consideration in their deliberations on the potential development of a global list of classified chemicals.

This report on the Proposal for Classification and Labelling (C&L) of Dimethyltin Dichloride was prepared by the European Chemicals Agency, with review and input from the project team established for this pilot project under the OECD Task Force for Hazard Assessment. It contains a C&L report as well as an Annex with additional background information.

The following two reports on the Proposal for Classification and Labelling (C&L) are published with this report:

1. Report on the Proposal for Classification and Labelling (C&L) of Dicyclopentadiene ENV/JM/MONO(2016)45, Series on Testing & Assessment No. 248.

2. Report on the Proposal for Classification and Labelling (C&L) of Dibutyl Phthalate ENV/JM/MONO(2016)46, Series on Testing & Assessment No. 249.

This document is being published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology.

Proposal for Classification and Labelling (C&L)

Based on the Globally Harmonized System of Classification and Labelling of Chemicals (GHS)

International Chemical Identification: Dimethyltin dichloride

CAS Number: 753-73-1

Contact details for dossier submitter:

European Chemicals Agency (ECHA)
P.O. Box 400
FI-00121 Helsinki
Finland

Version number: 4 **Date: 29/04/2016**

Note on confidential information

Please be aware that this report is intended to be made publicly available. Therefore it does not contain any confidential information.

Disclaimer: This proposal for classification and labelling, is for a candidate substance as identified by the UN Sub-Committee on GHS and contributes to the Joint GHS Sub-Committee/OECD Pilot classification exercise (work plan in UN/SCEGHS/28/INF.22, Annex I). It is not intended for any other purposes. The proposal does not represent an official position of the European Chemicals Agency.

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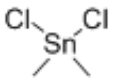
1. IDENTIFY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 1: Substance identity and information related to molecular and structural formula of the substance

International Chemical Identification - **Name(s) in the IUPAC nomenclature or other international chemical name(s)**	Dimethyltin dichloride
Other names (usual name, trade name, abbreviation)	DMTC
ISO common name (if available and appropriate)	Not applicable.
CAS number (if available)	753-73-1
Other identifier(s) (if available)	EC number: 212-039-2
In case the substance is already included in a classification list - identifier of the entry	EU Index number in Annex VI, CLP Regulation: 050-029-00-8
Molecular formula	$C_2H_6Cl_2Sn$
Structural formula	
SMILES notation (if available)	Not available.
Molecular weight or molecular weight range	219.67 g/mol
Information on optical activity and typical ratio of (stereo) isomers (if applicable and appropriate)	Not applicable.
Description of the manufacturing process and identity of the source (for UVCB substances only)	Not applicable.
Degree of purity (%) (if relevant for the classification proposal)	90% < conc. >100%

1.2 Composition of the substance

Table 2: Constituents (non-confidential information)

Constituent (Name and numerical identifier)	**Concentration range (% w/w minimum and maximum**
Dimethyltin dichloride	90% < conc. >100%

Table 3: Impurities (non-confidential information) if relevant for the classification of the substance

Impurity (Name and numerical identifier)	Concentration range (% w/w minimum and maximum)	The impurity contributes significantly to the classification and labelling
Monomethyltin trichloride (MMTC) (CAS 993-16-8).	Not disseminated	The impurity has a mandatory classification in the EU as toxic for reproduction with regard to developmental effects, category 2 (Annex VI, CLP Regulation, EU).

Table 4: Additives (non-confidential information) if relevant for the classification of the substance

Additive (Name and numerical identifier)	Function	Concentration range (% w/w minimum and maximum)	The additive contributes significantly to the classification and labelling (yes/no)
No data available.			

Table 5: Test substances (non-confidential information)

Identification of test substance	Purity	Impurities and additives (identity, %, classification if available)	Other information	The study(ies) in which the test substance is used
Not considered useful for this dossier				

2. PROPOSED CLASSIFICATION AND LABELLING

2.1 Proposed classification and labelling according to the GHS criteria (GHS revision number 6)

Table 6: Proposed classification and reason for not proposing a classification for a hazard class

GHS chapter ref.	Hazard class or differentiation	Proposed classification - Hazard Class and Category Code(s); Hazard statement Code(s)	Proposed Specific Concentration Limits (SCL(s)) and M-factor(s)	Reason for no proposed classification
2.1	**Explosives**	No classification.		Data lacking
2.2	**Flammable gases**	No classification.		Hazard class not applicable
2.3	**Aerosols**	No classification.		Hazard class not applicable
2.4	**Oxidising gases**	No classification.		Hazard class not applicable
2.5	**Gases under pressure**	No classification.		Hazard class not applicable
2.6	**Flammable liquids**	No classification.		Hazard class not applicable
2.7	**Flammable solids**	No classification.		Data conclusive but not sufficient for classification
2.8	**Self-reactive substances**	No classification.		Data lacking
2.9	**Pyrophoric liquids**	No classification.		Hazard class not applicable
2.10	**Pyrophoric solids**	No classification.		Data lacking
2.11	**Self-heating substances**	No classification.		Data conclusive but not sufficient for classification
2.12	**Substances which in contact with water emit flammable gases**	No classification.		Data lacking
2.13	**Oxidising liquids**	No classification.		Hazard class not applicable
2.14	**Oxidising solids**	No classification.		Data lacking
2.15	**Organic peroxides**	No classification.		Hazard class not applicable
2.16	**Corrosive to metals**	No classification.		Data lacking
2.17	**Desensitized explosives**	No classification.		Hazard class not applicable
3.1	**Acute toxicity - via oral route**	Acute Tox. 3; H301		
	- via dermal route	Acute Tox. 3; H311		
	- via inhalation route	Acute Tox. 2; H330		
3.2	**Skin corrosion/irritation**	Skin Corr. 1; H314		
3.3	**Serious eye damage/eye irritation**	Eye Dam. 1; H318.		
3.4	**Respiratory sensitisation**	No classification.		Data lacking.

	Skin sensitisation	No classification.		Data inconclusive.
3.5	**Germ cell mutagenicity**	No classification.		Data conclusive but not sufficient for classification.
3.6	**Carcinogenicity**	No classification.		Data inconclusive.
3.7	**Reproductive toxicity**	Repr. 2; H361 (developmental toxicity)		
3.8	**Specific target organ toxicity-single exposure**	No classification.		Data conclusive but not sufficient for classification.
3.9	**Specific target organ toxicity-repeated exposure**	STOT RE 1; H372 (nervous system, immune system)		
3.10	**Aspiration hazard**	No classification.		
4.1	**Hazardous to the aquatic environment**	Aquatic Acute 3; H402 Aquatic Chronic 3; H412		
4.2	**Hazardous to the ozone layer**	No classification.		Hazard class not applicable

Proposed labelling

Pictogram Code(s): GHS05, GHS06, GHS08

Signal Word Code(s): Danger

Hazard statement Code(s): H301, H311, H330, , H314, H318, H361 (developmental), H372 (nervous system, immune system), H412

Supplemental information: The additional hazard statement "Corrosive to the respiratory tract" is suggested to be added in the labelling based on the classification of DMTC as acutely toxic by inhalation and as skin corrosive (see section 8.2)

3. IDENTIFIED USES

Used as an intermediate to make heat stabilizers for PVC. There is no known use for the general public.

4. DATA SOURCES

- EU REACH registration dossier on DMTC, published 25 June 2013, modified 3 August 2015, as disseminated on ECHA's webpage (http://echa.europa.eu/information-on-chemicals)*
- PubMed search on DTMC (date 8 May 2015)
- The opinion of the ECHA's Committee for Risk Assessment proposing harmonised classification and labelling at EU level of Dimethyltin dichloride, adopted 30 November 2012 (including its Annexes of which Annex I is based on a proposal for a EU harmonised classification from the French Competent Authority) (http://echa.europa.eu/opinions-of-the-committee-for-risk-assessment-on-proposals-for-harmonised-classification-and-labelling/-/substance-rev/2066/del/50/col/staticField_-104/type/asc/pre/2/view)

* Please note that the term "registrant" in the following text, and in Annex I, means the registrant that has submitted the registration dossier as required according to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

5. PHYSICOCHEMICAL PROPERTIES

Table 7: Summary of physicochemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Physical state at 20°C and 101,3 kPa	Colourless/white solid	Harper et al. (2005), and Summer et al. (2003), OECD SIDS (2006)	References were assessed with a reliability of 4 (Klimisch score).
Melting/freezing point	Melting point of test substance determined as 105 ± 0.5 °C	Author not disseminated (2013); report date 2013-01-28.	The key study was conducted in accordance with the accepted EU A.1 & OECD Guideline 102 test methods and GLP compliant.
Boiling point	189°C	Harper et al. (2005), Dobson et al. (2006), Author not disseminated (1994), Hoch (2001), Summer et al. (2003), Author not disseminated (2006); report date 2006-07-23, OECD SIDS (2006).	References were assessed with a reliability of 4 (Klimisch score). No single study was robust enough to be considered a key study.
Relative density	1.4 g/cm3	Summer et al. (2003), Author not disseminated (1993); report date 1993-07-20, OECD SIDS (2006).	The density of the test substance was found to lie between 1 and 1.75 g/cm³. 1.4 g/cm³ was chosen as the key value for chemical safety assessment as it is the midpoint of this range. References were assessed with a reliability of 4 (Klimisch score). No single study was robust enough to be considered a key study.
Vapour pressure	0.04 hPa at 20°C,	Dobson et al. (2006), van Dokkum and Huwer (2005) Summer et al. (2003) and OECD SIDS (2006).	References were assessed with a reliability of 4 (Klimisch score). No single study was robust enough to be considered a key study.
Surface tension	Not applicable.		
Water solubility	823.0 g/l at 20.0 ± 0.5 °C	Author not disseminated (2003); report date 2003-04-09.	The key study was a reliable study (Klimisch score 1), conducted in accordance with OECD TG 105 and GLP compliant. However, this analysis method only measures the amount of the alkyltin moiety, but cannot identify the other ligands attached to the tin.
Partition coefficient n-octanol/water	-2.18 ± 0.17 (22.0 ± 1.0 °C)	Author not disseminated (2003). Report date 2003-04-09.	The key study was a reliable study (Klimisch score 1), conducted in accordance with OECD TG 107 and GLP compliant. However, in water,

			DMTC undergoes rapid degradation by hydrolysis and is expected to hydrolyze within minutes. The reported value may not be due entirely to the named substance and any subsequent use of the partition coefficient to predict environmental behaviour of the named substance must carefully consider the limitations inherent in the measurement of this parameter.
Flash point	Not applicable		As the substance is a solid, testing is technically not feasible.
Flammability	Non flammable	Author not disseminated (2013). Report date 2013-01-21.	In a reported flammability study (Klimisch 1) conducted in accordance with EU Method A.10 and CLP compliant, no evidence of flammability was observed.
Explosive properties	Non explosive		There are no chemical groups associated with explosive properties present in the molecule.
Self-ignition temperature	The substance has been determined not to have a relative self-ignition temperature below its melting temperature.	Author not disseminated (2013). Report date 2013-01-21.	Testing was conducted using a procedure designed to be compatible with Method Al6 Relative Self-Ignition Temperature for Solids of Commission Regulation (EC) No 440/2008 of 30 May 2008.
Oxidising properties			No studies are available.
Granulometry	Not applicable		The substance is marketed or used in a non solid or granular form.
Stability in organic solvents and identity of relevant degradation products			No studies are available.
Dissociation constant	pKa= 3.54	Vighi & Calamari, Chemosphere (1985).	No methodological information available. Klimisch 4 (not assignable).
Viscosity	Technically not feasible		The substance is unsuitable for viscosity testing as it is a solid.

6. EVALUATION OF PHYSICAL HAZARDS

6.1 Explosives

Table 8: Summary table of studies on explosive properties

Method	Results	Remarks	Reference
No studies are available.			

Short summary and overall relevance of the provided information on explosive properties

No studies are available.

According to the registrant it can be concluded from the structural formula that the substance is not explosive as it does not have functional groups associated with explosivity.

Comparison with the GHS criteria

A substance is not classified as explosive if there are no chemical groups associated with explosive properties present in the molecule (examples of groups which may indicate explosive properties are given in table A6.1 in Appendix 6 of the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria).

Conclusion on classification and labelling for explosive properties

From the structural formula it can be concluded that the substance is not explosive as it does not have functional groups associated with explosivity.

6.2 Flammable gases

Table 9: Summary table of studies on flammable gases

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on flammable gases

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for flammable gases

Not applicable.

6.3 Aerosols

Table 10: Summary table of studies on aerosols

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on aerosols

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for aerosols

Not applicable.

6.4 Oxidising gases

Table 11: Summary table of studies on oxidising gases

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on oxidising gases

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for oxidising gases

Not applicable.

6.5 Gases under pressure

Table 12: Summary table of studies on gases under pressure

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on gases under pressure

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for gases under pressure

Not applicable.

6.6 Flammable liquids

Table 13: Summary table of studies on flammable liquids

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on flammable liquids

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for flammable liquids

Not applicable.

6.7 Flammable solids

Table 14: Summary table of studies on flammable solids

Method	Results	Remarks	Reference
EU Method A.10	Not classified	The pile failed to ignite during the 2 minutes that the Bunsen flame was applied. The result of the preliminary screening test obviated the need to perform the main test.	Author not disseminated (2013), Report date 2013-01-21.

Short summary and overall relevance of the provided information on flammable solids

The test item has been determined to be not flammable as it failed to ignite in the preliminary screening test.

Comparison with the GHS criteria

If the test item does not ignite and propagate combustion either by burning with flame or smoldering along 200 mm within 4 minutes, the test item is not considered as highly flammable and no further testing is required. The flammability (solids) was determined by measuring the burning rate of test item prepared as a pile of set dimensions. The pile failed to ignite during the 2 minutes that the Bunsen flame was applied. The result of the preliminary screening test obviated the need to perform the main test.

The test item has been determined to be not highly flammable as it failed to ignite in the preliminary screening test.

Conclusion on classification and labelling for flammable solids

Not classified.

6.8 Self-reactive substances

Table 15: Summary table of studies on self-reactivity

Method	Results	Remarks	Reference
No studies are available.			

Short summary and overall relevance of the provided information on self-reactive substances

No studies are available.

Comparison with the GHS criteria

No studies are available.

Conclusion on classification and labelling for self-reactive substances

No studies are available.

6.9 Pyrophoric liquids

Table 16: Summary table of studies on pyrophoric liquids

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on pyrophoric liquids

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for pyrophoric liquids

Not applicable.

6.10 Pyrophoric solids

Table 17: Summary table of studies on pyrophoric solids

Method	Results	Remarks	Reference
No studies are available.			

Short summary and overall relevance of the provided information on pyrophoric solids

According to the registrant, in accordance with point 1, Annex XI of Regulation (EC) No. 1907/2006 (REACH), based on the known chemical and physical properties of the substance, its chemical structure and experience in handling the substance, testing in line with Method A13: Pyrophoric properties of solids and liquids of Commission Directive 92/69/EEC is expected to produce a negative results.

Comparison with the GHS criteria

No studies are available.

Conclusion on classification and labelling for pyrophoric solids

Not classified as no studies are available.

6.11 Self-heating substances

Table 18: Summary table of studies on self-heating substances

Method	Results	Remarks	Reference
A.16	The substance has been determined not to have a relative self-ignition temperature below its melting temperature		Author not disseminated (2013), Report date 2013-01-21.

Short summary and overall relevance of the provided information on self-heating substances

The substance has been determined not to have a relative self-ignition temperature below its melting temperature (105°C).

Comparison with the GHS criteria

A substance shall be classified as self-heating substance if a positive result at 140°C is obtained according to test method N4 described in the UN Recommendations on the TDG, Manual of tests and criteria, Part III, sub-section 33.1.6 used as the basis for the GHS criteria.

Not classified as the melting point temperature is below 140°C.

Conclusion on classification and labelling for self-heating substances

Not classified.

6.12 Substances which in contact with water emit flammable gases

Table 19: Summary table of studies on substances which in contact with water emit flammable gases

Method	Results	Remarks	Reference
No studies are available.			

Short summary and overall relevance of the provided information on substances which in contact with water emit flammable gases

No studies are available.

The substance is known to be highly soluble in water.

According to the registrant, in accordance with point 1, Annex XI of Regulation (EC) No. 1907/2006 (REACH), based on the known chemical and physical properties of the substance, its chemical structure and experience in handling the substance, testing in line with Method A.12: Flammability (contact with water) of Commission Directive 92/69/EEC is expected to produce a negative results.

Comparison with the GHS criteria

No studies are available, but the substance is known to be highly soluble in water.

Conclusion on classification and labelling for substances which in contact with water emit flammable gases

Not classified.

6.13 Oxidising liquids

Table 20: Summary table of studies on oxidising liquids

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on oxidising liquids

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for oxidising liquids

Not applicable.

6.14 Oxidising solids

Table 21: Summary table of studies on oxidising solids

Method	Results	Remarks	Reference
No studies are available.			

Short summary and overall relevance of the provided information on oxidising solids

No studies are available.

Comparison with the GHS criteria

No studies are available.

Conclusion on classification and labelling for oxidising solids

No studies are available.

6.15 Organic peroxides

Table 22: Summary table of studies on organic peroxides

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on organic peroxides

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for organic peroxides

Not applicable.

6.16 Corrosive to metals

Table 23: Summary table of studies on the hazard class corrosive to metals

Method	Results	Remarks	Reference
No studies are available.			

Short summary and overall relevance of the provided information on the hazard class corrosive to metals

No studies are available.

Comparison with the GHS criteria

No studies are available.

Conclusion on classification and labelling for corrosive to metals

No studies are available.

6.17 Desensitized explosives

Table 24: Summary table of studies on desensitized explosive properties

Method	Results	Remarks	Reference
Not applicable.			

Short summary and overall relevance of the provided information on desensitized explosive properties

Not applicable.

Comparison with the GHS criteria

Not applicable.

Conclusion on classification and labelling for desensitized explosive properties

Not applicable.

7. TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

Table 25: Summary table of toxicokinetic studies

Method	Results	Remarks	Reference
OECD TG 417, GLP compliant Rat SD, m/f , single dose, 10 mg/ kg bw	Bioavailability: 0.52/0.71 m/f Mean (±SD) apparent volume of distribution: intravenous: 44.3 (±26.7)/ 109 (±92.9) L/kg, m/f oral: 52.7 (±31.7)/138 (±98.1) L/kg Renal clearance: intravenous: 0.105/0.559 L/h/kg, m/f oral: 0.0816/0.282 L/h/kg, m/f t_{max} ranged from 10 minutes to 4 hour post dosing. mean (±SD) C_{max}: 3834 (±2983) / 1088 (±656) µg/mL m/f mean (±SD) $AUC_{0-\infty}$: 51.3 (±53.7)/11.0 (±0.31) µg-hour/mL m/f	Deviations: Three deviations not affecting the quality of the study were reported.	Author not disseminated (2001) Report date 2001-09-05.
No guideline, GLP compliance not reported Rat SD, f 40 mg tin/L/d phases I and II in drinking water; 0.8 mL/100 g bw/d in phase III by gavage. Radioactive dimethyltin dichloride in phase III only	Dimethyltin dichloride was transferred to the pups mainly during the gestation period. Transfer during lactation was limited.		Noland *et al.* 1983
OECD TG 428, GLP compliant dimethyltin dichloride 89%, monomethyltin dichloride 11% dose: 100 µg/cm² as a 10 µl/cm² dose of a 10000 µg/ml solution in ethanol	Human and rat skin, Wistar-derived rat strain. Dermal absorption was determined under occluded and unoccluded conditions. Percutaneous absorption rate at 24h: unoccluded human 20% and unoccluded rat 34%. In human skin the maximum absorption rate were 0.015 µg/cm²/h between 0-6h and 0.037 µg/cm²/h between 6-24h. In rat skin, the absorption rate was constant for the occluded skin (0.233 µg/cm²/h) during the whole exposure. While for the unoccluded skin the maximum rate was 1.07 µg/cm²/h, and the absorption was essentially complete within the first 3h.		Author not disseminated (1999) Report date: 1999-03-31.

Short summary and overall relevance of the provided toxicokinetic information on the proposed classification(s)

The absorption, distribution, metabolism and excretion (ADME) for dimethyltin dichloride was investigated in male and female Sprague-Dawley rats following administration of a single oral or intravenous dose of 10 mg/kg bw. Plasma and urine were collected at regular interval for analysis. Concentrations of tin were also generally higher in males than in females following the single oral dose. Smaller inter-animal variability was observed in the tin plasma concentrations following oral than intravenous administration. The distribution phase, for both routes of administration, lasted at least 8 hours. The tin plasma concentration decreased fast on the first 12 hour post-dosing, by approximately an order of magnitude, followed by a slower clearance rate. Tin plasma concentrations during the terminal elimination phase were higher for males than for females, but were similar between the two routes of administration.

The urinary clearance rate appeared to be influenced by the route of administration; biphasic after intravenous and triphasic after oral administration. Following the intravenous exposure, an initial faster clearance phase occurred within the first 24h, followed by slower elimination phase which coincided with the low plasma concentrations. After the oral dose, an additional phase, coinciding with the distribution phase, was observed.

Noland et al. (1983) investigated the dimethyltin dichloride gastrointestinal adsorption and trans placental transfer after oral administration in female Sprague-Dawley rats. The test substance was administrated to dams, two weeks prior breeding and continued through breeding and gestation, via drinking water on phases I and II and by gavage on phase III. The study showed that dimethyltin dichloride was able to cross the blood brain barrier and the placenta to reach the foetus. In pup the highest levels of tin were measured were measured at birth; tin levels were rapidly decreasing after birth demonstrating that exposure via lactation is limited.

Dermal absorption was investigated in vitro in human and rat skin. Percutaneous absorption rate in unoccluded and occulted human sample at 24 hours was 20% and 43%, respectively. While percutaneous absorption rate in unoccluded rat at 24 hours was 34%. For both species, the amount remaining in epidermis is considered potentially absorbable. After the 24h exposure, the overall recovery from the system was low: 55% and 67% of the occulted applied dose recovered in human and rat respectively while 31% and 48% was recovered from the unoccluded applications in human and rat respectively.

8. EVALUATION OF HEALTH HAZARDS

8.1 Acute toxicity - oral route

Table 26a: Summary table of animal studies on acute oral toxicity

Method, test guideline, and deviation(s) if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Value LD_{50}**	**Reference**
OECD TG 401 GLP compliant Oral gavage	Rat; Sprague-Dawley, 5 animals/sex and dose	Dimethyltin dichloride (DMTC)(85% DMTC: 15% monomethyltin trichloride). The [Di/Mono] Methyltin Chlorides Solution was a 50% organotin solution in an unspecified solvent.	Main study: 200, 300 and 500 mg/kg bw.	LD_{50} (male): 273 mg/kg bw (of 85% DMTC) LD_{50} (female): 164 mg/kg bw (of 85% DMTC) LD_{50} (male/female): 204.5 mg/kg bw (of 85% DMTC)	Elf Atochem NA, 1993
OECD TG 401 GLP compliance not reported Oral gavage	Rat; Sprague-Dawley, 5 animals/per sex and dose	dimethyltin dichloride 98.7%.	0, 100, 150, 200, 250 and 300 mg/kg bw	LD_{50} (male): 190 mg/kg bw LD_{50} (female): 160 mg/kg bw	Author not disseminated (1979). Report date: 1979-03-20.
Non-guideline GLP compliance not reported Oral gavage	Rat, Sprague-Dawley, 5 animals/per sex and dose	5% dimethyltin dichloride in corn oil (identity of test substance not the same as for substance defined in the SID part of registration dossier)	0.215, 0.464, 1.00, 2.15 and 4.64 mL/kg bw + controls	LD_{50} (male/female): 1.7 mL/kg bw	Author not disseminated (1978). Report date: 1978-05-25.
No guideline stated GLP compliance not reported Oral gavage	Rat, no strain data 6 males/dose	dimethyltin dichloride; purity not given	100, 200, 400, 800 and 1600 mg/kg bw No data on control animals.	LD_{50} (male): 141.4 mg/kg bw	Affiliated Medical Enterprises, 1971a .
No guideline stated. GLP compliance not reported (pre-GLP implementation) Oral gavage	Rat, Wistar, 10 males per dose	dimethyltin dichloride. Test material form: crystalline. 5% solution	48, 57, 69, 83, 100, 120 and 144 mg/kg bw No data on control animals.	LD_{50} (male): 73.86 mg/kg bw	Klimmer, O.R. 1971.

No methodological information. GLP compliance not reported. Oral	Rat, no further information given.	dimethyltin dichloride; purity not given	Not specified.	LD_{50}: 74 mg/kg bw	Hoch (2001) (from an overview in Applied Geochemistry)
No guideline followed, GLP compliance not reported. Acute oral test, with lower dosage groups repeated on 4th day. Animals observed for 10 days. Limited methodological information.	Rat, no data on strain, two females per dose.	dimethyltin dichloride. Test material form: crystalline.	Doses: 40, 80 and 160 mg/kg bw. 40 and 80 mg/kg bw given on 1st and 4th day; 160 mg/kg bw given on 1st day only.	Mortality: Both rats died in the 160 mg/kg bw group. LD_{50} to female rats was found to be between 80 and 160 mg/kg bw.	Barnes and Stoner (1958).
No guideline followed. Acute oral (gavage) LD50 determined as part of an in-vivo UDS study, in order to determine dosage levels for the study. GLP compliant.	Rat, Fischer 344, three males per dose.	Mixture of methyltin chloride compounds. Test material form: crystalline.	First range finding assay: 25, 50, 100, 200 and 400 mg/kg bw. Second range finding assay: 600 and 800 mg/kg bw.	LD_{50}: ca. 280 mg/kg bw (male).	Author not disseminated (1993). Report date: 1993-07-11.
Methodological information not available in English. GLP compliance not reported Route of administration: oral (unspecified).	Rabbit, no data on strain. Sex: male.	dimethyltin dichloride. Test material form: crystalline.	No data available.	Minimum lethal dose: 50 mg/kg bw (male).	Hashizume (1971).
No methodological information. GLP compliance not reported. Route of administration: oral (unspecified).	Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	No data available.	No LD_{50} given.	Author not disseminated (1978b). Reference type: review article or handbook.

No methodological information available. Route of administration: oral (unspecified). GLP compliance not reported.	Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	No data available.	LD_{50}: 88 - 119 mg/kg bw	van Dokkum, and Huwer (2005).
No methodological information available. Route of administration: oral (unspecified). GLP compliance not reported.	Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	No data available.	LD_{50}: 237 mg/kg bw.	Author not disseminated (1978c).
No methodological information. Route of administration: oral (unspecified). GLP compliance not reported.	Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	No data available.	LD50: 90 mg/kg bw.	Author not disseminated (1978d). Reference type: review article or handbook.
No methodological information. Route of administration: oral (unspecified). GLP compliance not reported.	Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	No data available.	LD50: 74 mg/kg bw.	Dean (1976).
No methodological information. Route of administration: oral (unspecified). GLP compliance not reported.	Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	No data available.	LD50: 74 mg/kg bw.	Author not disseminated (1992).

Table 26b: Summary table of human data on acute oral toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 26c: Summary table of other studies relevant for acute oral toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on acute oral toxicity

The oral toxicity of dimethyltin dichloride was evaluated in two OECD TG 401 studies in rats. In both studies, a difference in toxicity between male and female was observed, females being more sensitive than males. In Elf Atochem (1993), gross pathology effects were observed in the lungs, thymus, kidneys and stomach. Under the conditions of this test, the acute oral LD_{50} of [Di/Mono] Methyltin Chlorides Solution in the male rat was determined to be 546 mg/kg. In the female rat, the oral LD_{50} was determined to be 328 mg/kg. In the sexes combined, the oral LD_{50} was determined to be 409 mg/kg. According to the registrant, the [Di/Mono] Methyltin Chlorides Solution was a 50% organotin solution in an unspecified solvent and therefore the LD_{50} value achieved should be halved. The LD_{50} of 84.79 % pure Dimethyltin dichloride was therefore determined to be 273 mg/kg for male rats 164 mg/kg for female rats, with the combined LD_{50} being 204.5 mg/kg bw.

In the second study, effects were observed in the lungs (hemorragies) and in the stomach. The LD_{50} were 190 and 160 mg/kg bw for male and female rats, respectively. The REACH registration dossier contains additional studies with reliability scores of 3 or 4 (non-reliable or not assignable), most of them performed prior to GLP. In these studies, the LD_{50}-values ranged from 73.86 to 280 mg/kg bw; these values can thus be used as supportive evidence of the LD_{50} seen in the two OECD TG 401 studies in rats.

Comparison with the GHS criteria

In the two OECD TG 401 studies, the LD_{50} values were in the range between 160 and 273 mg/kg bw being within the range of $50 \leq ATE < 300$ mg/kg bw and thus supporting classification with Acute toxicity Category 3. In addition, the LD_{50} values ranged from 73.86 to 280 mg/kg bw in the non guideline studies providing further support for classification in Category 3.

Conclusion on classification and labelling for acute oral toxicity

Classification with category 3 is proposed for Acute toxicity via the oral route (Acute Tox. 3; H301).

Acute toxicity - dermal route

Table 27a: Summary table of animal studies on acute dermal toxicity

Method, test guideline, and deviation(s) if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Value LD_{50}**	**Reference**
OECD TG 402, EU Method B.3. GLP compliant. Deviations: The temperature and relative humidity of the animal room (66-72 °F and 30-60 %, respectively) exceeded the range specified in the protocol (61-70°F and 40-60%, respectively). The final body weight and method of euthanasia was not recorded for two males.	Rabbit, New Zealand White, male/female, 5 animals per sex and dose.	84.8 % DMTC in mixture with MMTC (Monomethyltin trichloride). Test material form: solution. Physical state: liquid.	200, 400 and 750 mg/kg bw. Occlusive, ca. 24 hours.	LD_{50}: 404 mg/kg bw (male/female).	Rush, E.R. (1993b).
No guideline followed. Very limited methodological information available. GLP compliance not reported.	Rat; no data on strain, 3 males per dose.	dimethyltin dichloride. Form: crystalline.	80 mg/kg applied on 5 successive days. Percutaneous application.	No LD_{50} determined.	Barnes and Stoner (1958).
OECD TG 402. Deviations: no information. GLP compliance not reported.	Rabbit: New Zealand White, male/female (six animals in total, no data on control animals).	Dimethyltin Dichloride: Methyltin Trichloride (90:10% mixture). Physical state: liquid.	2000 mg/kg bw.	LD_{50} > 2000 mg/kg.	Affiliated Medical Enterprises 1971b

Table 27b: Summary table of human data on acute dermal toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 27c: Summary table of other studies relevant for acute dermal toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on acute dermal toxicity

Three acute dermal toxicity studies are available. In the most reliable study, the GLP-compliant OECD TG 402 study in rabbits using DMTC at 84.8% in a mixture with MMTC (monomethyltin trichloride) (Rush 1993b), an LD_{50} value of 404 mg/kg bw has been determined. The other two studies have been insufficiently documented and are not considered sufficiently reliable for classification.

Comparison with the GHS criteria

The LD_{50} value of 404 mg/kg is within the range of values (200 ≤ ATE < 1000 mg/kg bw) warranting a classification in Category 3 for acute dermal toxicity according to the GHS criteria.

Conclusion on classification and labelling for acute dermal toxicity

Classification with Category 3 is proposed for Acute toxicity via the dermal route (Acute Tox. 3; H311).

Acute toxicity - inhalation route

Table 28a: Summary table of animal studies on acute inhalation toxicity

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance, form and particle size (MMAD)	Dose levels, duration of exposure	Value LC_{50}	Reference
Equivalent or similar to OECD TG 403. Inhalation (aerosol). GLP compliance not reported.	Rat, Tif: RAIf (SPF), 10 animals per sex and per dose.	dimethyltin dichloride. Form: crystalline. Aerosol.	44 ± 6, 90 ± 7, 121 ± 3 and 167 ± 23 mg/m³. Duration of exposure: 4 h.	LC_{50}: 115 mg/m³ air (analytical).	Ciba-Geiby (1977)

Equivalent or similar to OECD TG 403. Inhalation (aerosol). Deviations: only for 1 hour exposure. GLP compliance not reported.	Rat, no data on strain, 10 males per dose.	dimethyltin dichloride. Form: crystalline. Physical state: solid.	57.6 mg/l in air (with water as vehicle), 16.7 mg/l in air (with propylene glycol as vehicle). Duration of exposure: 1 h.	LC_{50} > 56.7 mg/L air (nominal). Calculated LC50 on 4 hour using Haber laws and n=1: **LC50 > 14.2 mg/L** LC_{50} > 16.7 mg/L air (nominal). Calculated LC50 on 4 hour using Haber laws and n=1**: LC50 > 4.2 mg/L**	International Bio-Research (1976).
Equivalent or similar to OECD TG 403. According to Federal Register August 12, 1961 et seq. FHSA. Deviations: no data. Inhalation (aerosol). GLP compliance not reported.	Rat, Wistar, 10 males per dose.	dimethyltin dichloride. Form: crystalline.	Concentrations: 100, 130 and 169 µl/l. Duration of exposure: 4 h.	LC_{50}: 139 µl/L air	Author not disseminated (1976).
Test type: standard acute method. GLP compliance not reported. Inhalation (aerosol). Duration of exposure: 1 h.	Rat, Sprague-Dawley, 10 males per dose.	dimethyltin dichloride. Form: crystalline. Aerodynamic mass median diameter (MMD): less than 5.0 µm in at least 80%.	For the first group the nominal aerosol concentration was 11.53 mg/litre. This aerosol delivery yielded a concentration of 5.77 mg/litre of test material. For the second group the nominal aerosol concentration was 15.02 mg/litre which was equivalent to 5.00 mg/litre of test material.	LC50 > 5.77 mg/L. Calculated LC50 on 4 hour using Haber laws and n=1**: LC50 > 1.44 mg/L**	Hazelton Laboratories 1976.

Equivalent or similar to OECD TG 403. Deviations: only 1 hour exposure duration. Inhalation (aerosol). GLP compliance not reported.	Rat, no data on strain, 10 rats per dose, mixture of sexes.	dimethyltin dichloride. Form: crystalline. Physical state: solid.	50, 100, 200 and 300 mg/l/hour.	LC50: 125 mg/L air (nominal). Calculated LC50 on 4 hour using Haber laws and n=1: **LC50= 31.25 mg/L.**	Wells Laboratories 1975
No methodological information. GLP compliance not reported. Inhalation (aerosol). Duration of exposure: 1 h.	Rat, no data on strain, male/female.	Monomethyltin trichloride + dimethyltin dichloride (21.5 : 78.5). Test material form: crystalline.	No information.	LC_{50}: 84 mg/L/hr.	Summer et al. (2003).
No methodological information available. Inhalation (vapour). GLP compliance not reported.	Species: rat. Strain: no data. Sex: no data.	dimethyltin dichloride. Form: crystalline.	No information.	LC_{50}: 1070 mg/L/hr.	Author not disseminated (1978e). Reference type: review article or handbook.
No methodological information available. Inhalation (aerosol). GLP compliance not reported.	Rat, male/female, no information on strain.	dimethyltin dichloride. Test material form: crystalline.	Concentrations: 1910 mg/m3. Duration of exposure: 1 h.	LC_{50} > 1910 mg/m³ air	Author not disseminated (2006). Report date: 2006-07-23. Reference type: review article or handbook.
No methodological information available. Inhalation (vapour). GLP compliance not reported.	Species: rat. Strain: no data. Sex: no data.	dimethyltin dichloride. Test material form: crystalline.	No information.	LC_{50} > 1.91 mg/L/hour.	Author not disseminated (1978f). Reference type: review article or handbook.

Similar to OECD 403 with shorter duration of exposure (1h).	Rat. No information on sex or strain.	Test substance: dimethyltin dichloride. (purity not known).	Doses: 640, 1679, and 3012 mg/m³. 1 h exposure to aerosol.	LC_{50} 1632 mg/m3, 1.6 mg/L. Calculated LC_{50} on 4 hour using Haber laws and n=1: **LC_{50} = 0.4 mg/L.**	Ciba-Geigy, 1977.

Table 28b: Summary table of human data on acute inhalation toxicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Case study of workers exposure. GLP compliance not reported.	mixture of half dimethyltin and half trimethyltin chloride vapour. Test material form: crystalline.	Route of administration: inhalation. Analytical verification of test atmosphere concentrations: no. Duration of exposure: 1.5 h. Remarks: over a 3 day working period.	1/6 workers died 12 days following the exposure. Symptoms preceding death: excretion of high levels of tin in the urine, respiratory depression, and coma. Autopsy results of the worker who died: massive fatty degeneration of liver cells and necrosis (shock kidneys i.e. proximal tubule degeneration). In two most severely affected surviving workers permanent neurological disabilities and non-persistent respiratory problems. All survuvung workers had high tin concentrations in the urine with the highest levels occurring in the most severely affected.	Harper, C. et al. (2005).

Table 28c: Summary table of other studies relevant for acute inhalation toxicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on acute inhalation toxicity

Acute inhalation studies with exposure to DMTC aerosol of unknown purity for 1 and 4 hours have been performed in rats. The only studies using a 4-hour exposure resulted in LC_{50} values of 0.115 mg/L and 0.139 mg/L. Both of these studies were equivalent or similar to OECD TG 403. The other LC_{50} values are based on 1-hour exposures, which have been extrapolated to 4 hours according to Haber's law. Only the studies with sufficient methodological information are considered as sufficiently reliable and the resulting extrapolated 4-hour LC_{50} values in these studies are 0.4, > 1.44 and 31.25 mg/L. The case study on workers is considered as a supporting study showing lethality in humans after an exposure to an unknown quantity of a mixture of dimethyltin and trimethyltin chloride vapour.

Comparison with the GHS criteria

The LC_{50} values of 0.115, 0.139 and 0.4 mg/L warrant classification in Acute Toxicity Category 2 (the range of values for classification in Category 2 for dust/mist is $0.05 \leq ATE < 0.5$ mg/L), the value of > 1.44 at

most in category 4, and the highest LC_{50} value of 31.25 mg/L warrants no classification. As three studies consistent with an OECD TG 403 warrant classification in Category 2, the Acute Toxicity Category 2 via inhalation route is proposed.

Conclusion on classification and labelling for acute inhalation toxicity

Classification with Category 2 is proposed for Acute Toxicity via inhalation route (Acute Tox. 2; H330).

8.2 Skin corrosion/irritation

Table 29a: Summary table of animal studies on skin corrosion/irritation

Method, test guideline, and deviation(s) if any	**Species, strain, sex, no/group**	**Test substance**	**Dose levels, duration of exposure**	**Results** **-Observations and time point of onset** **-Mean scores/animal** **-Reversibility**	**Reference**
According to OECD TG 404 and Guideline EU Method B.4 (Acute Toxicity: Dermal Irritation / Corrosion). Deviations: The relative humidity of the animal room (26-53%) exceeded the range specified in the protocol (40-60%). GLP compliant.	Rabbit, New Zealand White, 4 males, 2 females.	dimethyltin dichloride. Test material form: no data. Physical state: liquid.	Applied volume or weight with unit: 0.5 mL. Duration of treatment / exposure: 4 hours. Observation period: 72 hours. Area of exposure: 1" x 1". Semi-occlusive binding. Residual test article was removed where practical using gauze moistened with distilled water.	Mean erythema score of 24, 48 and 72 hours: 4, max. score 4. Not reversible. Remarks: Same score for all rabbits at all time points. Mean edema score of 24, 48 and 72 hours: 3.94, max. score 4. Not reversible. Remarks: Same scores (4) for all rabbits at all time points, except of one score of 3 in one rabbit at 48 hours. Necrosis and blanching with severe edema on 6/6 test sites at the 1 hour scoring interval. The dermal irritation progressed to eschar on 3/6 test sites by the 72 hour scoring interval.	Rush (1993b).

Type of method: in vivo. According to method described in 'Hazardous Substances Regulations' under the U.S. Federal hazardous Substances Labelling Act Sect. 191.11 (February 1965). Deviations: no data. GLP compliance not reported.	Rabbit, New Zealand White, no information on sex, 3 animals.	dimethyltin dichloride. Form: crystalline.	applied weight 0.5 g. Concentration: moistened with a 50% solution of ployethylene glycol in water. Duration of exposure: 24 hours. Area of exposure: 2.5 x 2.5 cm. Type of wrap: square gauze pad covered with aluminium foil secured with adhesive tape. No washing.	At 24 hours necrotic skin with deep fissuring into the subcutaneous tissue. No scores available as the test was ended early for humane reasons.	Author not disseminated (1973). Report date 1973-01-26.
Equivalent or similar to OECD TG 404 (Acute GLP compliance not reported.	Rabbit, New Zealand, 6 males.	dimethyltin dichloride. Form: crystalline.	Amount applied: 0.5 g of test substance. Duration of treatment / exposure: 24 hours. Observation period: 24 and 72 hours. Area of exposure: 1" x 1" Standard patch test plasters.	Mean erythema score of 24 and 72 hours: 3, max. score 3. Reversibility: not reversible. Scores were the same for all animals and for intact and abraded skin. Mean edema score at 24 hours: 1, max. score 1. Reversibility: fully reversible within 72 hours. Primary dermal irritation index: 1.75.	Affiliated Medical Enterprises Inc. 1971c.

Type of method: in vivo. According to Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics (1959) of the US Association of Food and Drug Officials. GLP compliance not reported.	Rabbit, Russian, 3 males, 3 females.	dimethyltin dichloride. Form: crystalline.	Concentration: 50% in PEG. Duration of treatment / exposure: 24 hours. Observation period: 72 hours. Area of exposure: 2.5 x 2.5 cm. Type of coverage: occlusive.	Mean primary dermal irritation index (PDII) of 24 and 72 hours: 0.8. Reversibility: no data.	Author not disseminated (1973). Report date 1973-04-10.

Table 29b: Summary table of human data on skin corrosion/irritation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 29c: Summary table of other studies relevant for skin corrosion/irritation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on skin corrosion/irritation

In Rush (1993b), blanching and necrosis with severe oedema were observed on all dermal sites within 1 hour after a four-hour exposure time, with irritation progressing to eschar in 3 sites by termination of the observation period (at 72 hours). Under the conditions of the test, the substance would be considered to be corrosive to rabbit dermal tissue.

In the report dated 1973-01-26 (Author not disseminated (1973)), the skin over the test sites was necrotic after 24 hours, with deep fissuring into the subcutaneous tissue, and all animals were killed early for humane reasons. The exposure period of 24 hours in this study is too long for the data to be used for classification of DMTC for skin corrosion.

In Affiliated Medical Enterprises Inc. (1971c), very slight oedema was observed on all animals at both intact and abraded skin sites at 24 hours. No oedema was observed at 72 hours. The Primary Dermal Irritation Index is evaluated at 1.75. Moderate to severe erythema and eschar formation were observed on all animals, at both skin sites, at 24 and 72 hours. According to the evaluation of Draize, the substance would be considered a moderate irritant to the skin. The exposure period of 24 hours in this study is too long for the data to be used for classification of DMTC for skin corrosion.

In the report dated 1973-04-10 (Author not disseminated (1973)), the mean primary dermal irritation index (PDII) of 24 and 72 hours was 0.8 after a 24 h exposure. There was no information on the reversibility of the effect. The available information on this study does not meet the classification criteria for skin corrosion/irritation.

Comparison with the GHS criteria

Although corrosive responses were noted during the observation period of 1 hour after the four-hour exposure in Rush (1993b), classification in category 1C for skin corrosion is not justified because none of the studies provide sufficient information on whether corrosive effects occur after a shorter exposure (i.e., ≤ 3 min for subcategory 1A, or between 3 min and 1 hr for subcategory 1B). Thus, no differentiation between the subcategories can be made and classification in category 1 without a subcategory is warranted.

Conclusion on classification and labelling for skin corrosion/irritation

Classification Skin Corr. 1; H314 according to the GHS criteria is warranted.

Supplemental labelling information

In addition, based on the classification as skin corrosive and acutely toxic via inhalation it is appropriate to add the hazard statement "Corrosive to the respiratory tract" (in the EU: EUH071) in the labelling.

8.3 Serious eye damage/eye irritation

Table 30a: Summary table of animal studies on serious eye damage/eye irritation

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results -Observations and time point of onset -Mean scores/animal -Reversibility	Reference
Equivalent or similar to OECD TG 405. GLP compliance not reported.	Rabbit, Russian, 3 males, 3 females.	dimethyltin dichloride. Form: crystalline.	0.1 g of test substance placed into left eye of rabbit with spatula. After application, the rabbits' eyelids were held open for a few seconds. Duration of treatment / exposure: 30 seconds. Observation period: 7 days.	(Results per animal in Annex I). Cornea score (mean of all time points): Score 80. Max. score 80. Reversibility: not reversible. Iris score (mean of all time points): Score 10. Max. score 10. Reversibility: not reversible. Conjunctivae score (mean of all time points): Score 12.5. Max. score 20. Reversibility: not reversible. 4/6 animals died during the 7-day observation period.	Author not disseminated (1973). Report date 1973-04-11.
Equivalent or similar to OECD TG 405. GLP compliance not reported.	Rabbit, New Zealand, 9 males.	dimethyltin dichloride. Form: crystalline.	Amount applied: 100 mg. Duration of treatment / exposure: 2 seconds. Removal of test substance: Washing. Time after start of exposure: three animals after two seconds; three animals after four seconds and three animals unwashed. Observation period: 72 hours. Scoring system: Draize (1956)	Cornea score (mean of 24, 48 and 72 hours): Score 4. Max. score 4. Reversibility: not reversible. Remarks: Score was the same for all rabbits at all time points. Iris score (mean of 24, 48 and 72 hours): Score 2. Max. score 2. Reversibility: not reversible. Remarks: scores were the same for all rabbits at all time points. Conjunctivae score (mean of 24, 48 and 72 hours): Score 3. Max. score 3. Reversibility: not reversible. Remarks: scores were the same for all rabbits at all time points. Chemosis score (mean of 24, 48 and 72 hours): Score 4. Max. score 4. Reversibility: not reversible. Remarks: scores were the same for all rabbits at all time points.	Author not disseminated (1971). Report date 1971-03-14.

Equivalent or similar to OECD TG 405. Deviations: no data. GLP compliance not reported.	Rabbit, New Zealand White, 3 males, 3 females.	dimethyltin dichloride. Form: crystalline powder. Physical state: solid.	Amount(s) applied: 100 mg. Duration of treatment / exposure: Eye held shut for 1 seconds, and then washed out after 30 seconds. Observation period: 1, 6 and 24 hours after application. The right eye served as a control. Removal of test substance: Washing with warm water.	At 1 h partial corneal destruction. Iris not visible in three animals and partly obscured in one. Marked chemosis and injection of the conjunctivae in all animals. Loss of sensation to touch over the cornea in five animals. Conjunctival mucosae of all rabbits was necrotic. At 24 hours moderate to severe necrosis of conjunctivae in all animals with severe periorbital oedema. Other effects: Instillation of the test compound caused pain. After 6 hours all animals appeared lethargic and had severe chemosis with blood stained discharge from the eyes. The cornea was completely opaque in five animals. Phlyctenar occurred on the cornea of one animal. An unpleasant odour was noted from all animals when examined at both 1 and 6 hours. Scores were not obtained as the animals were killed early for humane reasons.	Author not disseminated (1973). Report date 1973-01-26.

Table 30b: Summary table of human data on serious eye damage/eye irritation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 30c: Summary table of other studies relevant for serious eye damage/eye irritation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on serious eye damage/eye irritation

Dimethyltin dichloride is corrosive to skin and therefor deemed to cause serious eye damage. However, there are also three acute eye irritation / corrosion studies equivalent or similar to OECD TG 405. In all these studies dimethyltin dichloride caused irreversible effects on the eye within the observation period.

Comparison with the GHS criteria

A substance is classified for serious eye damage (Category 1) if the substance is corrosive to skin or if in at least one animal effects on the cornea, iris or conjunctiva are not expected to reverse or have not fully reversed within an observation period of normally 21 days or if corneal opacity ≥ 3, and/or iritis > 1.5 calculated as the mean scores following grading at 24, 48 and 72 hours after instillation of the test material occur in at least 2 of 3 tested animals. The observation period in the available studies did not reach 21 days, but in the report dated 1973-01-26 (Author not disseminated (1973)), the severity of the effects suggest that the effects were irreversible. Also the cornea score 4 and iris score 2 in all tested animals meet the criteria for

serious eye damage. Dimethyltin dichloride is also corrosive to skin and therefor deemed to cause serious eye damage.

Conclusion on classification and labelling for serious eye damage/eye irritation

Classification Eye Dam. 1; H318 according to the GHS criteria is warranted.

8.4 Respiratory or skin sensitisation

Respiratory sensitisation

Table 31a: Summary table of animal studies on respiratory sensitisation

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
No data available.					

Table 31b: Summary table of human data on respiratory sensitisation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 31c: Summary table of other studies relevant for respiratory sensitisation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on respiratory sensitisation

No data available.

Comparison with the GHS criteria

Not applicable because there is no data available.[

Conclusion on classification and labelling for respiratory sensitisation

Not applicable because there is no data available.

Skin sensitisation

Table 32a: Summary table of animal studies on skin sensitisation

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
Type of method: in vivo. Test system: Traditional sensitisation test. Type of study: Maurer optimisation test. Deviations: no information	Guinea pig, Albino (type not specified), no data on sex, 10 animals per dose.	dimethyltin dichloride.	Route of induction exposure: intradermal. Route of challenge exposure: intradermal. Vehicle: 1 part PEG to 7.3 parts water. Concentration: 0.1% solution. The first injection consisted of 0.05 mL, while the remaining nine were of 0.1 mL each. Ten sensitizing injections were given on alternative days during a three week period. Challenge controls: After an incubation period of two weeks, a final challenge dose of 0.05mL was injected.	From the first 10 induction exposures, the scores were as follows: Diameter: Average = 0.6, Maximum = 1. Colour: Average = 0.75, Maximum = 2 (in one animal only at one time point; all other scores were 1or less). Height: Average = 0.72, Maximum = 1. From the challenge exposure after 2 weeks incubation, no score greater than 1 was seen in any animal for either diameter, colour or height.	Author not disseminated (1973). Report date 1973-04-11.

Table 32b: Summary table of human data on skin sensitisation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 32c: Summary table of other studies relevant for skin sensitisation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on skin sensitisation

A Maurer optimisation test is available. The reactions elicited by the challenge dose were not substantially higher than the average of readings observed during the sensitizing period, and therefore the substance is not considered to have produced sensitization in the available test.

Comparison with the GHS criteria

Test methods for skin sensitisation are described in OECD TG 406, but other methods may be used provided that they are well-validated and scientific justification is given. The available Maurer optimisation test was negative.

Conclusion on classification and labelling for skin sensitisation

No classification is proposed for skin sensitisation as there are no positive studies available.

8.5 Germ cell mutagenicity

Table 33a: Summary table of mutagenicity/genotoxicity tests in vitro

Method, test guideline, and deviation(s) if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations	Reference
Bacterial reverse mutation assay OECD TG 472 No deviations. GLP-compliant.	Dimethyltin dichloride: Methyltin trichloride (72:28% mixture)	E. Coli WP2 uvr A; with and without metabolic activation Test concentrations: 10, 50, 100, 500, 1000, 5000 µg/plate	Genotoxicity: negative. Cytotoxicity: yes at 5000 µg/plate	Author not disseminated (1990). Report date 1990-07-24.
Chromosome aberration OECD TG 473 No deviations. GLP-compliant.	Mixes of methyltin compounds	Human peripheral lymphocytes. Test concentrations: Preliminary: 8, 40, 200, 1000, and 5000 µg/mL. Definitive experiment with metabolic activation: 10, 20, 40, 80, 160 µg/mL. Definitive experiment without metabolic activation: 2, 4, 8, 16, 32 µg/mL. Positive control, definitive experiment with metabolic activation: 11, 13, 15 µg/mL. Positive control, definitive experiment without metabolic activation: 150, 175, 200 µg/mL.	Genotoxicity: negative Cytotoxicity: yes, at ≥ 16 µg/mL	Author not disseminated (1990). Report date 1990-10-25.
Mammalian gene mutation assay OECD TG 476 No deviations. GLP-compliant.	Mixes of methyltin compounds	Chinese hamster ovary (CHO); with and without metabolic activation. Test concentrations: 0, 49, 61, 77, 96, 120 and 200 µg/mL (without metabolic activation); 0, 61.4, 76.8, 96, 120 and 150 µg/mL (with metabolic activation, replicate 1); 0, 31.4, 39.3, 49.2, 61.4, 76.8 and 96 µg/mL (with metabolic activation, replicate 2).	Genotoxicity: negative Cytotoxicity: yes	Author not disseminated (1990). Report date 1990-08-20.

Bacterial reverse mutation assay OECD TG 471 No deviations. GLP-compliant.	Dimethyltin dichloride:Methyltin trichloride (72:28% mixture)	Species/strain: S. typhimurium TA 1538; with and without metabolic activation Test concentrations: Range finding assay: 10, 50, 100, 500, 1000, and 5000 µg/plate. First mutagenicity assay: 10, 50, 100, 500, 1000, and 5000 µg/plate. Second mutagenicity assay: 5, 10, 50, 100, 500, and 1000 µg/plate.	Genotoxicity: negative Cytotoxicity: yes	Author not disseminated (1990). Report date 1990-07-18.
Spindle inhibition. No data on guideline or GLP-compliance.	Dimethyltin dichoride	Chinese hamster cells, without metabolic activation	Genotoxicity: no data Cytotoxicity: yes	Harper et al., 2005 (secondary source)
Three different genotoxicity tests. No data on guideline or GLP-compliance.	Dimethyltin dichloride	Three types of genotoxicty tests reported: 1) Induced mutation frequency (IMF) with Salmonella typhimurium TA100. 2) Rec assay with Bacillus subtiles H17 and M45 3) SOS chromotest with Echerichia coli PQ37	Genotoxicity: negative Cytotoxicity: no data	Author not disseminated (1992).
Genotoxicity of organotin compounds in SOS chromotest and rec-assay / DNA damage and repair. No guideline followed. GLP compliance not reported.	Dimethyltin dichloride	E. Coli, other: PQ37; without metabolic activation Bacillus subtilis (H17 Rec + and M45 Rec- strains); without metabolic activation	E. Coli: Genotoxicity: negative Cytotoxicity: no data Bacillus subtilis: Genotoxicity: positive Cytotoxicity: no data	Hamasaki et al., 1992

Study on induction of micronueli, chromosome aberrations and sister chromatid exchanges. GLP compliance not reported.	Dimethyltin dichloride	Chinese hamster Ovary (CHO) cells without metabolic activation. Test concentrations: 0.5 µM - 1.0mM.	Positive at a cytotoxic concentration of 1mM (chromosomal aberrations and sister chromatid exchanges).	Dopp et al., 2007.
Cytogenicity No guideline followed. GLP compliance not reported.	Dimethyltin dichloride	Human peripheral lymphocytes	Genotoxicity: negative Cytotoxicity: no data	Jensen et al., 1991
Bacterial reverse mutation assay. Equivalent or similar to OECD 471. With deviations. GLP compliance not reported.	Dimethyltin dichloride	S. typhimurium TA 98 S. typhimurium TA 100	S. Typhimurium TA 98: Genotoxicity: negative Cytotoxicity: no data S. typhimurium TA 100: Genotoxicity: positive in the presence of cytotoxicity Cytotoxicity: no data	Hamasaki et al., 1993

Table 33b: Summary table of mutagenicity/genotoxicity tests in mammalian somatic or germ cells in vivo

Method, test guideline, and deviation(s) if any	Test substance	Relevant information about the study including rationale for dose selection (as applicable)	Observations	Reference
Unscheduled DNA synthesis (UDS). Equivalent of similar to OECD TG 486. With deviations. GLP-compliant.	Mixture of methyltin chloride compounds	Fischer 344 rats, males. Oral gavage. Doses: Actual ingested: First range finding study: 25, 50, 100, 200 and 400 mg/kg. Second range finding study: 600 and 800 mg/kg. First definitive UDS assay: 90, 175 and 350 mg/kg. Second definitive UDS assay: 50, 110 and 225 mg/kg. First range finding assay: 3 males at each dose. Second range finding assay: 3 males at each dose. First definitive UDS assay: 3 males at each dose, except negative control with 0. First definitive UDS assay: 3 males at each dose, except highest dosage group with 4 and positive control with 0. Second definitive UDS assay: 3 males at each dose, except negative control with 0. Second definitive UDS assay: 3 males at each dose, except highest dosage group with 4 and positive control with 0.	Genotoxicity: negative Toxicity: yes	Author not disseminated (1993). Report date 1993-07-11.
Chromosome aberration / micronucleus assay. No data on method or GLP-compliance.	Monomethyltin trichloride and dimethyltin dichloride	SwissWebster, male/female, oral gavage. Doses: Actual ingested: 100, 200, 400 mg/kg bw in water, i.g. 15 animals per sex and dose.	Genotoxicity: negative Toxicity: no data	Summer et al., 2003

Table 33c: Summary table of human data relevant for germ cell mutagenicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data.				

Short summary and overall relevance of the provided information on germ cell mutagenicity

There are ten recorded mutagenicity or genotoxicity studies in vitro. All the Ames tests were negative. There was one positive chromosomal aberration test in human lymphocytes that shows positive results in the presence of metabolic activation. There is also one REC bacterial assay showing positive results. In vivo there is one UDS study (rat) and one poorly described MN study (mice) - both of which are negative.

Comparison with the GHS criteria

The GHS criteria requires positive results in vivo. No such evidence are seen although the data base is limited. The positive results seen in vitro is not of high concern, but it cannot be completely excluded that the substance may induce clastogenicity. However, in the in vivo clastogenicity study no evidence of effects were seen, although it should be noted that the study was not regarded as reliable.

Conclusion on classification and labelling for germ cell mutagenicity

No classification for germ cell mutagenicity is warranted as no positive animal or human data are available.

8.6 Carcinogenicity

Table 34a: Summary table of animal studies on carcinogenicity

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
No data on method or GLP-compliance.	Rat, male/female, 20 animals	dimethyltin bis(2-ethylhexylthioglycolate) + monomethyltin tris(2-ethylhexylthioglycolate)	Oral (feed), two years, 100 ppm	No malignant tumours.	Summer et al., 2003

Table 34b: Summary table of human data on carcinogenicity

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data.				

Table 34c: Summary table of other studies relevant for carcinogenicity

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data.				

Table 34d: Are the following factors taken into consideration in the hazard assessment (yes/no)?

Reference	Species and strain	Tumour type and background incidence	Multi-site responses	Progression of lesions to malignancy	Reduced tumour latency	Responses in single or both sexes	Confounding effect by excessive toxicity?	Route of exposure	MoA and relevance to humans
No applicable.									

Short summary and overall relevance of the provided information on carcinogenicity

One negative study with low reliability is available for the substance. The data is scarce and no proper evaluation can be done.

Comparison with the GHS criteria

There is no data supporting classification for this hazard class.

Conclusion on classification and labelling for carcinogenicity

No classification for carcinogenicity is warranted as no positive animal or human data are available.

8.7 Reproductive toxicity

Adverse effects on sexual function and fertility

No data on effects on fertility are available.

Short summary and overall relevance of the provided information on adverse effects on sexual function and fertility

No data on effects on fertility are available.

Comparison with the GHS criteria

No classification is proposed for fertility as no data on effects on fertility are available.

Adverse effects on development of the offspring

Table 35a: Summary table of animal studies on adverse effects on development of the offspring

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
US EPA, Developmental neurotoxicity study, Health effects TG, OPPTS 870.6300, EPA 712-C-98-239. No data on deviations or GLP compliance. Method: behavioural essays from PND 11 into adulthood and analysis of specific brain regions for apoptotic cell death and neuropathy.	SD rats. Experiment 1: 120 female rats (30 per dose) Experiment 2: 87 females (21 controls, 22 per dose)	Dimethyl tin (DMT)	Doses: 0, 3, 15 and 74 mg/L via drinking water. Exposure period: Experiment 1: 14 days premating – PND 21 Experiment 2: GD 6 – PND 21	<u>Experiment 1:</u> Maternal toxicity: ↓weight gain at highest dose. Fertility: low overall pregnancy rate (39%) in study but not treatment-related. Developmental toxicity: ↓brain weight (74 mg/L), mild vacuolation in the brain (all doses), slower learning in adult offspring in water maze (7 weeks old) maze (15 mg/L), no treatment-related difference in the incidence of non-learners in runway (PND 11). <u>Experiment 2:</u> Maternal toxicity: ↓body weight (lactation) as compared to controls (74 mg/L). Fertility: no effects seen. Developmental toxicity: ↓birth weight, ↓preweaning growth, ↓brain weight (only males, 74 mg/L), dose-dependent increase in no of animals that failed to learn to negotiate the runway (PND 11, n.s.) and in adult offspring (12 weeks old) water maze (15 mg/L)	Ehman *et al*., 2007

Similar to OECD TG 414; with deviations (exposure during GD 7-17, groups size below recommended in the TG); no data on GLP compliance	Wistar rats; **Study I**: 5 groups of 10 rats in each **Study II**: 8 groups of 8-11 rats in each.	Dimethyltin dichloride; purity ≥ 99%	**Study I**: 0, 5, 10, 15 and 20 mg/kg on GD 7-17; **Study II:** 0, 20 and 40 mg/kg On GD 7-9, 10-12, 13-15 or 16-17; controls were given vehicle on GD 10-12	**<u>Study I:</u>** *20 mg/kg bw/d:* - maternal toxicity (vaginal bleeding, tremors, convulsions, ataxia, other clinical signs of toxicity, severe thymus atrophy) generally appearing after GD15. - death of 2/10 pregnant rats, treatment-related - total resorption in 1/8 living pregnant rats (the dam had all clinical signs of toxicity, see above). - cleft palate in 21 foetuses (22%) in 5/7 pregnant rats with living foetuses. *15 and 20 mg/kg/day:* - significant ↓ mean body weight in living foetuses of both sexes, dose-dependent manner at. *15 mg/kg bw/day:* - two foetuses with omphalocele from one dam **<u>Study II:</u>** *40 mg/kg/day:* - slight maternal toxicity (reductions of the adjusted body weight gain and thymus weight) *All dose levels:* - no significant increase in the incidence of external, skeletal and visceral malformations at either dose in any group - no cleft palates - fetal body weight unaffected	Noda, 2001

Teratogenicity study. Limited data on methodology and results. GLP compliance not reported.	Wistar rats, 10 pregnant females per sex and dose	Dimethyltin dichloride	0, 5, 10, 15 and 20 mg/kg bw; GD 7-17 To clarify the teratogenic potential of DMTC, the compound was given at 20 ot 40 mg/kg for 2 or 3 consecutive days at 4 different periods of gestation (GD 7-9, 10-12, 13-15 or 16-17).	Dosing on GD 7-17: Vaginal bleeding, convulsion, ↓ body weight gain and dead dams (2/10) at 20 mg/kg in the late stage of gestation. On GD 20 the incidence of foetuses with cleft plate was sign. ↑ at 20 mg/kg bw. Dosing on GD 7-9, 10-12, 13-15 or 16-17 *(20, 40 mg/kg):* No maternal toxicity and no foetus with cleft plate was observed in any DMTC-treated group.	Noda & Morita, 1994 (study source was brief summary).
Sub-acute and developmental toxicity study. Non-guideline. GLP compliance not reported.	SD rats, male/female, adult: 24 rats per sex and dose, developmental: 8-9 dams per dose	Dimethyltin dichloride	20 and 40 mg/L (in water) Actual ingested: Male: 0, 1.7 and 3.4 mg/kg bw; Female: 2.4 and 4.6 mg/kg bw; Females from parturition until weaning: 3.6 and 6.9 mg/kg bw	No effects on body weight or body weight gain, humoral immunity examinations, specific cell-mediated immunity or non-specific cell-mediated immunity. Developmental effects: - at 40 mg/L, body weights of both male and female offspring was about 10% greater relative to controls on PND7-PND37 - body weights did not vary by dose for either sex when terminal weights were collected at PND44, 58, or 77 - pup mortality was limited to the 40 mg DMTC/L group; 2 pups from 1 litter died between PND14 and 17 and one pup from a second litter died on PND14.	DeWitt *et al*., 2007

Step 1: Study to determine whether DMTC was absorbed by the dam and transferred across the placenta to foetal blood and brain tissue. Step 2: Cross-fostering study Step 3: 14C-DMTC tracer study	SD rats, female	Dimethyltin dichloride (DMTC)	Step 1: 3 groups. Group 1: 40 mg/L DMTC in drinking water (n = 13). Group 2: 40 mg/L tin as stannous chloride (n = 13) Group 3: distilled water/control group (n = 12) Step 2: Group 1: 40 mg/L DMTC in drinking water Group 2: un-treated control Step 3: 14C-DMTC tracer administered by intubation to pregnant dams (GD 19)	Step 1: - DMTC was absorbed by the rat dam, transferred across the placenta to the foetus and into the brain of the prenatal animal Step 2: - significantly higher tin levels in pups from DMTC-exposed dams - highest levels of tin in blood at birth in gestationally exposed pups - DMTC mainly transferred to the pups during the gestation. - tin levels in brains of gestationally exposed pups highest at birth and different from controls - rapid clearance of the tin from the blood and brain in pups - ↓ DMTC concentration in pup brain and pup blood during post-natal period, indicating relatively unimpeded brain-to-blood transfer Step 3: - DMTC was absorbed in the gastrointestinal tract of the dam and transferred across the placenta to fetal blood and brain tissue - majority of the tin was transferred from the pups prenatally, rather than during lactation	Noland *et al.*, 1983

Table 35b: Summary table of human data on adverse effects on development of the offspring

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 35c: Summary table of other studies relevant for adverse effects on development of the offspring

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
In vitro examination of neurotoxic potential. Non-guideline. GLP compliance not reported.	Dimethyltin dichloride	7, 10, 15, 20 and 50 µM DMT to primed PC12 cells, observation of neurite outgrowth and cell viability/cytotoxicity	- addition of DMT to primed PC12 cells inhibited neurite outgrowth and ↓ cell viability in a concentration dependent manner - total neurite outgrowth sign. inhibited by 7.0 µM (43%↓), 10 µM (52%↓), 20 µM (64%↓), and 50 µM (93%↓) - no sign. effect at < 7.0 µM - the absence of NGF decreased neurite outgrowth - neurite branching prevented in a concentration-dependent manner; sign. inhibition at 7.0 µM (46%↓), 10 µM (50%↓), 15 µM (58%↓), 20 µM (62%↓), and 50 µM (93%↓) - removal of NGF ↓ the number of branch points - segment length sign. ↓ by 20 µM (28%↓) and 50 µM (32%↓) DMT - no sign. effects detected on segment length at concentrations of ≤ 15 µM - % of cells staining positively for trypan blue ↑ from 7.0% in control cells to 20%, 19%, 24%, and 47% in the presence of 10, 15, 20, and 50 µM DMT, respectively	Jenkins *et al*., 2004

Short summary and overall relevance of the provided information on adverse effects on development of the offspring

Summary and discussion of reproductive toxicity

In the **Ehman (2007)** study, developmental neurotoxicity of DMTC in drinking water was evaluated in two experiments. The two experiments utilized the same doses and the same route of exposure and vehicle, but they utilized different dosing regimens and therefore experiments 1 and 2 are not replicates. In the first experiment, DMTC toxicity was expressed as depressed maternal weight gain (74 mg/l), and in the offspring as decreased brain weight (74 mg/l), mild vacuolation in the brain of adult offspring (all doses), and slower learning in the water maze (15 mg/L).

In the second experiment, the high concentration lead to depressed maternal weight as compared to controls at the high dose, decreased offspring birth weight and preweaning growth as compared to controls, and as decreased brain weight (males only high dose). Learning deficits were observed in the runway at postnatal day 11 (15, 74 mg/L, no statistical significance) and again in the adult offspring in the water maze (15 mg/L).

The effect observed in the runway testing was identified only in experiment 2 but it may be due to the lower number of tested pups in the first experiment. In the second experiment, learning was not observed during

any reinforced-trial blocks in the 15 mg/L group, but learning was achieved at the last set of trials in the 74 mg/L group. In addition, only the 15 mg/L dose-group showed a decreased latency during the non-reinforced (extinction phase), which seems to be an aberration. The absence of dose-response therefore questions the significance of this finding. It is however noted that the trial did not follow the OECD TG 426 on the neurotoxicity for the development, the test was performed only at PND 11 although it also has to be done at PND 25 and at adult age. Moreover, it is not known whether each tested pup comes from different litters as it is recommended in the OECD TG 426. It is therefore difficult to conclude on the presence or the absence of a neurotoxic effect based on this result.

In the Morris water maze, the 15 mg/L group shows longer latencies to reach the platform than the 74 mg/L group in the first week for the experiment 1 and in the second week for the experiment 2. Thus, the effect in the 15 mg/L group seems to be reproducible but it is not observed at the higher dose. In the both experiments, the 15 mg/L group spent more time in the outer zone than in the middle one. According to the OECD TG 426, the trials have to be performed on 10 animals by sex and by litter, at PND 25 and adult age. However, in the experiment 1, there were only males rats, and a too small number of pups was tested (n= 11 control, 7 at 3 mg/L, 9 at 15 mg/L, and 11 at 74 mg/L). It may explain why the effect was not detected in experiment 1 at high dose. In experiment 2, the adequate number of pups was tested but it is not known whether they come from different litters.

Decreased brain weight was observed at 74 mg/L in the both experiment although only males were affected in the second experiment. Histopathological alterations in the brain of offspring of dams exposed to DMTC were noted in the cerebral cortex of rats sacrificed at PND 22 and as adults in experiment 1. Slight/mild vacuolation of the neuropil of the gray matter of the cerebral cortex were observed in 60% of adult offspring at 74 mg/L and 20% of PND 22 rats at 74 mg/L. Evaluations of the lower dose groups (at 3 and 15 mg/L) showed similar vacuolation.

In the first study of **Noda, 2001**, severe maternal toxicity occurred at the high dose of 20 mg/kg bw/d. These clinical signs of toxicity are vaginal bleeding, tremors and convulsions [30%], ataxia and other clinical signs of toxicity (severe thymus atrophy) [100%] and they generally appear after the 15th day of gestation. Oral administration of DMTC at 20 mg/kg bw/d resulted in the death of two pregnant rats [20%], caused by the DMTC treatment. Total resorption was observed in one of eight living pregnant rats, which exhibited all these clinical signs of toxicology at this level dose in the late stage of gestation.

Administration of DMTC at 20 mg/kg bw/d caused cleft palate in a high incidence i.e. in 21 foetuses (22%) in 5 out of 7 pregnant dams with living foetuses. Furthermore, cleft palate is a rare and serious malformation in the rat, which generally cannot be considered to be a secondary non-specific consequence to maternal toxicity However, according to the GHS criteria (GHS 3.7.2.4.4), maternal mortality greater than 10% is considered excessive and the data for that dose level should not normally be considered for further evaluation. In this case, the evidence on these serious malformations was not fully dismissed despite of ≥10% maternal mortality, i.e. excessive maternal toxicity. There were also two foetuses with omphalocele from one dam exposed to DMTC at 15 mg/kg bw/day in study 1 and this effect was not associated with maternal death or severe maternal toxicity. However, no omphaloceles were detected at the high dose and the biological relevance of such low incidence and in one litter only is questionable. Moreover, mean body weight in living foetuses of both sexes decreased in a dose-dependent manner with significance at 15 and 20 mg/kg/day.

In order to reduce maternal toxicity, shorter periods of DMTC treatment (two or three consecutive days at one of four different periods of gestation) and relative high doses of DMTC were chosen in a second study. The highest dose (40 mg/kg/day) of DMTC caused slight maternal toxicity as indicated by the reductions of the adjusted body weight gain and the thymus weight. No significant increase in the incidence of external, skeletal and visceral malformations were observed at either dose in any treatment period group, and no cleft palate was found. Fetal body weight was also unaffected.

The reliability of **Noda and Morita (1994)** cannot be assessed due to limited details on methodology and results. It cannot be excluded that Noda and Morita (1994) and Noda (2001) refer to the same study.

The study by **Dewitt et al. (2007)** did not provide evidence of an impaired immune function in Sprague–Dawley rats exposed to dimethyltin dichloride (DMTC) during development.

The study of **Noland et al. (1983)** is included in the section on toxicokinetics in Annex I (study 2). This study is relevant for the developmental neurotoxicity analysis of dimethyltin dichloride (DMTC). The results of this study have demonstrated that DMTC is absorbed in the gastrointestinal tract of the dam and DMTC is transferred across the placenta to fetal blood and brain tissue. The majority of the tin is transferred from the pups prenatally, during gestation rather than lactation.

In **Jenkins et al. (2004)** neurite outgrowth and cytotoxicity were examined in vitro using a split-plot design with subsampling. DMT inhibited neurite outgrowth and decreased cell viability in a concentration dependent manner, prevented neurite branching in a concentration-dependent manner, and decreased. segment length.

Overall, DMTC induced a high incidence of cleft palates in rat foetuses at 20 mg/kg/day, a dose level which also caused severe maternal toxicity (20% mortality) (Noda, 2001, first study). There were also two foetuses with omphalocele from one dam exposed to DMTC at 15 mg/kg bw/day in study 1 and this effect was not associated with maternal death or severe maternal toxicity. No significant increase in the incidence of cleft palates or other external, skeletal or visceral malformations were observed in a second study (Noda, 2001, second study) at similar or higher dose levels although the substance was administered for shorter durations but covering the whole embryogenesis period. Maternal toxicity and malformations were not observed in the Ehman (2007) study, which may be due to lower dosage (high dose between 4 and 12 mg/kg). In the study by Noda and Morita (1994) cleft palates were observed together with severe maternal toxicity. The reliability of the study cannot be assessed due to limited details on methodology and results, and it cannot be excluded that Noda and Morita (1994) and Noda (2001) refer to the same study. Altogether, the evidence on the serious malformations, i.e. cleft palates, was not fully dismissed despite of ≥10% maternal mortality, i.e. excessive maternal toxicity. The biological relevance of two incidences of omphalocele from one dam at 15 mg/kg bw/day only in study 1 is questionable.

DMTC induced a decrease in the body weight of living foetuses at 15 and 20 mg/kg as compared to controls (Noda, 2001, first study). Also maternal body weight gain was significantly reduced in pregnant rats treated with 15 or 20 mg/kg/day of DMTC and the maternal body weight on GD 20 was also significantly lower in the high dose group as compared to the control. These foetal effects did not occur in the second study at similar or higher dose levels although the substance induced significant decrease in maternal adjusted body weight gain. In Ehman (2007), a decrease in pup body weight was observed only at high dose (7-12 mg/kg) in the second experiment during lactation when maternal weight was also significantly decreased. The link between foetotoxicity and maternal toxicity is therefore likely.

DMTC showed developmental neurotoxic potential in the form of learning deficits consistently at the mid dose in water maze test in Ehman (2007). The maternal toxicity consisted on decreased maternal body weight gain only at the top dose (throughout the exposure in the first experiment and from lactation in the second experiment). There was also a dose-dependent but not statistically significant increase in the number of pups that failed to learn to negotiate the runway in one of two experiments in Ehman (2007). Developmental toxicity was also expressed in the offspring as a decreased brain weight (top dose only) and mild vacuolation in the brain (all doses, first experiment only) of adult offspring. DMTC inhibited neurite outgrowth and decreased cell viability in a concentration dependent manner, prevented neurite branching in a concentration-dependent manner, and decreasedsegment length in Jenkins et al. (2004) supporting the developmental neurotoxic potential. However, the absence of reproducibility and statistical significance of the effects observed in the runaway and the absence of effect at the top dose in water maze tests and the fact that the studies were not consistent with guideline requirements does not provide clear evidence of an adverse effect on development.

Comparison with GHS criteria

The GHS criteria for classification in Repr. 2 are as follows. Substances shall be classified in Category 2 for reproductive toxicity when there is some evidence from humans or experimental animals, possibly supplemented with other information, of an adverse effect on sexual function and fertility, or on development, in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of the other toxic effects, and where the evidence is not sufficiently convincing to place the substance in Category 1. For instance, deficiencies in the study may make the quality of evidence less convincing, and in view of this, Category 2 would be the more appropriate classification.

DMTC induced cleft palates on the foetuses at 20 mg/kg/day, in the presence of severe maternal toxicity (20% mortality) at this high dose level (Noda 2001, Experiment 1). Also in the study by Noda and Morita (1994), cleft palates were observed together with severe maternal toxicity, but the reliability of the study cannot be assessed due to limited details on methodology and results, and it cannot be excluded that Noda and Morita (1994) and Noda (2001) refer to the same study. Cleft palates are rare and serious malformations in the rat and are not considered as secondary to maternal toxicity. Additionally, the evidence on the serious malformations, i.e. cleft palates, was not fully dismissed despite of ≥10% maternal mortality, i.e. excessive maternal toxicity. The biological relevance of two incidences of omphalocele from one dam at 15 mg/kg bw/day only in study 1 is questionable. No significant increase in the incidence of cleft palates or other external, skeletal and visceral malformations were observed in a second study at similar or higher dose levels although the substance was administered for shorter durations but covering the whole embryogenesis period. Malformations were also not observed in Ehman 2007 but it may be due to lower dosage (high dose between 4 and 12 mg/kg). Therefore, considering the absence of reproducibility in both experiments of Noda 2001, the cleft palates occurring at a high dose which caused excessive maternal toxicity (20% mortality) (and the low incidence of omphaloceles at the second highest dose only), the evidence is not considered sufficient to place the substance in category 1B.

DMTC induced a dose-dependent reduction in mean body weight of living foetuses (both sexes), that was significant at 15 and 20 mg/kg/day (respectively 3.5g ±0.20, 3.4g ±0.22, 3.2g ±0.25, 2.9g ±0.16, and 2.2g ±0.46 in males and 3.3g ±0.16, 3.2g ±0.20, 3.2g ±0.27, 2.8g ±0.15, and 2.1g ±0.41 in females of the control, 5, 10, 15 and 20 mg/kg) (Noda 2001, Experiment 1). There was a dose-dependent reduction of maternal body weight gain of pregnant rats treated orally with DMTC during days 7-17 of gestation. Maternal body weight gain was significantly reduced in pregnant rats treated with 15 or 20 mg/kg/day of DMTC. Maternal body weight on GD 20 were also significantly lower in the high dose group (respectively 333g ±26.7, 334g ±21.9, 321g ±21.0, 315g ±9.2, and 252g ±41.1** in the control, 5, 10, 15 and 20 mg/kg groups, respectively). No effect on fetal body weight was observed in a second study at similar or higher dose levels although the substance was administered for shorter durations and induced maternal toxicity as evidenced by significant decrease in maternal adjusted body weight gain. In Ehman 2007, a decrease in fetal body weight was observed only at high dose (7-12 mg/kg) in the second experiment during lactation when maternal weight was also significantly decreased. The link between foetotoxicity and maternal toxicity is therefore likely and the effect on foetal body weight is considered to be a secondary non-specific consequence of maternal toxicity not warranting classification.

DMTC showed developmental neurotoxic potential in the form of learning deficits consistently at the mid dose in water maze test in Ehman (2007). The maternal toxicity consisted on decreased maternal body weight gain only at the top dose (throughout the exposure in the first experiment and from lactation in the second experiment). There was also a dose-dependent but not statistically significant increase in the number of pups that failed to learn to negotiate the runway in one of two experiments in Ehman (2007). Developmental toxicity was also expressed in the offspring as a decreased brain weight (top dose only) and mild vacuolation in the brain (all doses, first experiment only) of adult offspring. DMTC inhibited neurite outgrowth and decreased cell viability in a concentration dependent manner, prevented neurite branching in a concentration-dependent manner, and decreasedsegment length in Jenkins et al. (2004) supporting the developmental neurotoxic potential. However, the absence of reproducibility and statistical significance of the effects observed in the runaway and the absence of effect at the top dose in water maze tests and the fact

that the studies were not consistent with guideline requirements does not provide clear evidence of an adverse effect on development.

Altogether, considering the findings on rare and serious malformations (cleft palates) and learning deficits, but taking into account the absence of reproducibility of cleft palates in both experiments of Noda (2001) and the high dose causing excessive maternal toxicity (20 % mortality) at which cleft palates were reported, the low incidence of omphaloceles at the second highest dose only, the absence of reproducibility and statistical significance of the learning effects observed in the runaway test, the absence of learning effect at the top dose in water maze tests and the fact that the studies were not consistent with guideline requirements, do provide some evidence of an adverse effect on development supporting classification in Category 2 for developmental toxicity.

Conclusions on classification and labelling

Classification as **Repr. 2; H361** (for developmental toxicity) is proposed (i.e. with H361: "Suspected of damaging the unborn child). Data are available only by oral route and the route of exposure cannot be specified in the hazard statement.

Adverse effects on or via lactation

Table 36a: Summary table of animal studies on effects on or via lactation

Method, test guideline, and deviation(s) if any	Species, strain, sex, no/group	Test substance	Dose levels, duration of exposure	Results	Reference
No data available.					

Table 36b: Summary table of human data on effects on or via lactation

Type of data/report	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Table 36c: Summary table of other studies relevant for effects on or via lactation

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on effects on or via lactation

No data available.

Comparison with the GHS criteria

No data available.

Conclusion on classification and labelling for reproductive toxicity

Classification as **Repr. 2; H361** (for developmental toxicity) is proposed (i.e. with H361: "Suspected of damaging the unborn child). Data are available only by oral route and the route of exposure cannot be specified in the hazard statement.

8.8 Specific target organ toxicity-single exposure (STOT SE)

Table 37a: Summary table of animal studies relevant for STOT SE (oral route)

Method, test guideline, and deviation(s) if any, species, strain, sex, no/group	**Test substance, dose levels, duration of exposure**	**Effects**	**Reference**
OECD TG 401 GLP compliant Oral gavage Rat; Sprague-Dawley, 5 animals/sex and dose	dimethyltin dichloride (85% dimethyltin dichloride: 15% monomethyltin dichloride). The [Di/Mono] Methyltin Chlorides Solution is a 50% organotin solution in an unspecified solvent. Main study: 200, 300 and 500 mg/kg bw.	Mortality: Males: 0/5, 1/5 and 2/5 at 200, 300 and 500 mg/kg bw, respectively. Females: 0/5, 3/5 and 4/5 at 200, 300 and 500 mg/kg bw, respectively. Clinical abnormalities: decreased activity, salivation, rough haircoat, mucoid/soft stools, fecal/urine stain, hunched posture, dehydration, dark material around the facial area, decreased defecation and food consumption, gasping and rales. Body weight gain in the majority of surviving animals. Dark red medulla of the kidney, dark red foci on the thymus, mottled lungs, abnormal coloured mucoid/fluid contents and eroded area(s), reddened mucosa and dark red linear striations on the stomach in animals that died.	Elf Atochem NA (1993).
OECD TG 401 GLP compliance not reported. Oral gavage Rat; Sprague-Dawley, 5 animals/per sex and dose	dimethyltin dichloride 98.7%. 0, 100, 150, 200, 250 and 300 mg/kg bw	LD_{50} (male): 190 mg/kg bw. LD_{50} (female): 160 mg/kg bw. Sedation, piloerection and ptosis on day 0. Piloerection, decreased locomotor activity, ataxia, ptosis, oily ventral surface, reddish nasal discharge and shallow respiration on days 1-4/death. Most animals surviving the observation period exhibited normal behaviour and appearance on days 5 through 14. Hemorrhagic lungs, and small and large intestines filled with yellow gelatinous material in animals that died. No outstanding gross pathological organ changes in surviving animals. Controls: abnormal defecation, piloerection, decreased locomotor activity and oily ventral surface on day 1 and normal behaviour and appearance on days 2-14. No outstanding gross pathological organ changes.	Author not disseminated (1979). Report date: 1979-03-20.

Non-guideline. GLP compliance not reported. Oral gavage. Rat, Sprague-Dawley, 5 animals/per sex and dose.	5% dimethyltin dichloride in corn oil. 0.215, 0.464, 1.00, 2.15 and 4.64 mL/kg bw + controls.	LD_{50} (male/female): 1.7 mL/kg bw. 0.215 mL/kg bw: No deaths. 0.464 mL/kg bw: No deaths. 1.00 mL/kg bw: 1/5 females died. No male deaths. 2.15 mL/kg bw: 4/5 males and 3/5 females died. 4.64 mL/kg bw: All rats died. Males: 0.215 and 0.464 mL/kg bw: no effects. 1.00 mL/kg bw: depression, diarrhoea, bloody-appearing stains around the muzzle, urine stains, and piloerection. 2.15 mL/kg bw: depression, yellow mucoid diarrhoea, diarrhoea, bloody-appearing stains around the muzzle, urine stains, excessive nasal or salivation stains, piloerection, bloated appearance, emaciation, and mortality. 4.64 mL/kg bw: depression, depressed righting and placement reflexes, rapid respiration, shortness of breath, diarrhoea, bloody-appearing stains around the nose, comatose appearance, piloerection, hunched posture, emaciation, and shaking prior to complete mortality. Females: 0.215 and 0.464 mL/kg bw: no effects. 1.00 mL/kg bw: diarrhoea, depression, piloerection, urine stains and mortality. 2.15 mL/kg: depression, diarrhoea, piloerection, and mortality. 4.64 mL/kg bw: depression, diarrhoea, shortness of breath, and comatose appearance prior to complete mortality. Body weight gain in all animals. Gross pathology: Males: 2.15 mL/kg bw: Autolysis in 3/5 rats. 4.64 mL/kg bw: congested kidneys, stomach distended with gas, irritated intestines and mottled liver in 1/5 rats. Autolysis in 5/5 rats. Females: Autolysis in 1/5, 3/5 and 5/5 animals at 1.00, 2.15 and 4.64 mL/kg bw, respectively. 4.64 mL/kg bw: congested lungs, white lesions on lungs, congested kidneys, irritated intestines and intestines distended with gas in 1/5 rats.	Author not disseminated (1978). Report date: 1978-05-25.
No guideline stated. GLP compliance not reported. Oral gavage. Rat, no strain data 6 males/dose.	dimethyltin dichloride; purity not given. 100, 200, 400, 800 and 1600 mg/kg bw. No data on control animals.	LD_{50} (male): 141.4 mg/kg bw. Clinical signs: Depression, convulsions, death. Gross pathology: No significant findings.	Affiliated Medical Enterprises (1971a).

No guideline stated. GLP compliance not reported (pre-GLP implementation). Oral gavage. Rat, Wistar, 10 males per dose.	dimethyltin dichloride. Test material form: crystalline. 5% solution. 48, 57, 69, 83, 100, 120 and 144 mg/kg bw No data on control animals.	LD_{50} (male): 73.86 mg/kg bw. Preliminary study (if fixed dose study): 100 mg/kg bw: 2/3 dead. 200 mg/kg bw: 3/3 dead. Mortality: 48 mg/kg bw: 1/10 dead. 57 mg/kg bw: 2/10 dead. 69 mg/kg bw: 5/10 dead. 83 mg/kg bw: 6/10 dead. 100 mg/kg bw: 8/10 dead. 120 mg/kg bw: 8/10 dead. 144 mg/kg bw: 10/10 dead. Clinical signs: Lassitude, hypokinesia, lack of appetite, thirstiness, unkempt fur, general weakness, and sometimes a tendency to lay on their sides and death. Recovery in the surviving rats within 4-6 days. No gross pathological signs.	Klimmer, O.R. 1971.
No methodological information. GLP compliance not reported. Oral Rat, no further information given.	dimethyltin dichloride; purity not given.	LD_{50}: 74 mg/kg bw. No available data on other effects.	Hoch (2001).
No guideline followed, GLP compliance not reported. Acute oral test, with lower dosage groups repeated on 4th day. Animals observed for 10 days. Limited methodological information. Rat, no data on strain, two females per dose.	dimethyltin dichloride. Test material form: crystalline. Doses: 40, 80 and 160 mg/kg bw. 40 and 80 mg/kg bw given on 1st and 4th day; 160 mg/kg bw given on 1st day only.	Mortality: Both rats died in the 160 mg/kg bw group. LD_{50} to female rats was found to be between 80 and 160 mg/kg bw. Clinical signs: Marked weakness in rats at 160 mg/kg bw. Body weight: No weight loss at 40 or 80 mg/kg bw. Gross pathology: No bile duct lesion at any dose.	Barnes and Stoner (1958).

No guideline followed. Acute oral (gavage) LD50 determined as part of an in-vivo UDS study, in order to determine dosage levels for the study. GLP compliant. Rat, Fischer 344, three males per dose.	Mixture of methyltin chloride compounds. Test material form: crystalline. First range finding assay: 25, 50, 100, 200 and 400 mg/kg bw. Second range finding assay: 600 and 800 mg/kg bw. Definitive in vivo-in vitro hepatocyte DNA repair (UDS) assay: 90, 175, and 350 mg/kg bw 2 or 16 hours before sacrifice.	LD_{50}: ca. 280 mg/kg bw (male). 1st assay: 1 death at 400 mg/kg. Clinical signs of dosed rats: rough fur, diarrhoea, weakness, humped back, difficulty breathing, bloody nose, lacklustre eyes, and blood around eyes. Extreme weight loss in the surviving rats at 400 mg/kg. 2nd assay: all rats died. Clinical signs at 600 or 800 mg/kg bw: rough fur, weakness, diarrhoea, lacklustre eyes, humped back, hypoactive, and blood around eyes. (UDS) assay: 3 rats from the 16 hour 350 mg/kg bw methyltin chloride dose group were found dead on the morning after dosing. All rats from the 16 hour 175 mg/kg bw dose-group had rough fur on the morning after dosing. 1 rat from the 2 hour 90 mg/kg bw dose-group and 2 rats from the 2 hour 350 mg/kg bw dose-group had diarrhoea. The surviving rat from the 16 hour 350 mg/kg bw dose-group had rough fur, humped back, diarrhoea, laboured breathing, and was hypoactive.	Author not disseminated (1993). Report date: 1993-07-11.
Methodological information not available in English. GLP compliance not reported. Route of administration: oral (unspecified). Rabbit, no data on strain. Sex: male.	dimethyltin dichloride. Test material form: crystalline. No data available.	Minimum lethal dose: 50 mg/kg bw (male). No available data on other effects.	Hashizume (1971).
No methodological information. GLP compliance not reported. Route of administration: oral (unspecified). Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline. No data available.	No LD_{50} given. Clinical signs: General uncharacteristic illness. Gross pathology: Inflammatory lesion of bile duct.	Author not disseminated (1978b). Reference type: review article or handbook.

No methodological information available. Route of administration: oral (unspecified). GLP compliance not reported. Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline. No data available.	LD_{50}: 88 - 119 mg/kg bw. No available data on other effects.	van Dokkum, and Huwer (2005).
No methodological information available. Route of administration: oral (unspecified). GLP compliance not reported. Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	LD_{50}: 237 mg/kg bw. No available data on other effects.	Author not disseminated (1978c).
No methodological information. Route of administration: oral (unspecified). GLP compliance not reported. Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	LD_{50}: 90 mg/kg bw. No available data on other effects.	Author not disseminated (1978d). Reference type: review article or handbook.
No methodological information. Route of administration: oral (unspecified). GLP compliance not reported. Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline. No data available.	LD_{50}: 74 mg/kg bw. No available data on other effects.	Dean (1976).
No methodological information. Route of administration: oral (unspecified). GLP compliance not reported. Rat, no data on strain or sex.	dimethyltin dichloride. Form: crystalline.	LD50: 74 mg/kg bw. No available data on other effects.	Author not disseminated (1992).

Table 37b: Summary table of animal studies relevant for STOT SE (dermal route)

Method, test guideline, and deviation(s) if any Species, strain, sex, no/group	Test substance, dose levels, duration of exposure	Effects	Reference
OECD TG 402, EU Method B.3. GLP compliant. Deviations: The temperature and relative humidity of the animal room (66-72 °F and 30-60 %, respectively) exceeded the range specified in the protocol (61-70°F and 40-60%, respectively). The final body weight and method of euthanasia was not recorded for two males. Rabbit, New Zealand White, male/female, 5 animals per sex and dose.	84.8 % DMTC in mixture with MMTC. Test material form: solution. Physical state: liquid. 200, 400 and 750 mg/kg bw. Occlusive, ca. 24 hours.	LD_{50}: 404 mg/kg bw (male/female). In the animals that died or were sacrificed moribund during the study, slight to severe dermal irritation at the site of the test material application, urine/fecal stain, soft stool/diarrhoea, decreased food consumption, decreased activity, pale eyes, decreased defecation, tremors, wobbly gait, respiratory abnormalities, mucoid stools, reddened iris, prostration, partial immobility of the hindlimbs, dark material and swelling around the facial area, convulsions, dehydration, emaciation, red ocular discharge, apparent hypothermia, raised area on the abdominal region and grinding of teeth. Clinical abnormalities in the animals surviving to study termination included slight to severe dermal irritation at the site of test material application, decreased defecation, decreased activity, pale eyes, dark material around the facial area, partial immobility of the hindlimbs, tremors, wobbly gait, soft stool, mucoid stools, fecal stain, reddened iris, apparent decreased food consumption and raised area on the abdominal region. Body weight Body weight loss during the day 0-7 in1 male and 1 female at 400 mg/kg and in the one surviving male at 750 mg/kg (weight gain on day 7-14). Gross pathology Reddened mucosa in the digestive tract, petechial haemorrhages, abnormally coloured fluid/mucoid contents in the digestive tract, dark red foci on the mucosa of the stomach, mottled and/or dark red thymus, mottled and/or firm, consolidated lungs, clear amber or red fluid contents in the thoracic cavity and light red foamy contents in the trachea in animals that died. Cysts on the oviducts were noted in two surviving females.	Rush, E.R. (1993b).
No guideline followed. Very limited methodological information available. GLP compliance not reported. Rat; no data on strain, 3 males per dose.	dimethyltin dichloride. Form: crystalline. 80 mg/kg applied on 5 successive days. Percutaneous application.	No LD_{50} determined. Clinical signs: Necroses of superficial layer of skin with black eschar formation. No deep-seated inflammation. Body weight: Slight weight loss. Gross pathology: No bile duct lesions.	Barnes and Stoner (1958).

OECD TG 402. Deviations: no data. GLP compliance not reported. Reliability score 4 (not assignable). Rabbit: New Zealand White, male/female (six animals in total, no data on control animals).	Dimethyltin Dichloride: Methyltin Trichloride (90:10% mixture). Physical state: liquid. 2000 mg/kg bw.	LD_{50} > 2000 mg/kg. No available data on other effects.	Affiliated Medical Enterprises 1971b.

Table 37c: Summary table of animal studies relevant for STOT SE (inhalation route)

Method, test guideline, and deviation(s) if any Species, strain, sex, no/group	**Test substance, form and particle size (MMAD), dose levels, duration of exposure**	**Effects**	**Reference**
Equivalent or similar to OECD TG 403. Inhalation (aerosol). GLP compliance not reported. Reliability score 2 (reliable with restrictions). Rat, Tif: RAIf (SPF), 10 animals per sex and per dose.	dimethyltin dichloride. Form: crystalline. Aerosol. 44 ± 6, 90 ± 7, 121 ± 3 and 167 ± 23 mg/m³. Duration of exposure: 4 h.	LC_{50}: 115 mg/m³ air (analytical). Mortality 44 ± 6 mg/m³ : 0/10 males, 0/10 females within 14 days 90 ± 7 mg/m³ : 3/10 males, 1/10 females within 14 days 121 ± 3 mg/m³ : 5/10 males, 4/10 females within 14 days 167 ± 23 mg/m³ : 10/10 males, 10/10 females within 14 days Clinical signs Within 2 hours after starting the exposure the animals in concentrations where mortalities occurred showed dyspnoea, ventral position, tremor and ruffled fur. These symptoms became more accentuated as the concentration was increased. After the 4 hour exposure period all animals showed, in addition to the above symptoms edepla, in the head region. The surviving animals recovered within 6 to 7 days. They were submitted at random to a necropsy whenever they died, survivors at the end of the observation period.	Ciba-Geiby (1977).

Equivalent or similar to OECD TG 403. Inhalation (aerosol). Deviations: only for 1 hour exposure. GLP compliance not reported. Rat, no data on strain, 10 males per dose.	dimethyltin dichloride. Form: crystalline. Physical state: solid. 57.6 mg/l in air (with water as vehicle), 16.7 mg/l in air (with propylene glycol as vehicle). Duration of exposure: 1 h.	None of the animals died. **Dimethyltin Dichloride in Distilled Water:** Initial "excited" activity shown by all animals, the majority of the animals exhibited little or no activity throughout the period, depression, shallow respiration, serosanguineous stains around the nose, animals exhibited excessive masticatory movements, preening and lacrimation, and "squinting" of the eyes on occasion. Upon removal from the exposure chamber, all animals exhibited depression and shallow respiration, eight exhibited excessive lacrimation, nine exhibited serosanguineous stains around the nose and five exhibited wheezing. On the first post-exposure day, two exhibited serosanguineous stains around the nose and urine stains and one animal was wheezing. From the second day throughout termination of the study, all animals appeared grossly normal. An average bw gain of 82 g. No significant gross pathological alterations. **Dimethyltin Dichloride in Propylene Glycol:** Initial "excited" behaviour in all animals, little or no activity throughout the period, depression, laboured respiration, serosanguineous stains around the nose and/or mouth, excessive salivation, ataxia and damp haircoats in the majority of animals and occasional preening, excessive lacrimation, "squinting" of the eyes and masticatory movements. Upon removal from the exposure chamber, all animals exhibited depression, depressed righting and placement reflexes, excessive salivation and stains, damp haircoats, eight showed excessive lacrimation, seven serosanguineous stains around the nose and five exhibited wheezing. On the first and post-exposure day, two or three of the animals exhibited sero-sanguineous stains around the nose and one or two of the animals were wheezing. With the exception of one animal, which exhibited wheezing from day three through five, all animals exhibited normal appearance and behaviour until termination. An average bw gain of 107 g. No significant gross pathological alterations.	International Bio-Research (1976).

Equivalent or similar to OECD TG 403. According to Federal Register August 12, 1961 et seq. FHSA. Deviations: no data. Inhalation (aerosol). GLP compliance not reported. Rat, Wistar, 10 males per dose.	dimethyltin dichloride. Form: crystalline. Concentrations: 100, 130 and 169 µl/l. Duration of exposure: 4 h.	LC_{50}: 139 µl/L air. Mortality: 100 µl/l : No mortalities within 14 days 130 µl/l : 4/10 mortalities within 24 hours; no further mortalities. 169 µl/l : 8/10 mortalities within 24 hours; no further mortalities. Clinical signs A slight - medium degree of depression of the respiration, slight apathia and disturbances in coordination. The reflexes, urine and fecal deposition of the survived animals were normalised 24 hours after exposition. Body weight During the observation period of 14 days all the surviving animals showed a normal gain of body weight. Gross pathology At terminal autopsy no macroscopic pathological changes were observed in the cranial, abdominal and chest cavities. The animals which died during or shortly after the exposure time showed lung oedemas and lung emphysemas of a slight to moderate degree.	Author not disseminated (1976).
Test type: standard acute method. GLP compliance not reported. Inhalation (aerosol). Duration of exposure: 1 h. Rat, Sprague-Dawley, 10 males per dose.	dimethyltin dichloride. Form: crystalline. Aerodynamic mass median diameter (MMD): less than 5.0 µm in at least 80%. For the first group the nominal aerosol concentration was 11.53 mg/litre. This aerosol delivery yielded a concentration of 5.77 mg/litre of test material. For the second group the nominal aerosol concentration was 15.02 mg/litre which was equivalent to 5.00 mg/litre of test material.	Mortality: No deaths occurred in either of the groups. Clinical signs: All rats in both exposure groups exhibited inactivity during the exposure period. At the termination of the exposures, all 5.77 mg/litre animals and several animals exposed to 5.00 mg/litre of test material had a slight to moderate discharge around the muzzle and nasal areas. All animals in both groups exhibited normal appearance and behaviour throughout the 14-day post-exposure observation period. Body weight: NDA. Gross pathology: NDA.	Hazelton Laboratories 1976.

Equivalent or similar to OECD TG 403. Deviations: only 1 hour exposure duration. Inhalation (aerosol). GLP compliance not reported. Rat, no data on strain, 10 rats per dose, mixture of sexes.	dimethyltin dichloride. Form: crystalline. Physical state: solid. 50, 100, 200 and 300 mg/l/hour.	Mortality: 50 mg/l/hour: 2/10 100 mg/l/hour: 5/10 200 mg/l/hour: 7/10 300 mg/l/hour: 10/10 Clinical signs: Rats exposed to lower dose of the test material experienced CNS depression. After recovery from the state of depression, the rats became very aggressive and fought with each other. They were also very sensitive to sound and touch. This behaviour of aggressiveness was only observed in the male rats. Body weight: NDA. Gross pathology: Gross findings at autopsy on dead rats showed blood in the lungs and heart failure. Fluid was in the chest cavity. The spleen was very dark and the stomach was filled with gas.	Wells Laboratories 1975
No methodological information. GLP compliance not reported. Inhalation (aerosol). Duration of exposure: 1 h. Rat, no data on strain, male/female.	Monomethyltin trichloride + dimethyltin dichloride (21.5 : 78.5). Test material form: crystalline.	LC_{50}: 84 mg/L/hr. No data available on other effects.	Summer et al. (2003).
No methodological information available. Inhalation (vapour). GLP compliance not reported. Species: rat. Strain: no data. Sex: no data.	dimethyltin dichloride. Form: crystalline.	LC_{50}: 1070 mg/L/hr. No data available on other effects.	Author not disseminated (1978). Reference type: review article or handbook.
No methodological information available. Inhalation (aerosol). GLP compliance not reported. Rat, male/female, no information on strain.	dimethyltin dichloride. Test material form: crystalline. Concentrations: 1910 mg/m3. Duration of exposure: 1 h.	Mortality: no deaths observed after 21 days. Body weight: normal body weight gain reported. No information available on other effects.	Author not disseminated (2006). Report date: 2006-07-23. Reference type: review article or handbook.

No methodological information available. Inhalation (vapour). GLP compliance not reported. Species: rat. Strain: no data. Sex: no data.	dimethyltin dichloride. Test material form: crystalline.	LC_{50} > 1.91 mg/L/hour. No information available on other effects.	Author not disseminated (1978). Reference type: review article or handbook.
Similar to OECD 403 with shorter duration of exposure (1h). Rat. No information on sex or strain.	Test substance: dimethyltin dichloride. (purity not known). Doses: 640, 1679, and 3012 mg/m³. 1 h exposure to aerosol.	LC_{50} 1632 mg/m3, 1.6 mg/L. Calculated LC_{50} on 4 hour using Haber laws and n=1 as recommended in IR/CSA R7.4.4.1 for extrapolation to longer durations: **LC_{50} = 0.4 mg/L.** No information available on other effects.	Ciba-Geigy, 1977.

Table 37d: Summary table of human data relevant for STOT SE

Type of data/report	**Test substance**	**Route of exposure and relevant information about the study (as applicable)**	**Observations**	**Reference**
Case study of workers exposure. GLP compliance not reported.	mixture of half dimethyltin and half trimethyltin chloride vapour. Test material form: crystalline.	Route of administration: inhalation. Analytical verification of test atmosphere concentrations: no. Duration of exposure: 1.5 h. Remarks: over a 3 day working period.	1/6 workers died 12 days following the exposure. Symptoms preceding death: excretion of high levels of tin in the urine, respiratory depression, and coma. Autopsy results of the worker who died: massive fatty degeneration of liver cells and necrosis (shock kidneys i.e. proximal tubule degeneration). In two most severely affected surviving workers permanent neurological disabilities and non-persistent respiratory problems. All survuvung workers had high tin concentrations in the urine with the highest levels occurring in the most severely affected.	Harper et al. (2005), (study also referred to in section 8.9 STOT RE).

Table 37e: Summary table of other studies relevant for STOT SE

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Test type: acute. No guideline followed. Immunotoxicity study looking at DT-diaphorase activity and thymus atrophy. Male Wistar rats dosed via subcutaneous injection. GLP compliance: not reported.	Identity of Dimehyltin dichloride. Test material form: crystalline.	Single exposure. Doses / concentrations (actual injected): 11 mg/kg bw (50 µmoles/kg bw). No. of animals per sex per dose: 4 male rats per dose. Control animals: no. After treatment with organotin animals were killed by decapitation, and thymus and spleen were dissected out, washed with saline, blotted, and weighed. The liver was perfused in situ with a cold 0.9% saline and then removed, washed, blotted and weighed.	NOAEL (male) >= 11 11 mg/kg bw. Induction of heme oxygenase, peaking at 48 hours after treatment. No significant losses in cytochrome P-450. No significant changes in the DT-diaphorase activity at any time after injection. A good reciprocal correlation between DT-diaphorase activity and thymus weight (r=0.73, n=12).	Ariyoshi et al. (1991).

Short summary and overall relevance of the provided information on STOT SE

Oral route:

Dimethyl dichloride is classified as Acute Tox. 3; H301, and although some gross pathological organ changes were reported in animals that died, there is no clear evidence for a specific organ toxicity in the absence of lethality. Furthermore, the adaptive responses such as decreased activity, salivation, rough haircoat, mucoid/soft stools, fecal/urine stain, hunched posture, dehydration, dark material around the facial area, decreased defecation and food consumption, gasping and rales are not considered toxicologically relevant and do not warrant classification for STOT SE.

Dermal route:

Dimethyl dichloride is classified as Acute Tox. 3; H311 and Skin Corr. 1; H314, and apart from cysts on the oviducts in two female rabbits surviving to study termination (Author not disseminated (1993), report date 1993-07-25), there is no evidence for a specific organ toxicity in the absence of lethality or that would not be related to corrosive properties of the substance. However, cysts on the oviducts are not considered to warrant classification for STOT SE since they are commonly observed in New Zealand White rabbits.

Inhalation route:

The reversible activity changes, excessive salivation, ataxia and damp haircoats, depression, shallow respiration, serosanguineous stains around the nose, excessive masticatory movements, preening and lacrimation, and "squinting" of the eyes on occasion in the absence of lethality are considered adaptive responses that are not toxicologically relevant and do not warrant classification for STOT SE. Dimethyl dichloride is classified as Acute Tox. 2; H330, and no specific target organ toxicity was reported in the animal studies in the absence of lethality. In the human case study on six workers, unknown level of exposure over three days to a mixture of half dimethyltin and half trimethyltin chloride vapour caused death that was preceded by high levels of tin in the urine, respiratory depression, and coma, massive fatty degeneration of liver cells and necrosis or proximal tubule degeneration. The surviving workers, who were the most severely affected, developed permanent neurological disabilities, but respiratory problems did not

persist. Care should be taken not to assign classification for Acute Toxicity and STOT SE for the same effect. Specific target organ toxicity (single exposure) is defined as specific, non-lethal target organ toxicity arising from a single exposure to a substance, whereas acute toxicity classification is generally assigned on the basis of evident lethality or where the potential to cause lethality can be concluded from evident toxicity. In this case study on workers, unknown exposure levels over three days to a mixture of half dimethyltin and half trimethyltin chloride vapour caused one death and permanent neurological disabilities in the surviving workers. This human evidence is considered rather as contributing to the weight of evidence assessment the available information on animal studies supporting the classification as Acute Tox. 2; H330.

Other routes:
No evidence for immunotoxicity was observed in Ariyoshi et al. (1991).

Comparison with the GHS criteria

As dimethyl dichloride is classified as Acute Tox. 3; H301, Acute Tox. 3; H311 and Acute Tox 2; H330, and there is no clear evidence for a specific organ toxicity in absence of lethality, no classification for STOT SE is warranted.

Conclusion on classification and labelling for STOT SE

No classification is warranted for STOT SE.

8.9 Specific target organ toxicity-repeated exposure (STOT RE)

Table 38a: Summary table of animal studies relevant for STOT RE

Method, test guideline, and deviation(s) if any, species, strain, sex, no/group	Test substance route of exposure, dose levels, duration of exposure	Results	Reference
90-day repeated dose oral study Equivalent or similar to OECD TG 408. GLP-compliant. SD rats, male/female 15 animals per sex and dose in main study; 15 per sex and dose in neurotoxicity study.	methyltin chlorides (mixture of dimethyltin dichloride/methyltin trichloride). Oral in drinking water. 0, 25, 75, 200 ppm (reduced to 150 during 5th week of treatment and terminated during 6th treatment week).	NOAEL (males) < 25 ppm or 1.6 mg/kg bw/d NOAEL (females) < 25 ppm or 2.2 mg/kg bw/d *200 ppm:* - 7 males and 21 females died or were sacrificed between days 18 and 34, with severe treatment-related clinical signs - remaining animals sacrificed by day 36 of the study - sign. ↓ body weight - sign. ↓ food consumption - marked changes in various blood biochemical parameters - at day 92, the biochemical parameters were essentially the same between the control and treated groups - changes in various organ weights, including ↓ thymus and spleen weight at the interim sacrifice (males) - various gross pathology findings - in several preterminal non-perfused animals small thymus and/or spleen *Neurobehaviour:* Week 4: one male with slight ataxia ➢ slight overall gait incapacity, slight tremors at the limbs and clonus of the jaws (chomping), 3 females with slight/moderate tremors at the limbs or head and clonic convulsions, 2 animals with hunched posture and a severe overall gait incapacity attributed to a severe ataxia in one animal + red liquid material at the urogenital region. - incidence of a rearing body position in the home cage as well as average number of rearing incidents in the arena sign. reduced - hindlimb grip strength sign. decreased and body temperature sign. reduced in females *75 ppm:* - 1 male found dead on day 41, with e.g. tremors, hypersensitivity and thin dehydrated body condition - thin and dehydrated appearance for another male - abnormal gait/behaviour for a third male - one female with hypersensitivity, convulsions and reduced activity - changes in various organ weights, including ↓ absolute and relative thymus and/or spleen weight at the terminal sacrifice and ↑ brain weight (males, at end of recovery period it was comparable to controls) - histopath. changes in brain tissue --terminal evaluations indicated possible treatment-related lymphoid atrophy of the thymus *Neurobehaviour:* *FOB:* Week 4: one male with severe ataxia including falling over which resulted in a severe overall incapacity + several other neurological signs throughout the study - sign. lower body temperature Week 8 and 13: sign. decrease in rearing incidents in the arena (females) *Motor activity:* - sign. reductions in total activity counts *25 ppm:* - no mortalities - absolute and relative kidney weights (female) - treatment-related findings limited to reduced food (male) and water intake, neuropathological lesions and vacuolisation of white matter in the brain and spinal cord.	Rohm and Haas (1999).

90-day oral study in rat. OECD TG 408, with deviations. GLP-compliant. Wistar rat, male/female, 10 per sex and dose (main study), 6 per sex and dose (satellite groups).	MMTTC/DMDTC (30/70). Oral (feed). 0, 1, 6, 15 and 200 ppm. Actual ingested: Males: 0, 0.06, 0.39, 0.98, and 16.81 mg/kg bw/d. Females: 0, 0.07, 0.41, 1.02, and 17.31 mg/kg bw/d.	NOAEL (males) 15 ppm or 0.98 mg/kg bw/d NOAEL (females) 15 ppm or 1.02 mg/kg bw/d Both NOAELs based on neurological effects. *(actual dose received) based on test material 200 ppm: - neurological signs around week 4, including increased activity, rearing, convulsive activity (females), increased landing footsplay (males) - 3 females in the main group died towards the end of the first month and most of the females and a number of males showed severe neurological signs (incl. tremors and convulsions) ➢ all animals were considered moribund and killed for humane reasons - 1 animal in the subgroup found dead and the others killed for humane reasons (due to convulsions, blepharospasm, tremors) - treatment-related cell death, neuronal death (more pronounced in females) in various areas and submeningeal oedema in the brain - treatment-related tubular dilatation in the kidneys -females had an increased incidence of corticomedullary haemorrhage in the thymus. Most of the high-dose females also showed cortical lymphoid depletion in the thymus. -all animals showed decreased accumulation of brown pigment in the spleen. 15 ppm: - no clinical signs - no histopath. changes 6 ppm: - no clinical signs 1 ppm: - no clinical signs	Elf Atochem NA (1996).
7-day study to evaluate the palatability of a methyltin chloride mixture No guideline available. GLP-compliant. SD rats, female, 5 per dose	methyltin chlorides (mixture of dimethyltin dichloride/methyltin trichloride). Oral in drinking water. 0, 250 and 500 ppm. 7 days.	- no mortality/early sacrifices - signs of dehydration commencing from day 4 - no other clinical signs - changes in body weight - changes in food and water consumption	Author not disseminated (1997). Report date: 1997-08-26.
Subacute, 14-day study Non-guideline GLP-compliant. SD rats, male/female, 5 per sex and dose	methyltin chlorides (mixture of dimethyltin dichloride/methyltin trichloride). Oral in drinking water. 0, 25, 75, 150 and 200 ppm.	- no mortalities/early sacrifices - no clinical signs related to treatment - slightly lower (n.s.) mean body weight at the end of the study (200 ppm males, all dose group females) - some changes in food and water consumption - sign. (relative to bw) ↓ in kidney weight in 200 ppm females	Author not disseminated (1997). Report date: 1997-08-28.
90-day study in rats. OECD TG 408. GLP compliance not reported. Wistar rat, male/female, 10 per sex and dose	1175-114 Read across from 78/22 Mono/Di-methyltin dichloride. Oral (feed). 0, 20, 100 or 500 ppm.	- no deaths or signs of intoxication - treatment-related histopath. changes: hyperplasia of the urinary bladder epithelium (moderate to slight) in most animals at 500 ppm, in a number of animals at 100 ppm and 2 females at 20 ppm; slightly enlarged pale nuclei and foamy cytoplasm of the epithelial cells of the proximal tubules in the intercortico-medullary region of the kidney in 4 males and 1 female of the highest dose group.	Author not disseminated (1978). Report date: 1978-11-20.

Table 38b: Summary table of human data relevant for STOT RE

Type of data/report	Test substance	Route of exposure	Relevant information about the study (as applicable)	Observations	Reference
Poisoning incident report; secondary source.	Dimethyltin dichloride and trimethyltin chloride vapours		Occupational, unintentional exposure, inhalation	Two chemists who had been intermittently exposed to vapours of dimethyltin dichloride and trimethyltin chloride for about 3 months abruptly developed a status of mental confusion with generalized epileptic seizures. Before the acute episode, the subjects had complained of headaches, pain in various organs, and psychological disturbances such as memory defects, vigilance loss, insomnia, anorexia, and disorientation. Both patients recovered completely following removal from exposure.	Harper et al., 2005
Poisoning incident report; case study of workers exposure; secondary source.	Mixture of half dimethyltin and half trimethyltin chloride vapour		Occupational exposure, 6 workers (male and female), inhalation. Maximum exposure was a total of 1.5 hours over a 3 day working period. No estimates of exposure levels were given.	Six chemical workers exposed to methyltins primarily by inhalation experienced headache, tinnitus, deafness, impaired memory, disorientation, aggressiveness, psychotic and other severe neuropsychiatric behaviour, syncope and loss of consciousness as symptoms of exposure; one subject died. The two surviving workers with the highest urinary tin levels exhibited fixed neurological effects which were not resolved more than six years after exposure. The remaining three survivors returned to work, but had memory loss, which persisted for six months.	Harper et al., 2005 (study also referred to in section 8.8 STOT SE)

Table 38c: Summary table of other studies relevant for STOT RE

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
Publication/ literature paper.	dimethyltin dichloride	Investigating relationship between chemical structure of organotin compounds and thymolytic activity. Data considered in the review include: oral treatment studies, intravenous treatment studies and in vitro experiments. An intravenous treatment study and in vitro experiment included the assessment of dimethyltin dichloride Female rats, no strain data given; 0, 12, 24, 48 mg/kg bw/d i.v., 5-8 animals per dose. No further data on in vitro experiment methodology.	Intravenous Experiment: - DMTC did not affect the thymus. - No effects were seen on any of the lymphoid organs. - A single injection of 48 mg/kg bw caused 3 of the 8 animals to die within 2 days. - No liver or bile duct changes were found. - No other treatment-related histopathological changes were noted. In vitro experiment: - No effect in the cell count or viability was observed.	Seinen et al., 1977.
Subacute study; secondary source. No data on methodology or GLP compliance	dimethyltin dichloride	Rat, 5 mg/kg bw/d	NOAEL (no data on sex) ≥ 5 mg/kg bw/d based on test material. NOAEL based on thymus weight.	Dobson et al., 2006.

Short summary and overall relevance of the provided information on STOT RE

Two 90-day studies are considered as reliable: Rohm and Hass (1999) and Elf Atochem NA (1996).
In Rohm and Hass (1999) rats were treated with a methyltin chloride mixture containing 90% dimethyltin dichloride at concentrations of 25 (1.6 mg/kg bw/day in males; 2.2 mg/kg bw/day), 75 (5.2 mg/kg bw/day in males; 6.7 mg/kg bw/day in females) or 200 ppm (15.50 mg/kg bw/day in males; 19.5 mg/kg bw/day in females). At 200 ppm, 7 males and 21 females died or were sacrificed during the first 5 weeks due to poor condition. All remaining animals were sacrificed by Week 6. Animals in this group showed clinical signs of toxicity, including tremors, convulsions and aggression/ hypersensitivity/ difficulty when handled. Animals appeared to be weak, thin, and dehydrated, were cold to touch, were observed lying on their sides, and had decreased home-cage activity levels. An increased incidence of fur staining was also noted. Body weights and food intake were significantly lower at all intervals. At 75 ppm one male was found dead during week 6 (no other deaths occurred). Abnormal clinical signs were limited to tremors, hypersensitivity (difficulty when handled), a thin dehydrated body condition for the male that died, a transitory dehydrated appearance for another male, and hypersensitivity, convulsions, and reduced activity for one female. Body weights and food consumption were significantly lower for males at most intervals measured following treatment. At 25 ppm water consumption significantly decreased for all treated groups during most intervals measured; however, following treatment termination, water consumption values were generally comparable between the treated groups and the control.

Functional Observational Battery (FOB) tests indicated several findings, primarily affecting the 200 ppm group. At Week 4, females showed significantly reduced rearing, lower hindlimb grip strength, and decreased body temperature. Ataxic gait was observed for one male, along with tremors and clonus of jaws. Three females showed tremors and clonic convulsions. Hunched posture was observed for one male, and for one female ataxia was noted, as well as a red liquid material at the urogenital region. Significant findings for the 75 ppm group were limited to lower body temperature of females. One male showed ataxia and unusual hind limb movements (which were also observed for this animal on subsequent testing occasions). At Weeks 8, 13, and following recovery, rearing was significantly decreased for the 75 ppm females and their body temperature was significantly decreased at the week 13 assessment. At week 13, the rate of linear decrease was significantly lower for the 75 ppm females relative to the control group.

There were also significant blood biochemical changes for males in the 200 ppm group at week 4, which included increases in BUN, creatinine, and phosphorus and decreases in potassium levels. Many of the animals sacrificed by week 6 showed marked changes in various blood biochemical parameters, including increases in BUN, creatinine, AST, ALT, and phosphorus. Males in the 200 ppm group had an elevated urine pH at week 4. Absolute and relative thymus weights were significantly decreased for the 200 ppm (15.50 mg/kg bw/day in males) males at the interim sacrifice (week 4) and 75 ppm males at termination sacrifice. Absolute heart weight was decreased significantly for 25 and 75 ppm females at interim sacrifice, but not at terminal sacrifice.

Absolute and relative kidney weights were significantly increased for 25 ppm and 75 ppm females at terminal sacrifice. Gross pathological findings for preterminal animals included small thymus and/or spleen, emaciated carcass, dilation of digestive tract/discoloured digestive material, and dark areas on the stomach and/or lungs. A small thymus was also seen at the interim evaluation for 200 ppm males and at the terminal evaluation for the 75 ppm group. Results of the histopathological examinations indicated clear treatment related nervous system lesions for preterminal 200 ppm animals in various regions of the brain and spinal cord, characterized by slight to mild ventricular dilation, mild to moderate neuronal necrosis, and slight to mild white matter vacuolization. Nervous system changes were observed for 75 ppm animals at terminal examination (although slight and less frequent) and possible treatment-related lymphoid atrophy was observed for this group. Animals in the 25 ppm group showed slight to moderate vacuolization in brain and spinal cord tissue at the terminal examination.

Overall, treatment of male and female rats with a 90:10% mixture of dimethyltin: monomethyltin chloride (administered in drinking water) resulted in death, reduced body weight, decreased food and water intake, blood biochemical changes, behavioural effects, and neuropathological lesions at 200 ppm (equivalent to 15.5 and 19.5 mg/kg/day for males and females, respectively). At 75 ppm (equivalent to 5.2 and 6.7 mg/kg/day for males and females, respectively), one male died, body weights were reduced (males only), food and water intake were decreased, motor activity was reduced (females only), and neuropathological lesions were observed. For the 25 ppm group (equivalent to 1.6 and 2.2 mg/kg/day for males and females, respectively), no mortality occurred and treatment-related findings were limited to reduced food (males only) and water intake and neuropathological lesions. The no-observed-adverse-effect level (NOAEL) was considered to be less than 25 ppm.

In Elf Atochem NA (1996), 1, 6, 15, and 200 ppm (equivalent to 0.06, 0.39, 0.98 and 16.81 mg/kg bw/day in males and 0.07, 0.41, 1.02 and 17.31 mg/kg bw/day in females) of Dimethyltin Dichloride: Methyltin Trichloride (66.5:33.5% mixture) was given by oral route in diet. Three females of the 200 ppm group died during the first month and most males, and remaining females in this group showed severe neurological and neurobehavioural signs, including tremors, convulsions, and increased footsplay. All remaining animals of the 200 ppm group were sacrificed. Mean body weight for males of the 200 ppm group on days 7 and 28 were significantly lower. Food consumption on day 7 was significantly decreased in animals (both sexes) of the 200 ppm group and increased in females on Day 28. Food conversion efficiency was significant only for high-dose males on Day 21. Mean water consumption was significantly reduced in females (6 ppm group) on day 6 only. Mean intake of the test substance in animals receiving 1, 6, 15, or 200 mg/kg diet were 0.06, 0.39, 0.98, and 16.81 mg/kg bw/day in males and 0.07, 0.41, 1.02, and 17.31 mg/kg bw/day in females.

There was a significant increase in alanine aminotransferase and aspartate aminotransferase in males of the 1 ppm group. The specific gravity of urine was significantly increased in females of the 6 ppm dose group.

Upon microscopic examination, treatment-related histopathological changes were observed in the brain, the kidneys, and the thymus of animals treated with 200 ppm of the test substance. Macroscopic pathological observations showed some gross skin changes at 200 ppm that were probably treatment-related. Animals below 15 ppm were not examined microscopically because no microscopic changes were found at 15 ppm as compared to the control group. Females at 200 ppm (17.31 mg/kg bw/day) had an increased incidence of corticomedullary haemorrhage in the thymus and most of these high-dose females also showed cortical lymphoid depletion in the thymus. All females and males (16.81 mg/kg bw/day) treated with 200 ppm showed decreased accumulation of brown pigment in the spleen. Neuropathological examinations showed that animals in the high dose group showed signs of convulsions, tremors, blepharospasm, and hunched posture, and microscopic observations showed pronounced neuronal death in a number of areas of the cerebellum (more pronounced in females). The areas with predominant lesions were the hippocampal region, the piriform, entorhinal, and perirhinal cortices, the amygdala, the olfactory nuclei and the tenia tecta. Also a slight increase in swollen axons in the spinal cord was observed in this high dose group. Based on the effects described above, particularly the neurotoxic effects observed in the high dose group, the NOAEL was placed at 15 ppm equivalent to 0.98 mg/kg bw/day (males) and 1.02 mg/kg bw/day (females) of the test mixture or 0.62 mg/kg bw/day (males) and 0.65 mg/kg bw/day (females) for the dimethyltin dichloride component of the mixture.

Together, these two oral 90-day studies on DMTC indicate that the main target organ is the nervous system. Deaths and severe neurological signs occurred from 75 ppm (5.2/6.7 mg/kg) in Rohm and Hass (1999) and at 200 ppm (16.81/17.31 mg/kg) in Elf Atochem NA (1996). Besides, neuropathological lesions were observed from the lowest dose of 25 ppm (1.6/2.2 mg/kg) in Rohm and Hass (1999) as evidenced by moderate vacuolization in the brain and spinal cord tissue and ventricular dilation and neuronal necrosis at highest doses. Neuronal death was found at 200 ppm (16.81/17.31 mg/kg), but no dose-response was observed in neuronal micro-vacuolization or degeneration in Elf Atochem NA (1996). The absence of neurological findings in the shorter-term studies and in the unreliable 90-day study do not decrease the concern for clear adverse effects on the nervous system supported also by human data. In the poisoning incident report on six workers (Harper et al., 2005), unknown exposure to a mixture of half dimethyltin and half trimethyltin chloride vapour over three days caused death that was preceded by high levels of tin in the urine, respiratory depression, and coma, massive fatty degeneration of liver cells and necrosis or proximal tubule degeneration. The surviving workers, who were the most severely affected, developed permanent neurological disabilities, but respiratory problems did not persist. In the other poisoning incident report reviewed in Harper et al. (2005), two chemists who had been intermittently exposed to vapours of dimethyltin dichloride and trimethyltin chloride for about 3 months abruptly developed a status of mental confusion with generalized epileptic seizures. Before the acute episode, the subjects had complained of headaches, pain in various organs, and psychological disturbances such as memory defects, vigilance loss, insomnia, anorexia, and disorientation. Both patients recovered completely following removal from exposure. No estimates of exposure levels were given in the poisoning incident reports (Harper et al., 2005), but the observed neurological effects contribute to the weight of evidence assessment of the available information on animal studies supporting a classification with STOT RE 1 with the nervous system as the target organ.

Also, the absolute and relative weights of the thymus were reduced in the 90-day oral studies at 75 ppm in males (about 5 mg/kg bw/day), indications of a possible treatment-related lymphoid atrophy of the thymus were observed in animals in the mid dose group of 75 ppm (below 10 mg/kg bw/day), and a smaller spleen was also observed in females in the mid and low groups (Rohm and Haas 1999). In Elf Atochem NA (1996), females at 200 ppm (17.31 mg/kg bw/day) had an increased incidence of corticomedullary haemorrhage in the thymus and most of these high-dose females also showed cortical lymphoid depletion in the thymus. All females and males (16.81 mg/kg bw/day) treated with 200 ppm showed decreased accumulation of brown pigment in the spleen. Accumulation of brown pigment is a normal phenomenon in rats, which gradually increases with age. The 200 ppm animals were killed at an early stage of the study, at which they had not yet accumulated pigment in the spleen. Therefore, the decreased splenic pigment was not considered to be an effect of the treatment, but rather a consequence of the difference in age between these animals and those of

the other treatment groups and the controls, that were killed two months later. No histochemical changes were observed at the lower dose of 1 mg/kg bw/day in Elf Atochem NA (1996). However, the effects on thymus observed at 75 ppm in Rohm and Haas (1999) supported by the effects on spleen justify the STOT RE 1 classification also for the immune system as this dose level is within the range of guidance values for category 1 classification. The effects observed on the thymus and spleen are consistent with a known class effect of organotins on the immune system, and it is to be noted that reduced thymus weights (atrophy) were also observed in the two prenatal developmental rat studies (Noda 2001) on day 20 of gestation of females treated at 15 and 20 mg/kg although these dose levels are above the guidance value range for classification in Category . No examination of spleen was conducted.

Comparison with the GHS criteria

According to the GHS criteria in Figure 3.9.1 in section 3.9.2.1, classification in category 1 is justified if: "substances that have produced significant toxicity in humans, or that, on the basis of evidence from studies in experimental animals can be presumed to have the potential to produce significant toxicity in humans following repeated exposure". The guidance dose value for this category for a rat 90 day study is ≤ 10 mg/kg bw/day. The effects seen in the thymus (and to a lesser extent in the spleen) as well as in the nervous system in the two rat 90-day studies justify classification in STOT RE Category 1 according to the GHS criteria with the central nervous system and the immune system as the specific target organs/systems (see Note to Figure 3.9.1). The observed neurological effects in humans contribute to the weight of evidence assessment of the available information on animal studies supporting a classification with STOT RE 1 with the nervous system as the target organ.

Conclusion on classification and labelling for STOT RE

Classification as STOT RE 1; H372 (nervous system, immune system) is considered warranted. No specific concentration limit is proposed.

8.10 Aspiration hazard

Table 39: Summary table of evidence for aspiration hazard

Type of study/data	Test substance	Relevant information about the study (as applicable)	Observations	Reference
No data available.				

Short summary and overall relevance of the provided information on aspiration hazard

Not applicable as there is no data available.

Comparison with the GHS criteria

Not applicable as there is no data available.

Conclusion on classification and labelling for aspiration hazard

Not applicable as there is no data available.

9. EVALUATION OF ENVIRONMENTAL HAZARDS

9.1 HAZARDOUS TO THE AQUATIC ENVIRONMENT

9.1.1 Rapid degradability of organic substances

Table 40: Summary of relevant information on rapid degradability

Method, test guideline, and deviation(s) if any	Results	Remarks	Reference
OECD Guideline 111 (Hydrolysis as a Function of pH)	Hydrolysis DT_{50} at 25°C: pH 4 > 1 year pH 7 > 1 year pH 9 > 1 year	Several deviations from the guideline but considered not to impact the validity of the study	Author not disseminated (2004). Report date 2004-06-17.
Secondary source with no methodological information	In a literature source with limited detail, the photodegradation constant was reported to be 1.8 x 10-12 cm^3/ molecule/second (25 °C).		Secondary source (Dobson et al (2006)).
OECD Guideline 301 F (Ready Biodegradability: Manometric Respirometry Test)	The determination was performed with a single concentration of dichlorodimethylstannane: 14-d biodegradation: 3% 28-d biodegradation: 3% 35-d biodegradation: 3% Not readily biodegradable	Minor deviations from standard test guidelines and/or minor methodological deficiencies, which do not affect the quality of the relevant results	Author not disseminated (2003). Report date 2003-06-22.

Hydrolysis

Hydrolytic stability of dimethyltin dichloride was tested according to the OECD TG 111 at three pHs (4, 7, 9). The study can be considered as a valid test in spite of several deviations from the TG protocol. The result of the study showed that dimethyltin dichloride is hydrolytically stable.

Photochemical degradation

The included photo degradation information originates from secondary source and the applied methodology in the study is not known. Based on this information it can be concluded that there is no indication of photo degradation of dimethyltin dichloride.

Ready biodegradability

Ready biodegradation of dimethyltin dichloride was tested according to the OECD TG 301 F (Manomeric respiratory test) and only minor deviations to the TG protocol were reported. For example, additional $NaNO_3$ was added to the mineral medium to prevent nitrogen limitation during the test. The test was performed at one concentration (0.111 mg/L) in three replicate flasks and oxygen concentration was measured every 4 hours. Inoculum activity and toxicity controls contained 100 mg/L of reference substance (two replicates for each). After 28 days of incubation it was decided to extend the test with two weeks because the oxygen consumption had not reached the plateau phase. The actual termination was after 35 days.

Very low degradation (3%) of dimethyltin dichloride was observed through the study. Based on this, the substance has not achieved oxygen depletion of more than 60% within 28 days and cannot, be considered as readily and, thus, rapidly degradable in the environment in line with the GHS criteria.

BOD_5/COD

Not available.

Aquatic simulation tests

Not available.

Field investigations and monitoring data (if relevant for C&L)

Not available.

Inherent and Enhanced Ready Biodegradability tests

Not available.

Soil and sediment degradation data

Not available.

9.1.2 Environmental transformation of metals or inorganic metal compounds

Summary of data/information on environmental transformation

Not relevant for an organic tin compound.

9.1.3 Environmental fate and other relevant information

Not considered in this document.

9.1.4 Bioaccumulation

Table 41: Summary of relevant information on bioaccumulation

Method, test guideline, and deviation(s) if any	Species	Results	Remarks	Reference
A non-guideline study	Natural community of algae	BCF after five (5) days exposure = 1.6 - 5.9.	Limited information provided on the study methods and results to conclude on the validity of the provided information.	Hall & Pinkey (1985)
A non-guideline study	*Artemia franciscana* (Crustacea)	BCF (24h) at 10 mg Sn/L exposure = 50 BCF (24h) at 100 mg Sn/L = 6	Limited information provided on the study methods and results to conclude on the validity of the provided information.	Hadjispyrou et al. (2001)
EPIWIN estimate		BCF = 3.16 L/kg	Low reliability as the EPIWIN model has not been developed and validated for organometallic substances	Review article or handbook (2006): 2006-07-23

Estimated bioaccumulation

An EPIWIN estimation is available that derived a BCF value of 3.16 L/kg. The results are not relevant for classification purposes.

Measured partition coefficient and bioaccumulation test data

Dimethyltin dichloride has a very low octanol-water partition coefficient, i.e. log K_{ow} = -2.18 measured at 22^{o}C (OECD TG 105, Spruit & Schilt 2003).

Two experimental aquatic bioaccumulation studies are considered. A non-guideline study on bioaccumulation of dimethyltin dichloride in algae resulted a BCF ranging from 1.6-5.9 (Hall & Pinkey, 1985). The available summary of the study in Annex I does not provide sufficient details to evaluate its reliability and therefore the study is considered as a supportive study only, for classification purposes.

Another non-guideline bioaccumulation study tested bioaccumulation of dimethyltin dichloride to an aquatic crustacean *Artemia franciscana* (Hadjispyrou et al. 2001). The test was performed at two concentrations (10 and 100 mg/L). The BCF factor of dimethyltin dichloride was reported to be 50 at 10 mg Sn/L to 6 at 100 mg Sn/L (Sn = tin). Also this study is not reported in detail and it is considered as a supportive study for classification purposes.

9.1.5 Acute aquatic hazard

Table 42: Summary of relevant information on acute aquatic toxicity

Method, test guideline, and deviation(s) if any	Species	Test material	Results	Remarks	Reference (NA = not available)
Fish					
OECD TG 203	*Danio rerio* (formerly *Brachydanio rerio*)	Dimethyltin dichloride	The 96h LC_{50} and 96h NOEC were determined to be >100 and ≥ 100 mg/l, Based on nominal concentrations (measured concentrations were >80% of nominals and therefore no reason to use measured concentrations)	GLP, minor deviations	Author not disseminated (2003). Report date 2003-09-14.
OECD TG 203	red killifish *Oryzias latipes*	Dimethyltin dichloride	LC_{50}(48h): 6 mg/L; not known if the values were based on nominal or measured conc.	GLP compliance not reported; methods not reported in detail	Nagase et al. (1991)
Review article with no methodological information.	*Misgurnus fossilis*	Dimethyltin dichloride	Maximum acceptable concentration for development: 100-1000 mg/L; not known if the values were based on nominal or measured conc.	NA, No GLP	Summer et al. (2003)
Invertebrates					
OECD TG 202	*Daphnia magna*	Dimethyltin dichloride	**EC_{50}(48h): 17 mg/L.** The value is based on nominal concentrations (measured concentrations were >80% of nominals and therefore no reason to use measured concentrations)	GLP compliant	Author not disseminated (2003). Report date 2003-09-14.
Proposed OECD Acute Immobilization Test (1981)	*Daphnia magna*	Dimethyltin dichloride	EC_{50}(24h): 88 mg/L. Based on nominal concentrations.	No GLP compliance	Vighi & Calamari (1985)
A non-guideline study	*Daphnia magna*	Dimethyltin dichloride	EC_{50}(24h): 19.27 mg/L. Based on nominal concentrations.	GLP compliance not reported.	Kungolos et al. (2004)
A non-guideline study conducted in accordance with generally accepted scientific principles	*Artemia franciscana*	Dimethyltin dichloride	LC_{50}(24h): 80.7 mg/L.	GLP compliance not reported.	Hadjispyrou et al. (2001)
A result quoted in a review paper	Aquatic crustacea: *Rithropanopeus harrisil*	Dimethyltin dichloride	LC_{50}(14d): 10-20 mg/L.	GLP compliance not reported.	Eisler (1989)
no information on method (value taken from a review	*Brachionus plicatilis*	Dimethyltin dichloride	LC_{50}(24h): 74 mg/L.	No GLP compliance	Summer et al. (2003)

paper)					
OECD TG 201	*Desmodesmus subspicatus*	Dimethyltin dichloride	ErC_{50}(72h): 37 mg/L ErC_{90}(72h): >110 mg/L EbC_{50}(72h): 11.8 mg/L EbC_{90}(72h): 47 mg/L All values based on measured (geom. mean) concentrations.	GLP compliant	Author not disseminated (2003). Report date 2003-09-08.
Non-standard test method	*Scenedesmus obliquus* and *Platyrnonas* sp.	Dimethyltin dichloride	*S. obliquus:* ErC_{50}(96h) = 805.84 ng/L 0.000806 mg/L *Platymonas* sp.: ErC_{50}(96h) = 988.69 ng/L 0.000988 mg/L Based on nominal concentrations.	No GLP compliance	Huang et al. (1996)
Non-standard test method	*Scenedesmus quadricauda, Ankistrodesmus falcatus and Anabaena flos-aquae*	Dimethyltin dichloride	*S. quandricuada*: IrC_{50}(4h) = 4.1 mg/L *A. falcatus:* IrC_{50}(4h) = 21 mg/L *A. flos-aquae:* IrC_{50}(4h) > 5 mg/L	No GLP compliance	Wong et al. (1982)
OECD TG 201	*Skeletonema costatum*	Dimethyltin dichloride	EbC_{50}(72h) > 9.8 mg/L (cell number) EbC_{50}(96h) > 9.8 mg/L (cell number) ErC_{50}(72h) > 9.8 mg/L (growth rate) ErC_{50}(96h) > 9.8 mg/L (growth rate) Based on nominal concentrations.	GLP compliant	Author not disseminated (1996). Report date 1996-03-12.
Non-standard test method	*Scenedesmus obliquus*	Dimethyltin dichloride	ErC_{50}(96h) = 1118.4 µg/L = 1.118 mg/L based on nominal conc.	No GLP compliance	Huang et al. (1993)
No methodological information reported	*Skeletonema costatum* and *Thalassiosira pseudonana*	Dimethyltin dichloride	EC_{50}(72h) > 0.93 mg/L	GLP compliance not reported	based on secondary source (Dobson et al. (2006))

The study results that were the basis for the proposed classification are highlighted in bold letters in the Table above.

Acute (short-term) toxicity to fish

Three acute toxicity studies in fish are available.

The study in zebrafish (*D. rerio*) was performed according to the OECD TG 203 and GLP principles. Several minor deviations from the standard protocol were reported (deviations in aeration regime, storage, temperature, etc.) but were assumed to have no major impact on the results of the study. Only one concentration of the test substance was applied and no mortality was observed in control or at 100 mg/L exposure to dimethyltin dichloride during the 96-h study. The test fulfilled the validity criteria as required in the relevant OECD Guideline.

The acute toxicity study in red killifish (*Oryzias latipes*) was also performed according to OECD TG 203. The fish were exposed to five concentrations of dimethyltin dichloride for 96 h. The LC_{50} (48 h) was reported to be 6 mg/L. For unknown reasons, the 96-h LC_{50} value was not reported. The overall documentation and reporting of the study methods and results was not sufficient, namely information on

exposure conditions, data on controls, analytical monitoring and maintenance of test concentrations, etc. is missing. Furthermore, both section 4.1.1.3 of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) and the relevant OECD Guideline 203 indicate that a 96 hour LC_{50} value should be reported. As such, the study results were not considered relevant for classification purposes.

The third acute toxicity study in fish (Misgurnus fossilis) was not performed according to any standard protocols and GLP principles. The test type, exposure duration, analytical monitoring methods have not been described, whilst no LC_{50} value was reported. As such, the study results were not considered relevant for classification purposes.

Acute (short-term) toxicity to aquatic invertebrates

Six studies are available on acute toxicity of dimethyltin dichloride to aquatic invertebrates.

One study followed the OECD Guideline 202 and GLP principles. The study is well reported and considered as fully reliable and EC_{50}(48h) for *D. magna* was 17 mg/L.
Due to methodological and reporting deficiencies (e.g. shorter test duration, no information on analytical monitoring, etc.) the results from the other five studies on aquatic invertebrates have only been considered in a supportive capacity, for classification purposes. It is noted that the EC_{50} values derived from these studies ranged between 10 and 88 mg/L.

Acute (short-term) toxicity to algae or aquatic plants

Two available algae studies were performed according to the OECD Guideline 201 and GLP principles. Both studies have been considered as relevant for classification purposes

Firstly, in the 72-h study, *Desmodesmus subspicatus* was exposed to five concentrations (0, 1.1, 3.6, 11, 36 and 111 mg/L) of dimethyltin dichloride. The resulting toxicity values were ErC_{50}(72h): 37 mg/L (growth rate) and EbC_{50}(72h): 11.8 mg/L (biomass) based on the mean measured concentration of the substance.

Secondly, in the 96-h study, *Skeletonema costatum* was exposed to five nominal concentrations (0.098, 0.49, 0.98, 4.9, and 9.8 mg/L) of dimethyltin dichloride. The recorded acute toxicity was too low to define reliable EC_{50} values (both cell numbers and growth rate).

The remaining algae studies were not performed according to internationally recognised study guidelines, there was no analytical monitoring, no information on results other than the toxicity values and their reporting was limited. Consequently the study results were not considered relevant for classification purposes. It is noted that the EC_{50} values derived from these studies ranged between 0.8 μg/L and 4.1 mg/L.

Acute (short-term) toxicity to other aquatic organisms

Not available.

9.1.6 Long-term aquatic hazard

Table 43: Summary of relevant information on chronic aquatic toxicity

Method, test guideline, and deviation(s) if any	Species	Test material	Results	Remarks	Reference
OECD TG 201	*Desmodesmus subspicatus*	Dimethyltin dichloride	NOErC (72h): 1.1 mg/L ErC_{10}(72h): 5.7 mg/L EbC_{10}(72h): 2.9 mg/L NOEC not defined for the biomass endpoint. All values based on measured (geom. mean) concentrations.	GLP compliant	Author not disseminated (2003). Report date 2003-09-08.
OECD TG 201	*Skeletonema costatum*	Dimethyltin dichloride	NOEbC(72h) = 4.9 mg/L (cell number) NOEbC(96h) = 0.98 mg/L (cell number) NOErC(72h) = 4.9 mg/L (growth rate) NOErC(96h) = 4.9 mg/L (growth rate) Based on nominal concentrations.	GLP compliant	Author not disseminated (1996). Report date 1996-03-12.

Chronic toxicity to fish

Not available.

Chronic toxicity to aquatic invertebrates

Not available.

Chronic toxicity to algae or aquatic plants

NOEC and ErC_{10} values are available for two algae studies performed according to the OECD Guideline 201 and GLP principles (the same studies as for acute toxicity). For *Desmodesmus subspicatus* the defined NOErC (72h) was 1.1 mg/L and ErC_{10} (72h) was 5.7 mg/L (growth rate). For *Skeletonema costatum* NOErC (72h) was 4.9 mg/L based on nominal concentration. Both studies are considered relevant to be used for classification purposes.

Chronic toxicity to other aquatic organisms

Not available.

9.1.7 Comparison with the GHS criteria for hazardous to the aquatic environment

Acute aquatic hazard

There are several acute toxicity studies available for all trophic levels (see section 9.1.5 and Table 42 for more details).

In fish, only the study performed according to the OECD TG 203 and GLP principles and a reported 96h LC50 value of above 100 mg/L was deemed relevant to be used for classification purposes.

In crustacea, only the study performed according to OECD TG 202 and GLP principles and a reported 48h EC50 value of 17 mg/L in Daphnia magna was deemed relevant to be used for classification purposes. This was also the basis for the proposed acute classification.

In algae, two studies were performed according to OECD TG 201. The lowest concentration for which toxicity was observed was 37 mg/L.

Comparing the information derived from the most reliable and fully documented acute aquatic toxicity studies available with the GHS criteria (Table 4.1.1.(a)), a classification as Category Acute 3 [acute aquatic toxicity value above 10 but below (or equal to) 100 mg/L] applies.

Long-term aquatic hazard (including bioaccumulation and degradation)

Bioaccumulation

The available information on bioaccumulation (experimental log Kow = -2.18; two non-guideline studies showing BCF from 1.6 to 50) indicate that dimethyltin dichloride has low potential for bioaccumulation since the substance does not meet the GHS criteria (log Kow ≥ 4 or BCF ≥ 500) to be considered potentially bioaccumulative.

Rapid degradation

The available studies on hydrolysis (DT_{50} > 1 year) and ready biodegradability (degradation ~ 3% in the 35 d extended test according to OECD Guideline 301F) indicate that dimethyltin dichloride should be considered as not rapidly degradable according to the GHS criteria.

Chronic aquatic toxicity

As mentioned in section 9.1.6, chronic aquatic toxicity of dimethyltin dihclorate is available only for one trophic level: algae. As both studies were deemed as relevant for classification purposes, the results from the most sensitive one [NOErC (72h) = 1.1 mg/L] were considered in classification for long-term aquatic hazard. This results in no classification for long-term aquatic hazards.

Table 4.1.1 (b) (i) of GHS applies and based on this no chronic classification should be appointed. However, since there are no adequate chronic data available for fish and crustacea, the surrogate approach should be considered for those trophic levels. Based on the acute toxicity in *D. magna* (EC50(48h) = 17 mg/L) and non-rapid degradation, the classification based on Table 4.1.1 (b) (iii) applies and the substance should be classified in Category Chronic 3. Since this is more stringent than the classification based on the available chronic data, dimethyltin dichloride should be classified as Category Chronic 3 for long term (chronic) hazard according to GHS.

9.1.8 Conclusion on classification and labelling for hazardous to the aquatic environment

Based on the presented information classification as Category Acute 3 and Category Chronic 3 are proposed for dimethyltin dichloride.

9.2 HAZARDOUS TO THE OZONE LAYER

9.2.1 Conclusion on classification and labelling for hazardous to the ozone layer

Dimethyltin dichloride is not included in *The Montreal Protocol on Substances that Deplete the Ozone Layer* and therefore it is not proposed to be classified in this hazard class.

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