Committee for Risk Assessment

RAC

Annex 1

Background document

to the Opinion proposing harmonised classification and labelling at Community level of

2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate / (MMT(EHMA))

ECHA/RAC/CLH-O-0000001981-71-01/A1

EC number: 260-828-5
CAS number: 57583-34-3

Adopted
14 September 2011

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PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

Substance Name: 2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate / (MMT (EHMA))

EC Number: **260-828-5**

CAS number: 57583-34-3

Registration number (s):

Purity: 90 % w/w

Impurities: 2-ethylhexyl mercaptoacetate, trimethyltin chloride, dimethyltin dichloride, trichloromethylstannane

A classification proposal was submitted and discussed at ECB (TC C&L) for health endpoints in October 2006. Classification for health was concluded by TC C&L in September 2007 and the classification that was finally agreed in September 2007 is proposed in the present dossier. For information, discussions and conclusions of the TC C&L as reported in summary records and follow-up of the corresponding meetings are presented in Annex I of the present report.

In agreement with article 36 (1) of CLP, only mutagenicity and developmental toxicity are proposed for harmonisation in this dossier. Toxicokinetic information and repeated toxicity data are displayed for information so as to provide a general toxicological profile on MMT(EHMA) but are not proposed for harmonisation.

Classification & Labelling in accordance with the CLP Regulation

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
	2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate; MMT (EHMA)	260-828-5	57583-34-3	Repr. 2	H361d[1]	GHS08 Wng	H361d			

[1] It is the view of RAC that hazard statement H361d is the most appropriate, given the available toxicological profile of MMT(EHMA), but RAC recognised that H361 could be applied if the available criteria are applied strictly

Classification & Labelling in accordance with Directive 67/548/EEC:

Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling	Concentration Limits	Notes
	2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate; MMT (EHMA)	260-828-5	57583-34-3	Repr. Cat. 3; R63	Xn R: 63 S: (2)-22-36/37		

JUSTIFICATION

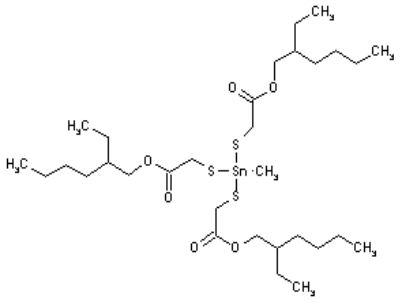
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Chemical Name:	2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate
EC Number:	260-828-5
CAS Number:	57583-34-3
IUPAC Name:	8-Oxa-3,5-dithia-4-stannatetradecanoic acid, 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-, 2-ethylhexyl ester

1.2 Composition of the substance

Constituent

Chemical Name:	2-ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate
EC Number:	260-828-5
CAS Number:	57583-34-3
IUPAC Name:	8-Oxa-3,5-dithia-4-stannatetradecanoic acid, 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]thio]-4-methyl-7-oxo-, 2-ethylhexyl ester
Molecular Formula:	C31H60O6S3Sn
Structural Formula:	
Molecular Weight:	743.7 g/mol
Typical concentration (% w/w):	Not known
Concentration range (% w/w):	> 80%

Impurities

Information on impurities based on the MMT(EHMA) registration dossier has been included in the the IUCLID 5 CLH dossier (confidential).

Several impurities can have a possible influence on hazard properties and classification of MMT(EHMA) depending on their concentration in MMT(EHMA).

However, the classification proposed in this dossier as displayed above does not take into account additional classifications based on impurities as impurity content can vary depending on the production process and its possible improvements.

According to articles 10 and 11 of Regulation (EC) No 1272/2008 (CLP Regulation), the potential influence of impurities on classification remains of the responsibility of the manufacturer/importer.

1.3 Physico-chemical properties

REACH ref Annex, §	Property	IUCLID section	Value	[enter comment/reference or delete column]
VII, 7.1	Physical state at 20°C and 101.3 KPa	3.1	Liquid	
VII, 7.2	Melting/freezing point	3.2	- 85 to - 65 °C	Crompton GmbH 2001
VII, 7.3	Boiling point	3.3	≥ 260 °C	Crompton GmbH 2001
VII, 7.4	Relative density	3.4 density	1.18 g/cm³ at 20 °C	BASF 2000
VII, 7.5	Vapour pressure	3.6	No data	
VII, 7.7	Water solubility	3.8	2.4 mg/l (25°C)	de Roode and de Haan 2004; Migchielsen 2004; Oldersma et al. 2004
VII, 7.8	Partition coefficient n-octanol/water (log value)	3.7 partition coefficient	10.98	Calculated USEPA 2000b

Table 1: Summary of physico- chemical properties

2 MANUFACTURE AND USES

2.1 Manufacture

No data available

2.2 Identified uses

Used as a heat stabilizer in PVC.

No use known for general public.

3 CLASSIFICATION AND LABELLING

3.1 Classification in Annex I of Directive 67/548/EEC

No current classification in Annex VI of CLP regulation.

3.2 Self classification(s)

No information available.

4 ENVIRONMENTAL FATE PROPERTIES

Not covered by this dossier.

5 HUMAN HEALTH HAZARD ASSESSMENT

5.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

MMT(EHMA) (purity 78.6%) was tested under low pH (0.6-0.7) conditions (0.07 N HCl) at 37°C in order to simulate the possible hydrolytic action on mammalian gastric contents (Schilt, 2004). Under acidic conditions it is expected that the tin-EHMA bond breaks, leading to formation of the corresponding alkyltin chloride and release of the ligand EHMA. The liberated EHMA may hydrolyse further, forming thioglycolic acid (TGA) and 2-ethylhexanol (EH). The degree of hydrolysis was studied by determination of the sum of amounts of EHMA and EH formed after 0.5, 1.0, 2.0 and 4.0 hours, using GC-FID. The experiment were performed in duplicate.

The conversion of MMT(EHMA) to EHMA+EH and MMTC was rapid. The calculated percentage of hydrolysis was 93.9% after 0.5 hours (87.0% EHMA and 6.9% EH). Assuming first-order kinetics, the half-time of the simulated gastric hydrolysis of MMT(EHMA) was estimated to be 0.27 hours. An apparent decrease of the percentage of hydrolysis in time was observed: 90.6% at 1h (82.1% EHMA and 8.5% EH), 84.8% at 2h (72.0% EHMA and 12.8% EH) and 78.0% at 4h (58.6% EHMA and 19.4% EH). It is possible that with increased time, other hydrolysis product are formed from the initial hydrolysis products EHMA and EH.

It should be noted that taken into account an hydrolysis of 94% and the respective molecular weight of MMT(EHMA) (744 g/mol) and of MMTC (241 g/mol), 1 mg MMTC is expected to be released from 3.28 mg MMT(EHMA).

5.2 Acute toxicity

5.2.1 Acute toxicity: oral

Species	LD_{50}	Observations and remarks	Ref.
Rat 5/sex/dose	880 mg/kg bw	Test substance: MMT(EHMA) (purity not known) Doses: 0.50, 0.80, 1.25, and 3.15 g/kg bw Mortality: 0.50 g/kg: Males: no mortality; Females: 1 dead at 24 h 0.80 g/kg: Males: no mortality; Females: 2 dead at 24 h, 2 dead at 48 h 1.25 g/kg: Males: 3 dead at 24 h; Females: 4 dead at 24 h, 1 dead at 48 h 3.15 g/kg: Males: 5 dead at 24 h; Females: 5 dead at 24 h Body weight generally increased for all animals in the 0.50 and 0.80 g/kg dose groups, as well as for males in the 1.25 and 3.15 g/kg dose groups. A slight decrease was noted in the body weights of females in the dose groups >=1.25 g/kg. Clinical observations included depression, comatose, piloerection, eye squinting, hunched posture, labored breathing, ataxia, fecal stains, urine stains, and masticatory movement. Signs of systemic toxicity increased with increasing dose levels.	Morton, 1996a

		Gross necropsy results (animals that died during the test): Lungs: pale, reddened, or mottled Liver: pale or mottled with darkened edges, or white/blanched areas Speen: pale, darkened, or mottled Pancreas: darkened Kidneys: enlarged, pale, and/or congested Stomach: distended Intestines: reddened, distended, and contained a viscous yellow/orange fluid Bladder: contained a red fluid, external staining noted	

5.2.2 Acute toxicity: inhalation

Not covered by this dossier

5.2.3 Acute toxicity: dermal

Species	LD_{50}	Observations and remarks	Ref.
Rabbit	LD_{50} (males) = 2150 mg/kg LD_{50} (females) = 1000 mg/kg	Test substance: MMT(EHMA):DMT(EHMA); actual purity not reported but MMT(EHMA) predominant Cumulative mortality (total number of deaths/total number dosed), by sex and dose level: 215 mg/kg: 0/2 females 464 mg/kg: 0/2 females 1000 mg/kg: 1/2 females (day 3); 0/2 males 2150 mg/kg: 2/2 females (days 3, 6); 1/2 males (day 4) 4640 mg/kg: 2/2 males (days 4, 6) 10,000 mg/kg: 2/2 males (day 3) Clinical signs included death, uncoordinated movements, and shaking and hypersensitivity to external stimuli. All clinical symptoms of toxicity disappeared in surviving animals by the end of the exposure period. Irritative effects were erythema, edema, atonia, desquamation, and blanching. Gross necropsy results for animals that died during observation included irritated intestines, blanched stomach, reddened lungs, pale or congested kidneys, and oral, ocular, and/or nasal discharge.	Hill Top Research, 1983
Rabbit	>1050 mg/kg	Test substance: DMT(EHMA):MMT(EHMA); (70:20%) Dose: 1050 mg/kg, undiluted Patches removed after 24-hrs No deaths or test substance-related systemic effects were observed over the 14-day observation period. Male and	SRI Interna-tional, 1993

		female rabbits in the treatment group showed varying degrees of skin irritation including thickened skin and chapped and flaky skin, as early as day 2 of observation; all signs of irritation had disappeared by day 12.	

5.2.4 Summary and discussion of acute toxicity

By oral route, a single acute toxicity study is available and reports a LD_{50} of 880 mg/kg in rats.

By dermal route, an acute toxicity study is available on a mixture of MMT(EHMA): DMT(EHMA) of unknown ratio but containing mainly MMT(EHMA). It reports a LD_{50} of 1000 mg/kg in female rabbits. No death was reported in male and female rabbits at 1050 mg/kg in a dermal acute toxicity study on a mixture of DMT(EHMA):MMT(EHMA); (70:20%). Results from these two studies indicate that toxicity seen in females in the mixture with unknown ratio can be attributed to MMT(EHMA).

Information on acute toxicity is reported here for information only, so as to provide a general toxicological profile on MMT(EHMA).

This point is however not proposed for harmonisation.

5.3 Irritation

Not covered by this dossier

5.4 Sensitisation

Not covered by this dossier

5.5 Repeated dose toxicity

5.5.1 Repeated dose toxicity: oral

A simulated gastric hydrolysis study of methyltin tris(EHMA) found that under low pH conditions (similar to mammalian gastric systems) all of the available EHMA ligands had been released and there was >90% hydrolysis of the test substance (Schilt, 2004). The results of this simulated gastric hydrolysis study of methyltin tris(EHMA) support the use of the chloride derivative, methyltin trichloride (MMTC), as the anchor compound for the mono-methyltin family of compounds to the extent possible for the repeated dose, mutagenic and developmental effects endpoints. Available data on EHMA are also presented.

Species	Dose mg/kg body weight, mg/kg diet	Duration of treatment	Observations and Remarks	Ref.
Rat (n=10/s	30, 150, 750	13 weeks	Test substance: MMTC:DMTC; (82.85:9.29%) Impurity profile is presented in a confidential	Appel, 2004

ex/dose plus 10 females for the satellite group)	ppm (equivalent to 1.9, 9.8 and 49.7 mg/kg bw/day in males and 2.1, 10.2 and 53.6 mg/kg bw/day in females)		Appendix I of the present report (separate file). The possible sub-chronic toxicity of the test substance in rats was examined using continuous administration via the diet for 13 consecutive weeks (OECD 408). In satellite groups of female rats, a reproduction/developmental screening test (OECD 421) was performed to provide initial data on possible reproductive and developmental effects of trichloromethylstannane. The 13-week study comprised four groups of 10 rats/sex and the satellite study used four groups of 10 female rats. Male rats from the main study were mated, after a premating period, with female rats of the satellite groups which were fed the same dose of test diets. (See section 5.8.2 Developmental Toxicology) **Range Finding:** Dietary doses of 50, 250, 750, and 1500 ppm trichloromethylstannane were administered in diet for 14 days. The body weights were sporadically decreased in males of the 750 ppm group and throughout at 1500 ppm. Food consumption was significantly decreased in males of the 750 and 1500 ppm groups on day 7 and 14. Food consumption was significantly increased in females of the 50 and 250 ppm groups (day 7) and significantly decreased in females of the 750 ppm group (days 7 and 14) and the 1500 ppm group (day 7). Food conversion efficiency was significantly decreased in males of the 1500 ppm group (days 7 and 14). The absolute weights of the testes were significantly decreased in the males of the 50 and 1500 ppm groups. Absolute spleen weights, relative kidney weights and absolute and relative liver weights were significantly decreased in the males of the 1500 ppm group. Absolute weights of the ovaries were significantly increased in the females of the 250 ppm group and decreased in the females of the 1500 ppm group. Absolute and relative spleen weights were significantly decreased in females of the 750 and 1500 ppm groups. Dietary exposure of trichloromethylstannane up to 1500 ppm for 14 days was tolerated; however, the body weight and food consumption decreases were deemed palatability effects at 750 and 1500 ppm. The low food intake, low food efficiency, and organ weight effects at these doses were suggestive of a toxic response threshold. **Main Study:**	

			TEST SUBSTANCE INTAKE: Overall intake of the test substance for the 30, 150 and 750 ppm groups was 1.9, 9.8 and 49.7 mg/kg bw/day, respectively, in males and 2.1, 10.2 and 53.6 mg/kg bw/day, respectively, in females. - Body weight gain: Similar among the groups in males and females throughout the study. - Food consumption: Similar among the groups in males throughout the study. Food consumption was slightly higher (ca. 8%) in females of the 750 ppm group. This difference was statistically significant during the last three weeks of the study. - Food conversion efficiency: Similar among the groups in males and females throughout the study. An occasional significant difference was seen. - Neurobehavioral testing: In animals of the 750 ppm group, some statistically significant effects were observed during neurobehavioural testing at the end of the study in week 13. In males, increases in forelimb gripstrength, landing footsplay and body temperature were measured, and a marginal effect was shown on click response. Hyperactivity was clearly observed in both males and females. The changes were considered related to treatment and toxicologically relevant. - Clinical chemistry: At the end of the treatment period the following statistically significant differences (relative to the control group) were observed: ALP: increased in males of the 750 ppm group and decreased in females of the 30 ppm group; ASAT: increased in males and females of the 750 ppm group; Albumin: increased in males of the 750 ppm group; Albumin/globulin ratio: decreased in females of the 750 ppm group; Urea: increased in males of the 750 ppm group; Creatinin: increased in males of the 750 ppm group; Total bilirubin: decreased in females of the 750 ppm group; Cholesterol: increased in males of the 750 ppm group Phospholipids: increased in males of the 750 ppm group; Chloride: increased in males of the 750 ppm group; Potassium: decreased in males of the 750 ppm group.	

			- Haematology: RBC, Hb and PVC were statistically significantly increased in females and MCV and MCH were statistically significantly increased in males of the 750 ppm group. Thrombocytes (females) and prothrombine time (males and females) were statistically significantly decreased in the 750 ppm group. Absolute and relative numbers of eosinophils were significantly decreased in females of the 750 ppm group. Haematology parameters were similar among the control, 30 and 150 ppm groups, with the exception of a statistically significantly lower number of neutrophils in males of the 30 ppm groups, which was considered a chance finding. - Urinalysis: Urinary pH and urinary crystals were statistically significantly increased in males and females of the 750 ppm group. Other semiquantitative and microscopic urinary observations were similar among the groups. - Renal concentration test: Urinary volume was statistically significantly increased and urinary density was statistically significantly decreased in males and females of the 750 ppm group. - Organ weights: The following organ weights were statistically significantly increased in the 750 ppm group: · Absolute (males and females) and relative (males) adrenal weights; · Absolute and relative kidney weights (males and females). The following organ weights were statistically significantly decreased in the 750 ppm group(49.7 mg/kg bw/day males; 53.6 mg/kg bw/day females): · Absolute and relative thymus weights (males and females); · Absolute and relative brain weights (females); · Absolute and relative spleen weight (males); · Absolute and relative epidydimidal weights At microscopical examination, treatment related histopathological changes were observed in the thymus and the brain. Six males of the 750 ppm group showed a decreased cortex/medulla ratio in the thymus. This change was also present in three females. The treatment related histopathological changes in the brain consisted of loss of perikarya of neuronal cells in specific areas of the brain. All females and all but one male showed loss of perikarya in the pyramidal layer of the Hippocampus	

			CA1/2. In addition, four males of the 750 ppm group demonstrated loss of perikarya in the piriform cortex, which was also considered related to treatment. Based on the changes in neurobehavioural parameters, haematology, clinical chemistry, urinalysis and organ weights and the associated histopathological findings in thymus and brain in animals of the 750 ppm group (49.7 mg/kg bw/day males; 53.6 mg/kg bw/day females), the NOAEL in the sub-chronic toxicity study was placed at 150 ppm (equivalent to 9.8 mg/kg bw/day in males and 10.2 mg/kg bw/day in females).	
Rat (n=10/sex/dose)	20, 100 and 500 ppm (in feed) Estimated to be equivalent to 1.2, 6 and 30 mg/kg bw/day in males and 1, 5 and 25 mg/kg bw/day in females	13 weeks	Methyltin Trichloride : Dimethyltin Dichloride (78:22%) mixture Decreased mean body weight gain at 500 ppm (males), decreased mean specific gravity of urine from rats fed 500 ppm test substance (both sexes); decreased volume of urine at 100 ppm (males) and increased volume of urine at 500 ppm (males); increased relative kidney weight at 20 and 500 ppm (females); increased relative thymus weight at 100 ppm (females). Histopathological observations considered treatment-related included slight to moderate epithelial hyperplasia in the bladder (males in the 100 and 500 ppm groups; females in all treatment groups) and enlarged epithelial nuclei and foamy cytoplasm of the proximal tubules in the intercortico-medullary region of the kidneys (males and females in the 500 ppm group). The NOAEL of the methyltin mixture was less than the 20 ppm test concentration.	Til, 1978
Rat 5/sex/dose	0, 0.05, 0.1 and 0.2% (actual dose received: males: 42, 82, and 168 mg/kg/day; females: 45, 87, and 173 mg/kg/day)	28 days	2-ethylhexyl mercaptoacetate; Purity >98% Body weight : There were no statistically significant differences between the bodyweights of EHMA treated groups. - Food consumption: There were no statistically significant differences between the food intakes of male control rats and male rats treated with the three dose levels of EHMA. Female rats treated with EHMA consistently consumed more diet than the control group throughout the study. These differences were statistically significant for female rats treated with 0.05 % EHMA on study days 20-24 and 24-27 respectively, and for animals given 0.1 % EHMA on study days 20-24. - Clinical signs: no abnormalities of condition or	BIBRA, 1998

			behavior related to treatment were seen in rats given EHMA. - Hematological findings : The white blood cell and lymphocyte counts for EHMA treated male rats were lower than the controls, and these differences were statistically significant for the 0.1 % and 0.2 % EHMA dose groups. The mean cell haemoglobin for male rats treated with 0.2 % EHMA was statistically significantly lower than the controls. Female rats treated with 0.2% EHMA had statistically higher haematocrit values, mean cell volumes and platelet counts than the control animals. - Clinical biochemistry findings: There were no statistically significant differences between control and EHMA treated female rats, in the three dose groups, for any of the serum chemical measurements. For male rats the only statistically significant difference between control and EHMA treated animals was an increase in aspartate aminotransferase activity in the 0.2 % EHMA group. - Mortality : none - Gross pathology incidence : no change related to treatment. - Organ weight changes: Male rats administered 0.05 % and 0.2% EHMA had statistically significantly higher relative kidney weights than the controls, but these differences were not apparent from the statistical analysis of the absolute kidney weights. Female rats treated with 0.1 % EHMA had significantly higher absolute and relative kidney weights than the control animals. The absolute kidney weights of female rats treated with 0.05 % EHMA were also statistically significantly higher than those of the control females. Male liver weights were not affected by treatment with EHMA. In the EHMA treated female groups, the only statistically significant effect on liver weights was an increase in the relative liver weights of animals given 0.1 % EHMA, compared with controls. These changes did not exhibit a dose-response relationship and are not considered to be biologically relevant. - Biochemical examination of the liver: Hepatic protein concentrations were slightly higher than controls in male and female rats treated with the two top doses of EHMA (0.1 % and 0.2 %, though the	

			differences were not statistically significant. Treatment with EHMA did not produce any statistically significant increases in cyanide-insensitive palmitoyl-CoA oxidation or lauric acid 11- and 12-hydroxylation in male or female rats. There were no significant changes in microsomal protein concentrations of EHMA treated male and female rats compared with the control group. - Histopathology : Histopathological examination of the kidneys from female rats treated with the three dose-levels of EHMA showed a statistically significant incidence of nephrocalcinosis. Nephrocalcinosis was not seen in male rats treated with EHMA. Nephrocalcinosis is not uncommon in female rats and is not considered to be treatment related. Examination of the lungs from animal numbers 1 and 34 showed interstitial pneumonitis and perivascular cuffing. Microgranuloma were also seen in the lungs from animal n°1. Haematoxylin and eosin stained liver sections from male and female rats treated with EHMA did not show any significant histological changes compared with the control groups. Oil red O stained sections of control livers from both sexes showed large amounts of fat in the periportal areas. Treatment with 0.2 % (168 mg/kg/day in males; 173 mg/kg/day in females) EHMA and 0.05% (42 mg/kg/day in males; 45 mg/kg/day in females) EHMA produced little reduction in the amount of periportal fat in the livers from male and female rats compared with the controls. Treatment with 0.1 % (82 mg/kg/day in males; 87 mg/kg/day in females) EHMA gave a variable reduction of periportal fat. In some male and female rats a slight reduction was seen, while in others no change occurred. Statistical analysis showed no significant trend for the reduction in periportal fat with increasing dose of EHMA. - Electron microscopic examination : Peroxisomes in liver cells from control male rats appeared as small spherical structures of fairly regular size scattered throughout the cytoplasm of the hepatocytes. Most contained a prominent electron dense core and the number and morphology of peroxisomes appeared similar in both portal and centrilobular areas. Administration of 0.2 % EHMA to male rats appeared to have little effect on the peroxisome population of hepatocytes. The peroxisomes remained small and were scattered throughout the	

			cytoplasm but showed a variation in the numbers per cell. Portal and centrilobular areas were similar and most peroxisomes appeared to have electron dense cores. In livers from control female rats the appearance of peroxisomes was similar to those of the male rats. The peroxisomes were small and scattered throughout the cytoplasm. The appearance of electron dense cores in the peroxisomes was variable, and the nature of peroxisome size and distribution was similar in portal and centrilobular areas. The administration of up to 0.2 % EHMA in the diet of rats for 28 days does not lead to a proliferation of hepatic peroxisomes, and does not produce any treatment-related effects.	

5.5.2 Repeated dose toxicity: inhalation

Not covered in this dossier

5.5.3 Repeated dose toxicity: dermal

Not covered in this dossier

5.5.4 Summary and discussion of repeated dose toxicity:

Information on repeated dose toxicity by oral route is reported here for information only, so as to provide a general toxicological profile on MMT(EHMA) and assist evaluation of developmental effects.

This point is however not proposed for harmonisation.

5.6 Mutagenicity

5.6.1 In vitro data

Test	Species Test system	Conc.	Metabol. activ.	Observations and Remarks	Ref.
Ames assay	Salmonella typhimurium TA1535, TA1537, TA98, TA100, and TA102; Escherichia coli	16.7, 50, 167, 500, 1670, and 5000 µg/plate	With and without S9 (from Aroclor 1254-induced male rat	Test substance: MMT(EHMA) (purity not known) Negative The test article was evaluated	Morton International, 1996b

	WP2 uvrA		liver)	using both liquid pre-incubation and plate incorporation treatment. Except for strain WP2 uvrA, inhibited growth was observed at the highest 1-3 doses evaluated. In addition, the test article was found to be incompletely soluble at doses ≥ 500 µg/plate. Statistically significant increases in revertant frequencies, to approximately 1.6- to 2.0-fold control values were observed in strains TA1537 and TA1535 at a dose of 16.7 µg/plate without S9 under liquid pre-incubation and plate incorporation conditions, respectively. However, these increases were not dose dependent, and the observed revertant frequencies approximated historical control values. Revertant frequencies for all other doses and strains approximated or were less than control values. All positive and negative control values were within acceptable ranges. Thus, the slight increase observed in strains TA1537 and TA1535 was considered spontaneous.	

5.6.2 In vivo data

A simulated gastric hydrolysis study of methyltin tris(EHMA) found that under low pH conditions (similar to mammalian gastric systems) all of the available EHMA ligands had been released and there was >90% hydrolysis of the test substance (Schilt, 2004). The results of this simulated gastric hydrolysis study of methyltin tris(EHMA) support the use of the chloride derivative, methyltin trichloride (MMTC), as the anchor compound for the mono-methyltin family of compounds to the extent possible for the repeated dose, mutagenic, and developmental effects endpoints.

Test	Species Test system	Conc.	Observations and Remarks	Ref.
Micronucleus assay (n= 10 males	Rat Gavage	37, 111, 333, 1000 mg/kg	Test substance: MMTC(purity 98.53%; DMTC 1.32%) Solvent: 0.9% sodium chloride	deVogel, 2003

in the 333 mg/kg, 1000 mg/kg and vehicle control groups and n=5 males/group in the 37 mg/kg, 111 mg/kg and positive control groups)		(single dose)	Positive. A rat micronucleus assay, conducted according to OECD Test Guideline 474, demonstrated that methyltin trichloride (98.53% purity) produced a statistically significant increase in the number of micronucleated polychromatic erythrocytes (MPE) at dose levels of 37 mg/kg bw and above. The MPE response did not increase with increasing dose and was transient, appearing only 24 hours after treatment, but not at 48 hours after treatment. These results could be judged equivocal or characterized as weakly positive for induction of MPE from bone marrow cells in rats. Methyltin trichloride did not increase the number of polychromatic erythrocytes (PE) in the dosed animals and no clinical signs were observed. Lowest concentration at which a weak genotoxic effect was observed, was 37 mg/kg bw. Mean number of MPE per 2000 polychromatic erythrocytes in negative control, 37, 111, 333 and 1000 mg/kg MMTC and mitomycin C (1.5 mg/kg): 24h-harvest: 1.2±0.4, 3.0±1.2*, 1.8±0.4, 3.0±1.4*, 3.4±1.7*, 26.8±3.3* 48h-harvest: 2.4±1.8, -, -, 1.8±1.1, 1.6±0.9, - * $p<0.05$ (t-tests)	

5.6.3 Human data

No data available

5.6.4 Summary and discussion of mutagenicity

Originally the weak genotoxic effect of MMTC *in vivo* has been considered relevant to classify Muta. cat. 3; R68 (cf CLH dossier for MMTC). This classification was agreed at TC C&L of October 2006. RAC has re-evaluated these data and concluded that as supported by the *in vitro* data MMTC is not considered genotoxic and that the proposed classification (Muta 2; H341 according to the CLP criteria, and Muta. cat. 3; R68 according to the DSD criteria) is not warranted. (see RAC CLH opinion for MMTC).

It should be noted that in the *in vivo* test, MMTC contains a low proportion of DMTC. The available data suggests that DMTC is not mutagenic *in vivo* (DMTC classification proposal, 2006).

5.7 See Carcinogenicity

No data available

5.8 Toxicity for reproduction

5.8.1 Effects on fertility

Not covered in this dossier

5.8.2 Developmental toxicity

A simulated gastric hydrolysis study of methyltin tris(EHMA) found that under low pH conditions (similar to mammalian gastric systems) all of the available EHMA ligands had been released and there was >90% hydrolysis of the test substance (Schilt, 2004). The results of this simulated gastric hydrolysis study of methyltin tris(EHMA) support the use of the chloride derivative, methyltin trichloride (MMTC), as the anchor compound for the mono-methyltin family of compounds to the extent possible for the repeated dose, mutagenic, and developmental effects endpoints. Available data on EHMA are also presented.

Species	Route	Dose	Exp. time	Exp. period	Observations and Remarks	Ref.
Rats (n=10 females for the satellite group)	Oral feed	30, 150, 750 ppm (equivalent to 1.2-2.1, 6.2-11.7 and 26.5-53.6 mg/kg bw/day)	Daily	ca. 5 weeks	Test substance: MMTC:DMTC; (82.85:9.29%). Impurity profile is presented in a confidential Appendix I of the present report (separate document). The possible sub-chronic toxicity of the substance in rats was examined using continuous administration via the diet for 13 consecutive weeks (OECD 408). In satellite groups of female rats a reproduction/ developmental screening test (OECD 421) was performed to provide initial data on possible reproductive and developmental effects of trichloromethylstannane. The main study comprised four groups of 10 rats/sex and the satellite study used four groups of 10 female rats (13-week study). (See section 5.5.1 Repeated dose toxicity: oral) In the satellite study female rats were fed their respective test diets beginning two weeks prior to the mating period, and continued on test diets through mating, gestation and up to PN 4or shortly thereafter. Male rats from the main study	Appel, 2004

					were mated after a premating period with female rats of the satellite groups. **TEST SUBSTANCE INTAKE:** The test substance intake of the female animals of the 30, 150 and 750 ppm dose groups was respectively: Premating period days 0-7: 1.8, 9.0 and 44.5 mg/kg bw/day days 7-14: 1.8, 8.8 and 43.9 mg/kg bw/day Gestation period GD 0-7: 1.9, 9.6 and 44.5 mg/kg bw/day GD 7-14: 2.0, 9.6 and 45.8 mg/kg bw/day GD 14-21: 1.2, 6.2 and 35.9 mg/kg bw/day Lactation period PN 1-4: 1.7, 11.7 and 26.5 mg/kg bw/day **MATERNAL TOXIC EFFECTS:** - Mortality and day of death: One animal of the 750 ppm group was found dead on GD 22 (i.e. 37 days after the start of exposure). The animal found dead on day 37 was necropsied. Findings included yellow patches on the liver, yellow appearance of the small intestines, haemorrhagic discharge from the vagina and a haemothorax. The haemothorax was considered to be the probable cause of death. Most probably the haemothorax was caused by severe dystocia, since at necropsy the uterus contained 12 dead fetuses. - Maternal Body weight: Increased body weight change from GD 7-14 of the females of the 30 ppm group, which was considered a chance finding. Mean body weights (change) of the females were similar among the control, 30 and 150 mg/kg group during the entire study. Mean body weight (changes) between PN 1-4 of the 750 ppm group was decreased; however, no statistical significance was reached for these findings. - Food consumption: Food consumption of the female animals of the 750 ppm group was decreased (not statistically	

					significantly) during the lactation period. During the premating and gestation periods food consumption of the females was similar in the control, 30, 150 and 750 ppm groups. - Mating index: 100, 90, 100 and 100% in the control, 30, 150 and 750 ppm groups, respectively. - Fertility index: 90, 80, 90 and 80% in the control, 30, 150 and 750 ppm groups, respectively. - Mean number of implantations: 11.2 (control group), 10.8 (30 ppm), 11.6 (150 ppm), 10.5 (750 ppm). - Gestation index: 89, 100, 100 and 88% in the control, 30, 150 and 750 ppm groups, respectively. - Number of pups born (number of litters): 90(8), 86(8), 99(9) and 50(7) for the control, 30, 150 and 750 ppm groups, respectively - Number of stillborn pups (number of litters): 2(1), 3(2), 0 and 2(2) for the control, 30, 150 and 750 ppm groups, respectively. - Live birth index: 98, 97, 100 and 96% in the control, 30, 150 and 750 ppm groups, respectively. - Post implantation losses [total implantation sites minus total live births at the first observation]: 13(18.6%), 16(15.3%), 5(4.7%) and 36*(42.9%) for the control, 30, 150 and 750 ppm groups, respectively. (* $p<0.001$) **FETAL DATA:** - Litter size: The mean number of pups delivered per litter amounted to 11.2, 10.8, 11.0 and 7.1 for the control, 30, 150 and 750 ppm groups, respectively. - Litter weight: The mean pup weights and pup weight changes were similar in the treated groups when compared to the	

					control group. - Pup mortality: 2.2, 3.5, 0 and 4% for the control, 30, 150 and 750 ppm groups, respectively at PN 1; 16, 25, 3 and 16% for the control, 30, 150 and 750 ppm groups, respectively at PN 4 (at 750 mg/kg, $p<0.001$ for difference in pups lost between PN1 and PN4 compared to controls). - Number viable: The viability index (PN 1-4) was 84, 75, 97 and 35% in the control, 30, 150 and 750 ppm groups, respectively. - Number live pups per litter: 11.0, 10.4, 11.0 and 6.9 for the control, 30, 150 and 750 ppm groups, respectively at PN 1; 10.6, 7.8, 10.7 and 4.2 for the control, 30, 150 and 750 ppm groups, respectively at PN 4. Interpretation of these data was complicated by the incidence of missing pups across groups. A variable incidence of pups "missing" after birth was recorded. The number of missing pups at PN 4 was 14 in controls (16% of pups born alive), 21 (25%) in the low-dose group, 3* (3%) in the mid-dose group and 30* (62%) in the high-dose group (*statistically different from controls). The missing pups were presumed to have been cannibalized by the dams, but it is not known if the missing pups were alive or dead. It is also not known if some pups were cannabilized prior to being counted for litter size at birth. This could account for the slightly lower number of recorded live births and the slightly higher post-implantation loss in the high-dose versus controls. The reason for missing pups can not be determined on the basis of the data within the study. Missing pups could be due o a toxic behavioral effect on dams which caused a lack of, or abnormal, nurturing. No malformations were noted at any observation point for any of the missing	

					pups and no overt behavioral effects were noted, however some other toxic effect on the pups could have caused the dam to eat them. NOAEL (prenatal toxicity): Based on the increase in post-implantation loss in the 750 ppm group, 150 ppm can be considered as a NOAEL for postnatal toxicity. NOAEL (prenatal toxicity): Based on the decrease of viability index in the 750 ppm group, 150 ppm can be considered as a NOAEL for postnatal toxicity. NOAEL (maternal toxicity): Based on the effects observed on body weight and food consumption in the 750 ppm group, 150 ppm (equivalent to 6.2 - 11.7 mg/kg bw/day in females) was considered to be the NOAEL for maternal toxicity.	
Rats (number not given)	Oral – drinking water	12.0, 40 or 120 mg/L tin;	Females exposed for 14 days before breeding and through breeding, gestation, birth and nursing until the pups were weaned at 21 days.		Test substance: MMTC (purity not given but verified before use according to the article) Male rat pups were exposed to monomethyltin trichloride (MMTC) via their dam's drinking water throughout gestation and post partum until 21 days of age. At 11 days of age, the pups were tested for acquisition and extinction learning ability in an appetitive learning paradigm, and at 21 days for learning ability in a one trial swim escape learning test. At 11 days, pups from dams exposed to 120 mg/L Sn as MMTC displayed significantly significant increases in acquisition time, while all dose groups (12, 40, 120 mg/L MMTC) displayed significant decreases in extinction learning ability as compared to controls. At 21 days of age, animals exposed to 12 mg/L and 120 mg/L MMTC displayed higher escape times than controls.	Noland, 1982
Rats Sprague-Dawle	Oral-drinking water	Experiment #1 0, 10, 50, 245 ppm in	14 days pre-mating, through Day 11 post natal [ca. 7 weeks]		Test substance: MMTC (purity 97%) The possible developmental neurotoxicity of MMTC in rats was examined using continuous administration via drinking	Moser, 2005

y (CD-CRL) 53-54 days old (n=30 females/group)		water (equivalent to 1.0-1.8, 5.3-10.6 and 23.3-41.6 mg/kg bw/day) Purity of test substance 97%.		water beginning 14 days prior to cohabitation & mating through Day 21 of the post natal period. The study complied with the US EPA Developmental Neurotoxicity Test [DNT] guideline [US EPA 870.6300 which us equivalent to the OECD 426. Four groups of 30 female rats/group were used. Litters were culled to 8 males on PND1. **MATERNAL ENDPOINTS:** There were no changes in maternal Body weight throughout the study. - Number of dams delivering litters: 10 (control group), 11 (10 ppm), 11 (50 ppm), and 12 (245 ppm). Necropsy of all non-pregnant dams or dams not delivering revealed resorptions in only two control rats and one rat from the low dose group. Incidence of pregnancy, late delivery, and resorptions were not statistically different across treatment groups. **DATA ON OFFSPRING:** - Litter size: The mean number of pups per litter was: 12.5 (control group), 15.2 (10 ppm), 13.1 (50 ppm), and 13.4 (245 ppm). Litter birth weights and body weights across time were similar across treatment groups throughout the entire study. In addition, there were no differences in weights of the pups selected for each behavioral test. Live birth index and Viability index were not provided in the published article, but the author stated there were no differences across groups. There was any cannibalization in any group. There were no effects on any measure of growth, development, cognitive function, or apoptosis following MMTC exposure. There was a trend towards decreased brain weight in the high dose group. In addition,	

				there was vacuolation of the neuropil in a focal area of the cerebral cortex of the adult offspring in all MMT dose groups (1–3 rats per treatment group). This is a mild neuropathological lesions observed in the offspring at PND85-90. The finding was called ”restricted” by the author and was given no weight in the overall conclusion. The finding is of uncertain biological significance and its relation to treatment was unclear. The author concluded that perinatal exposure to MMTC did not result in neurobehavioral, or cognitive deficits. The NOEL was 245 ppm [23.3-41.6 mg/kg bw], the highest dose tested.	
Rats Sprague-Dawley (CD-CRL) timed-pregnant (n=17-18 females/group)	Oral drinking water	Experiment #2 0, 500 ppm in water (equivalent to 55.8-94.3 mg/kg bw/day) Purity of test substance 97%.	Gestation Day 6 [GD6] through Postnatal Day 21 [PND21] [ca. 5 weeks]	Test substance: MMTC (purity 97%) This experiment is a second developmental neurotoxicity assessment of MMTC in rats. MMTC was administered via drinking water from GD6 through PND21. This study complied with the US EPA and OECD Developmental Neurotoxicity Test [DNT] guidelines.Two groups [17 control and 18 treated] of female rats were used. Litters were culled to 8 [4 males and 4 females] on PND4 and weaned on PND21. **MATERNAL ENDPOINTS:** There was a significant depression of fluid intake across all but one day of treatment with MMTC at 500 ppm. This indicates that the “tolerated dose” was reached or exceeded. Only the intake measured 3 days post-parturition was not different than controls. During gestation, MMTC consumption was about 80–88% of control levels, and during lactation, 82–88% of control. Despite the lowered intake, body weight was not different in the treated group. All of the timed-pregnant females in the control group delivered, but two in the MMTC group did not. These rats were not evaluated for implantation sites. All of the deliveries occurred when expected. In the	Moser, 2005

				MMTC group, one litter was killed by the dam shortly after birth and another litter consisted of all females and was not used. Live birth index and Viability index were not provided in the published article, but the author stated there were no differences across groups. **DATA ON OFFSPRING:** - Number of pups per litter: 11.9 (control group), 12.2 (500 ppm). Body weight changes during the lactation period showed no differences except on PND11, male and female pups in the control group were different by about 4g. This was within biological variability. There were no treatment effects on body weight after weaning. Behavioral assessments included the runway task (PND11), motor activity habituation (PND17), and Morris water maze (PND 85-90 (adults)). MMTC exposure did not alter pup runway performance, motor activity, or cognitive function. The NOEL was 500 ppm [55.8-94.3 mg/kg bw], the highest dose tested.	
Rat 12/sex/ group	Gavage	10, 50 and 150 mg/kg bw /day	Males received 15 daily doses prior to mating. Males were dosed throughout the mating period for a total of 54 doses. Females received a minimum of 15 daily doses prior to pairing and were dosed through lactation	2-ethylhexyl mercaptoacetate; Purity >98% **Parental toxicity:** Three males and 3 females in the 150 mg/kg/day group were found dead or euthanized in extremis. Males died on study days 4 or 14 while females died on gestation days 21 or 22. Prior to death/euthanasia, 2 of these males and 1 female had marked body weight losses; these males also had decreased defecation, unkempt appearance and/or red or yellow material on various body surfaces. The female that was euthanized in extremis had signs of dystocia (hypoactivity, an unkempt appearance, piloerection, soft stool, drooping eyelids, hypothermia and was recumbent and unresponsive to	Wil Research, 2005

				handling). These premature deaths were attributed to the test article. In addition, 1 female in the 150 mg/kg/day group was euthanized due to total litter loss on lactation day 1. All other animals survived to the scheduled necropsies. Clear material around the mouth and/or nose was observed in the 50 mg/kg/day group males and the 150 mg/kg/day group males and females following dose administration. There were no test article-related clinical findings in the 10 mg/kg/day group males and females or in the 50 mg/kg/day group females. There were no test article-related effects on male and female mating and fertility indices, male copulation index or female conception index. The mean number of days between pairing and coitus in the test article-treated groups were similar to the control group value. Mean body weights and/or body weight gains in the 150 mg/kg/day group males were generally reduced throughout the study. Mean food consumption in these males was similar to that in the control group during the pre- and post-mating periods. During the pre-mating period, no test article-related effects on body weight gain and food consumption were observed in the 150 mg/kg/day group females. However, mean maternal body weight gain in these females was lower during gestation days 17-20; the reduction was attributed to a female with a small litter size (8 corpora lutea) and 1 of the females that was found dead on gestation day 21 (lost 21 g during gestation days 17-20). Gestation food consumption was unaffected by test article administration in this group. During lactation, mean body weight gain and food consumption in the 150 mg/kg/day group were similar to that in the control group. There were no test article-related effects on mean body weights or food consumption in the 10 and 50 mg/kg/day group males and females	

				throughout the study. Mean gestation lengths in the test article-treated groups were similar to that in the control group. Two females in the 150 mg/kg/day group were found dead on gestation day 21, near the time of expected parturition, 1 female was euthanized in extremis on gestation day 22 with signs of dystocia, and 1 female was euthanized due to total litter loss on lactation day 1. Pale liver and/or white areas in the liver were observed in 2 males and 1 female in the 150 mg/kg/day that were found dead or euthanized in extremis. These findings correlated to hepatocellular vacuolization and were considered test article-related. At the scheduled necropsies, no test article-related macroscopic lesions were observed, including in the liver; this precluded further evaluation of the liver for microscopic lesions. However, mean relative (to final body and brain weight) liver weights in the 150 mg/kg/day group males and females were increased, and the increase was considered related to the lesions observed in the unscheduled death animals. Mean relative (to final body weight) kidney weight was increased in the 150 mg/kg/day group males. Mucification of the cervical and vaginal epithelium was noted microscopically in the 150 mg/kg/day group gravid females that died or were euthanized in extremis prior to the scheduled necropsy on lactation day 4. This finding may be a morphologically normal peri-parturitional phenomenon, but since there were no control group animals examined at that age, this cannot be unequivocally established. However, there was a dose-related increase in incidence and severity of mucification compared to the control group at the scheduled necropsy on lactation day 4. Although this finding itself was not considered abnormal morphologically, its presence on lactation day 4 was clearly increased compared to the control group. Taken in context of the maternal mortality, dystocia and adverse effects on pup growth and survival,	

				mucification of the vaginal epithelium in the 150 mg/kg/day group was considered test article-related. No test article-related effects on the mean numbers of corpora lutea, implantation sites or unaccounted-for sites were observed at any dosage level. Slight reductions in the mean numbers of corpora lutea and implantation sites were observed in the 150 mg/kg/day group. The decreases resulted in a reduced mean number of pups born and corresponded to lower mean maternal body weight gain late in gestation. These slight reductions in mean numbers of corpora lutea and implantation sites and the number of pups born was not considered test article-related as these decreased mean values were attributed primarily to a single female with only 8 corpora lutea. Decreased viability and growth of the F1 animals through post-partum day 4 also occurred at the 150 mg/kg/day dose. There were no test article-related effects on the general physical condition of the pups or pup body weights in the 10 and 50 mg/kg/day groups. At the necropsy of pups that were found dead, there were no internal findings that were related to parental treatment with the test article. In this study, decreased viability and growth of the F1 animals through post-partum day 4 occurred in the 150 mg/kg/day dose but marked parental systemic toxicity was also observed in this group. It was characterized by: mortality, moribundity, decreased mean body weight gain, decreased consumption of feed, increased liver and kidney weight, or hepatocellular vacuolization in at least one sex of the F0 animals; and increased mucification of the cervical and vaginal epithelium in post-partum F0 dams. Within the limits of the experimental design, a dosage level of 50 mg/kg/day was considered to be the no-observed-adverse-effect level (NOAEL) for	

				developmental, systemic and neonatal toxicity resulting from exposure to EHMA when administered orally by gavage to rats.	

5.8.3 Human data

5.8.4 Other relevant information

5.8.5 Summary and discussion of reproductive toxicity

An OCDE 421 study provides an indication of an adverse effect of MMTC on development (decreased viability and post-implantation loss) in the absence of maternal toxicity but the interpretation of the study is not clear due to postnatal cannibalization by the dams and a classification Repro. Cat. 3 – R63 is warranted (cf CLH dossier for MMTC) and was agreed at TC C&L of September 2007.

It should be noted that in the OECD 421 study (Appel, 2004), MMTC contains *ca.* 10% of DMTC. However, the data available on DMTC suggests that DMTC is foetotoxic with a LOAEL of 15 mg/kg and a NOAEL of 10 mg/kg in rat (DMTC classification proposal, 2006). In OECD 421 study, effects of MMTC are seen at the highest dose of *ca.* 50 mg/kg, which contains around 5 mg/kg of DMTC and the effects seen with MMTC can therefore not be attributed to DMTC.

Due to the high degree of hydrolysis of MMT(EHMA) in EHMA and monomethyltin and the developmental effect observed on MMTC, a classification **Repro. Cat. 3 – R63** is also warranted for MMT(EHMA) and was agreed at TC C&L of September 2007 (CLP Repr. 2 – H361d) .

6 HUMAN HEALTH HAZARD ASSESSMENT OF PHYSICO-CHEMICAL PROPERTIES

Not covered in this dossier

7 ENVIRONMENTAL HAZARD ASSESSMENT

Not covered in this dossier.

JUSTIFICATION THAT ACTION IS REQUIRED ON A COMMUNITY-WIDE BASIS

The substance has CMR properties, i.e. mutagenicity and developmental toxicity that justify harmonising its classification and labelling.

In this aim, a classification proposal was submitted and discussed at ECB (TC C&L) for health endpoints in October 2006. Classification for health was concluded by TC C&L in September 2007 and the classification that was finally agreed in September 2007 is proposed in the present dossier.

For information, discussions and conclusions of the TC C&L as reported in summary records and follow-up of the corresponding meetings are presented in Annex I of the present report.

In agreement with article 36 (1) of CLP, only mutagenicity and developmental toxicity are proposed for harmonisation in this dossier. Toxicokinetic information and repeated toxicity data are displayed for information so as to provide a general toxicological profile on MMT(EHMA) but are not proposed for harmonisation.

OTHER INFORMATION

No other information relevant

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ANNEX I

Collection of discussions of MMT(EHMA) classification at ECB

For health effects, MMT(EHMA) classification was first discussed at the Technical Committee of Classification and Labelling (TC C&L) in October 2006. Health classification was concluded at the TC C&L in September 2007.

Environmental effects were not discussed at ECB.

Extract from document ECBI/13/07 Rev. 2 - Draft Summary Record - Meeting of the Technical Committee C&L on the Classification and Labelling of Dangerous Substances - Arona, 4-5 October 2006

Methyltin tris(2-ethylhexyl- mercaptoacetate, MMT (EHMA) (F051) [4]

EC number: 260-828-5, CAS number: 57583-34-3

Classification proposal : [Muta. Cat. 3; R68 - Repr. Cat. 3; R63 - Xn; R21/22 - Xn; R48/20/21/22 - Xi; R43]

ECBI/25/06 Add 1	F, differences in opinion for MMTC, MMT (EHMA) and TERP
ECBI/26/06	French C&L proposal, as prepared by IND, for MMT (EHMA)
ECBI/26/06 Rev. 1	French revised C&L proposal for MMT (EHMA)

Acute toxicity:

Xn: R21/22 was proposed. It has to be controlled if data exist for the dermal route, since DMTC was not classified for this route. Xn; R22 was agreed and Xn; R21 was postponed to the next meeting.

Sensitisation:

R43 was proposed, but **D** and **BE** did not agree. No classification for sensitization was agreed by the Group.

Long term toxicity:

Xn; R48/20/21/22 was proposed, but no classification was agreed, due to lack of data of this specific compound.

Reprotoxicity:

The reprotoxicity discussion was postponed, as for MMTC.

Mutagenicity:

R68 was agreed without further discussion.

Conclusion:

The **TC C&L** agreed not to classify **Methyltin tris(2-ethylhexyl- mercaptoacetate, MMT (EHMA)** with Xn; R48/20/21/22 and R43. The TC C&L agreed to classify **Methyltin tris(2-ethylhexyl- mercaptoacetate, MMT (EHMA)** with **Muta. Cat. 3; R68 - Xn; R22**.

The **reprotoxicity discussion and acute dermal toxicity were postponed to the next meeting** to allow the experts to look once more into the data.

Extract from : Follow-up III of the meeting of the Technical Committee on Classification and Labelling in Arona, 26-28 September 2007

Methyltin compounds: **F049 [1]** **Methyltin trichloride, MMTC** **CAS: 993-16-8** **EC: 213-608-8** **Classification:** Muta. Cat. 3; R68 *Agreed 1006* Repr. Cat. 3; R63 *Agreed 0907* Xn; R22 *Agreed 1006* [N; R50/53] *To be discussed* **Labelling:** Xn R: 22-63-68[-50/53] S: (2-)36/37[-60-61] **Classification assigned in accordance with the CLP Regulation:** Muta. 2; H341 Repr. 2; H361d Acute Tox. 4; H302 [Aquatic Acute 1; H400] [Aquatic Chronic 1; H410] FR confirms that the acute tox. data are consistent with the classification shown. **F051 [2]** **Methyltin tris(2-ethylhexyl-mercaptoacetate, MMT(EHMA)** **CAS: 57583-34-3** **EC: 260-828-5** **Classification:** Muta. Cat. 3; R68 *Agreed*	*In October 2006* the TC C&L on the basis of the F proposal (ECBI/27/06) it was agreed to classify MMTC for mutagenicity in category 3 and with Xn; R22 for acute toxicity. It was agreed not to classify for corrosivity and repeated dose toxicity. *In October 2006* the TC C&L on the basis of the F proposal (ECBI/26/06 Rev. 1) it was agreed to classify MMT(EHMA) for mutagenicity in category 3 and with Xn; R22 for acute toxicity. It was agreed not to classify for sensitisation and repeated dose toxicity. (*In October 2006* the discussion of the classification for the two dimethyltin compounds: Dimethyltin dichloride, DMTC (EC No: 212-039-2, CAS No: 753-73-1) and Dimethyltin bis(2-ethylhexyl- mercaptoacetate, DMT(EHMA) (EC No: 260-829-0, CAS No: 57583-35-4) were concluded) **IND** gives in their paper ECBI/27/06 Add. 1 information on maternal toxicity and reprotoxicity of MMTC. Document ECBI/27/06 Add. 2 is a scientific paper on Evaluation of developmental neurotoxicity of organotins via drinking water in rats. Furthermore the following documents were sent by IND: ECBI/27/06 Add. 3 parts I, II, III and IV on reprotoxicity of MMTC as well. **S** commented by email on the reprotoxicity of MMTC (ECBI/27/06 Add. 4) and re-submitted the expert report ECBI/30/04 and the Guidelines for Developmental Toxicity Risk Assessment from the EPA (ECBI/27/06 Add. 5). **IND** sent further information requested by the TC C&L in documents ECBI/27/06 Add. 6 (I-IV) and ECBI/27/06 Add. 7 (I, II) distributed with Revision 2 of the September agenda *MS were asked to send their comments to the new information forwarded by IND within the deadlines for the September meeting.* **F** sent further comments developmental toxicity in their document ECBI/27/06 Add. 8 confirming their position to classify both substances with Repr. Cat. 3; R63. ***In September 2007*** the TC C&L agreed to classify MMTC and MMT(EHMA) with Repr. Cat. 3; R63 (Repr. 2 H361d).

1006 Repr. Cat. 3; R63 *Agreed 0907* Xn; R21/22 *Agreed 0907/1006* [NC for ENV] *To be discussed* **Labelling:** Xn R: [21]/22-63-68[-50/53] S: (2-)36/37[-60-61] **Classification assigned in accordance with the CLP Regulation:** Muta. 2; H341 Repr. 2; H361d Acute Tox. 4; H312 Acute Tox. 4; H302 *ENV still to be discussed* FR confirms that the acute tox. data are consistent with the classification shown.	In addition it was agreed to classify MMT(EHMA) with Xn; R21. ⇨ **Next ATP if ENV classification is concluded.** ECB will evaluate whether to make a written procedure and ask the TC C&L Environmental experts to agree on classification for F049 (N; R50-53 proposed by FR in ECBI/27/06) and F051 (NC proposed by FR in ECBI/26/06) for environment, else the partial classification concerning the environment should be handed over for discussion at ECHA with support of an Annex XV dossier**.** **After FU II:** **A written procedure for ENV has not been made and consequently the issue of classification of these substances for environmental effects will be discussed further.** ⇨ **Hand-over to ECHA**