

Europe's Grouping Strategy and the Chemical Universe:

All Organotin Compounds Are Not The Same

Donna Mondimore, Dieter Drohmann, Kevin Ross*

To speed up the identification of chemicals that need regulatory action, authorities may decide to address groups of structurally related substances rather than single substances. ECHA, EU Member States and the European Commission have developed an approach to assess groups of substances as a starting point where eventually regulatory action may be needed.¹ This activity has prompted harmonised classification and labelling and may potentially identify substances of very high concern (SVHCs²) leading to restrictions and an outright ban with no relevant scientific evidence.

I. Introduction

In 2022, the EU Commission tasked the European Chemicals Agency (ECHA) to prepare an investigation report on the potential risk posed by PVC additives used in PVC and PVC itself throughout the complete life cycle of PVC articles. Further, the Commission encouraged ECHA to apply a grouping approach due to the large number of substances concerned. The final report was issued in November of 2023.³ Supporting this grouping approach, in May 2024, Germany's Federal Institute for Occupational Safety and Health (BAuA) suggested grouping of substances as a whole instead of focusing only on their presence in PVC.⁴

In the last few years, ECHA's approach was to address groups of structurally related substances rather than single substances, in order to speed up the identification of chemicals that need regulatory action.⁵

The investigation report groups organotin stabilisers present in PVC and rates them with a 'higher health hazard' which 'may support the prioritisation of the substance groups from the point of view of potential further regulatory work'. The suggestion from BAuA can be interpreted to include the universe of organotin compounds for regulatory restrictions using hazard classifications that may be inaccurate and therefore inappropriate.

The opinion of Regulators to assess the organotins as groups and not as individual substances is a worrisome development. The proposed grouping approach is not supported by recognised scientific ev-

idence from recent toxicological information generated on organotin compounds. As an example, the approach for other substance groups goes so far that, in the case of Per- and polyfluoroalkyl substances [PFAS], a group of more than 10,000 substances is dealt with in a restriction proposal,⁶ which includes Polymers of Low Concern.

II. What Are Organotin Compounds?

Organotin compounds,⁷ or stannanes, are chemical compounds based on the tin element bonded to car-

* Dieter Drohmann is Founder and CEO of Chemservice. For correspondence: <d.drohmann@chemservice-group.com>; Donna Mondimore is Regulatory Manager at Chemservice Americas LLC. For correspondence: <d.mondimore@chemservice-group.com>; Dr. Kevin Ross is Global Director, Technical Service PMC Organometallics, Inc. For correspondence: <kross@pmc-group.com>.

1 Working with Groups, ECHA, see <<https://echa.europa.eu/working-with-groups>>.

2 Substances of Very High Concern.

3 Investigation Report on PVC and PVC Additives; European Chemicals Agency, P.O. Box 400, FI-00121, Helsinki, Finland ECHA.EU-ROPA.EU, Version Number: 1.0 (Final); Date 22/11/2023.

4 51st Meeting of Competent Authorities for REACH and CLP – open session REACH DE CA comments on Agenda Item 10.1 Investigation report on PVC and PVC additives.

5 Working with Groups, ECHA, see <<https://echa.europa.eu/working-with-groups>>.

6 Per- and polyfluoroalkyl substances (PFAS), ECHA, see <<https://echa.europa.eu/hot-topics/perfluoroalkyl-chemicals-pfas>>.

7 Organotin chemistry is the scientific study of the synthesis and properties of organotin compounds or stannanes, which are organometallic compounds containing tin-carbon bonds.

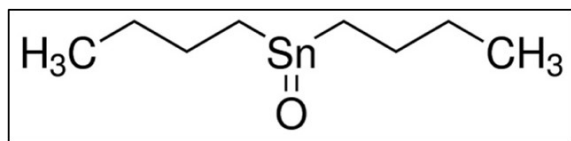


Figure 1: Chemical structure of Dibutyltin oxide (DBTO).

bon. These compounds are classified by the number of organic functional group's bond to tin (mono-, di-, tri-, and tetra-organotin compounds). Compounds with one 'carbon-tin' (C-Sn) bond are referred to as mono-substituted organotin compounds; two 'C-Sn' bonds are known as di-substituted tin compounds and three 'C-Sn' bonds are known as tri-substituted organotin compounds. Figure 1 illustrates the structural diagram of a di-substituted tin: dibutyltin oxide.

III. How Are Organotin Compounds Used?

The first patent for the use of organotin compounds in stabilising PVC was awarded in 1936.⁸ The heat that is needed during the processing of PVC causes polymer decomposition. Black coloration can be seen when as little as 0.1% of the polymer decomposes. To prevent colour formation during manufacture of articles such as window casings, film, etc. and to preserve the appearance of the PVC article during its life cycle, organotin compounds are used primarily as colour stabilisers, but they also improve the physical properties like tensile strength, impact resistance, and flexibility.

As the chemistry of organotin compounds became better understood, their application expanded to catalytic agents. Commercial uses include use in urethane systems, esterification, transesterification, silicone crosslinking, etc. Organotin catalysts are an essential component for the Electrodeposition Coatings [e-Coatings] that are applied to motor vehicles, automotive parts and appliances to provide corrosion protection.

The commercial organotin products currently available have been proven to work well in their respective applications. Mono-substituted organotin compounds e.g., methyltin (MMT), butyltin (MBT), octyltin (MOT), are used as heat stabilisers for polyvinyl chloride (PVC). Di-substituted organotin compounds e.g., dimethyltin (DMT), dibutyltin (DBT), dioctyltin (DOT), are used as catalysts and as heat stabilisers for polyvinyl chloride (PVC). Tri-substituted organotin compounds e.g., tributyltin (TBT), triphenyltin (TPhT) are used as biocides.

IV. What Is the Issue?

The overall toxicity picture for any substance depends on its own toxicity and on the toxicity of the degradation products formed under the conditions of use. For organotin compounds, great differences in toxicity exist among tetra-, tri-, di- and mono-organotin compounds.

Many research publications on the toxicology of organotin compounds study the organotin chloride species rather than the substance itself. Historically, the organotin industry assumed that all organotin compounds convert to their chloride analogue when ingested by mammals. For example, a typical PVC stabiliser, dimethyltin bis(2-ethylhexyl thioglycolate) [DMTE], would convert to dimethyltin dichloride due to the presence of hydrochloric acid in a mammal's stomach. Industry decided in the early days of REACH implementation that it would be cost effective (and save animals) to test the respective chloride species and use the toxicity data generated to conduct a read across to the other alkyltin compounds. Consequently, the assessments from regulators on critical health effects including genotoxicity, reproductive toxicity and immune system toxicity for the chloride species were applied to the whole substance group.

In 2017, industry took a new approach to the development of toxicity information for organotin compounds. Instead of assuming that a common surrogate compound could represent the family of organotin compounds, industry conducted toxicity testing on a specific organotin compound and augmented it with analysis of the gastric hydrolysis by-products of the compound. The first project used a sophisticated analytical method, Sn NMR spectroscopy, and demonstrated that dioctyltin bis(2-ethylhexyl thio-

⁸ US2219463A Application filed by Carbide and Carbon Chemicals Corp.

glycolate) [DOTE] hydrolysed to form dioctyltin chloro-(2-ethylhexyl thioglycolate) [DOTCE] under simulated gastric conditions. Additionally, developmental toxicity studies in rabbits and mice with DOTE demonstrated a substantially different toxicity profile of the substance compared to its surrogate: dioctyltin dichloride.⁹ This discovery then led a consortium of organotin producers to begin toxicity testing on specific organotins used in commerce in order to remove the surrogate data derived from alkyltin chloride compounds which has proven to be inaccurate. Consequently, the same testing protocol was conducted on dibutyltin bis(2-ethylhexyl thioglycolate) [DBTE] in 2021¹⁰, and dimethyltin bis(2-ethylhexyl thioglycolate) [DMTE] in 2023.¹¹ The results demonstrated that dialkyltin chloride compounds are not appropriate surrogates to represent the toxicity of all organotin compounds.

V. Response Through Advocacy

A European Union Harmonised Classification & Labelling has been assigned to dimethyltin bis(2-ethylhexyl thioglycolate) (DMTE: EC 260-829-0) in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation) during ATP o6. The harmonised classification and labelling of hazardous substances is updated through an 'Adaptation to Technical Progress (ATP)', which is issued yearly by the European Commission. Following the adoption of the opinion on the harmonised classification and labelling of a substance by the Committee for Risk Assessment (RAC), the European Commission takes a decision and publishes the updated list in an ATP.

At the time that ATP o6 was published in 2014, the only data available for use in classifying DMTE came from dimethyl tin dichloride. As such, the following classifications were assigned:

- Repr. 2 and H361: Suspected of damaging fertility or the unborn child
- STOT Rep. Exp. 1 and H 372: Causes damage to organs

In compliance with EU REACH compliance check, industry generated a 90-day toxicity study combined with a neurotoxicity study which provided a no-observed adverse-effect level (NOAEL) of 60 ppm (approximately 5.74 mg/kg/day) in females and 175 ppm (14.96 mg/kg/day) in males. An OECD 489 Comet As-

say (In Vivo Mammalian Alkaline Comet Assay) was completed in 2023. The test result was negative (indicating that DMTE is not mutagenic).

These new studies showed no test material-related or toxicologically significant changes in any of the developmental parameters investigated for DMTE. According to the new data, the classifications should be:

- Repr. – NOT CLASSIFIED
- STOT Rep. Exp. 2 and H373: May cause damage to nervous system and immune system through prolonged or repeated exposure

Following a CLH proposal in 2022 by Austria for Dibutyltin oxide (DBTO; EC Number: 212-449-1, CAS Number: 818-08-6), RAC concluded on a classification as Repr. 1B for both fertility and development (H360FD) using a category approach. This classification was finalised in the 21st ATP to the EU CLP Regulation published on January 5, 2024.¹² It will be legally enforced beginning on September 1, 2025.

Recent toxicity testing including a study on the reproductive and developmental toxicity of DBTO itself (OECD 422) showed the classification is unjustified. Moreover, unlike the test results from the analogue, dibutyltin dichloride, DBTO shows no effects regarding the fertility endpoints and also no induction of any foetal malformations.

The EU REACH registrants intend to challenge inaccurate harmonised classifications. The process does not allow industry to submit a proposal for change; only EU Member States can start the process. But, dossier preparation and submission is not the only challenge because any Member State can influence the decision to accept or reject a CLP dossier. Industry will have to engage individual Member State authorities to consider the view of industry as listed in the CLP dossier.

9 Costlow et al, 'Simulated gastric hydrolysis and developmental toxicity of dioctyltin bis(2-Ethylhexylthioglycolate) [DOTE] in rabbits and mice', *Regulatory Toxicology and Pharmacology*, Volume 87, 2017, 23-29.

10 Costlow RD, Nasshan H, Frenkel P, Salsbury J. Simulated gastric hydrolysis and developmental toxicity of dibutyltin bis(2-ethylhexyl thioglycolate) in rats. *J Appl Toxicol*. 2021 Nov;41(11):1794-1802.

11 Kirf et al, 'Simulated gastric hydrolysis and developmental toxicity of dimethyltin bis(2-ethylhexylthioglycolate) in rats', *Front. Toxicol.*, 21 February 2023. Sec. Developmental and Reproductive Toxicology. Volume 5 – 2023.

12 Commission Delegated Regulation (EU) 2024/197 of 19 October 2023 amending Regulation (EC) No 1272/2008 as regards the harmonised classification and labelling of certain substances.

VI. Conclusion

Harmonised classifications have global implications because authorities with limited capacity in toxicological evaluations (e.g., Southeast Asia) tend to adopt them. In the EU, Repr. 1B classifications are a stepping stone to move substances into the SVHC list and potential bans. The market deselection that follows

tends to be global and based on flawed regulatory decisions.

CLP criteria guidance clearly states that 'Good quality data on the substance itself have more weight than such data extrapolated from similar substances'.¹³ As outlined herein, grouping substances is not appropriate when scientific evidence demonstrates toxicological differences among the group of substances. In the case of organotin compounds, any grouping exercise should be based on accurate scientific evidence.

Industry is therefore called upon to conduct toxicological tests in good time and to take action against unfair substance classifications, since these will 'travel' globally.

¹³ Guidance on the Application of the CLP Criteria Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures Version 6.0 Jan 2024 [3.4.2.2.3.7. Weight of evidence].