

What does it mean?

Simulated gastric hydrolysis and developmental toxicity of dimethyltin bis(2-ethylhexylthioglycolate) in rats¹

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Substance: Dimethyltin bis(2-ethylhexylthioglycolate) (DMTE; CAS 57583-35-4)

Study type: Simulated gastric hydrolysis + prenatal developmental toxicity in rats (OECD TG 414, GLP)

Purpose: To test whether DMTE forms dimethyltin dichloride (DMTC) in the stomach and whether DMTE causes developmental toxicity².

1. Background and regulatory context

Multiple dimethyltin compounds have been classified as developmental toxicants based on **read-across** data from dimethyltin dichloride (DMTC), a compound known to cause developmental effects in animals. Historically, DMTE had been assumed to behave like **dimethyltin dichloride (DMTC)** in the stomach, with DMTC considered the toxicologically relevant breakdown product. That assumption underpinned prior regulatory concern for developmental toxicity. The present work directly tests this assumption using modern analytical methods and a guideline-compliant developmental toxicity study in a sensitive species.

2. Key questions addressed

- Does DMTE convert to DMTC under stomach-like conditions?
- Does DMTE cause maternal or developmental toxicity when administered orally during pregnancy?

¹ [Frontiers | Simulated gastric hydrolysis and developmental toxicity of dimethyltin bis\(2-ethylhexylthioglycolate\) in rats](#)

² Developmental toxicity is defined as the study of adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation (US EPA 1991)

- Is read-across from DMTC to DMTE scientifically justified for hazard classification?

3. Simulated gastric hydrolysis³

- DMTE was exposed to acidic conditions representative of the mammalian stomach (pH 1.2, 37°C for 72 hours).
- The study used ¹¹⁹Sn-NMR, which directly detects tin-containing species allowing unambiguous detection of DMTC if formed.
- Results:
 - DMTE did not convert to dimethyltin dichloride (DMTC) under simulated gastric conditions.
 - Instead, DMTE rapidly formed dimethyltin chloro-(2-ethylhexyl thioglycolate) (DMTEC).
 - DMTC was not detected, with an analytical detection limit of 0.5%.
- Regulatory relevance: These results show that the key assumption underlying the use of toxicity data produced for DMTC and subsequently used to classify the hazards for DMTE is not supported. DMTE does not generate the known developmental toxicant DMTC under gastric conditions.

4. Prenatal developmental toxicity study (rats)

Pregnant Wistar Han rats were dosed at 0, 5, 10, or 25 mg/kg bw/day by oral gavage from gestation day 6 to 20 following OECD Test Guideline 414 and GLP principles. Maternal health, pregnancy outcomes, and detailed foetal examinations were performed.

- Maternal findings:
 - No maternal deaths at any dose.
 - At 25 mg/kg bw/day, mild maternal toxicity was observed:
 - Reduced food intake
 - Reduced maternal body-weight gain
 - Reduced thymus weight
 - No changes in thyroid hormones (T3, T4, TSH).

³ Simulated gastric hydrolysis of chemicals is an in vitro (laboratory-based) procedure designed to mimic the digestive processes of the human stomach—specifically the breakdown of chemical compounds (drugs, food components, or nutrients).

- Developmental findings:
 - No effects on fertility, implantation, or litter size.
 - No treatment-related effects on foetal weight, growth, or sex ratio.
 - No dose-related increase in external, visceral, or skeletal malformations.
 - Observed foetal findings were isolated, non-dose-related, and within historical control ranges, supporting an incidental rather than treatment-related interpretation.
- NOAELs:
 - No observed adverse effect level (NOAEL)⁴: 10 mg/kg bw/day
 - Developmental NOAEL: 25 mg/kg bw/day (highest dose tested)
- Conclusion: DMTE was not teratogenic and not developmentally toxic in rats.

5. Overall regulatory conclusion

- DMTE does not hydrolyse to dimethyltin dichloride under simulated gastric conditions.
- The developmental toxicity profile of DMTE differs from that of DMTC.
- **DMTC is not a relevant metabolite of DMTE** under gastric conditions; therefore, DMTC is not an appropriate surrogate for hazard identification.
- Based on guideline-compliant animal data, **DMTE does not meet criteria for classification as a developmental or reproductive toxicant.**

6. Implications for read-across and classification

- Read-across from DMTC to DMTE **lacks mechanistic and empirical support.**
- DMTE shows a **distinct metabolic and toxicological profile** compared with chlorides.
- On the basis of these data, **classification of DMTE as a reproductive or developmental toxicant is not supported** under standard hazard classification frameworks (e.g., EU CLP / GHS).

7. Regulatory significance

⁴ Highest dose at which there was not an observed toxic or adverse effect.

These studies provide direct, substance-specific evidence addressing both metabolic behaviour under gastric conditions and in vivo developmental toxicity. The results demonstrate that prior hazard assumptions based solely on structural analogy to DMTC are not scientifically justified for DMTE. The data support the conclusion that DMTE is not teratogenic nor is it a developmental toxicant in rats which is relevant for risk assessment and classification decisions.

About GOSC

The [Global Organotin Stewardship Council](#), established in 2021, aims to enhance understanding of the intrinsic health and environmental properties of organotin compounds while highlighting their benefits. It actively communicates this information to stakeholders, ensuring scientific consistency and clarity.

Additionally, GOSC represents the major organotin manufacturers and technology sector in order to support Members and market organizations in their engagement globally with policy makers and regulatory authorities. The Global Organotin Stewardship Council (GOSC) consists of manufacturers of organotin manufacturers: Galata Chemicals, Gulbrandsen, Nitto Kasei Co., Ltd., PMC Group, Reagens S.p.A, Songwon Industrial Group, and TIB Chemicals AG.

GOSC monitors and responds to global Regulations on Organotins with the following objectives:

- Develop scientific and socioeconomic data to accurately assess organotin-based substances.
- Demonstrate that organotin-based substances can be safely handled.
- Assess if Organotin-based substances are easily replaced in the applications in which they are used and where they show outstanding performance or are critical in certain applications.
- Recommend justifiable regulatory action and/or appropriate risk management measures for organotin based substances.
- Promote the most appropriate regulatory management option for any initiative that may be triggered on organotin-based substances and develop regulatory consensus on it.