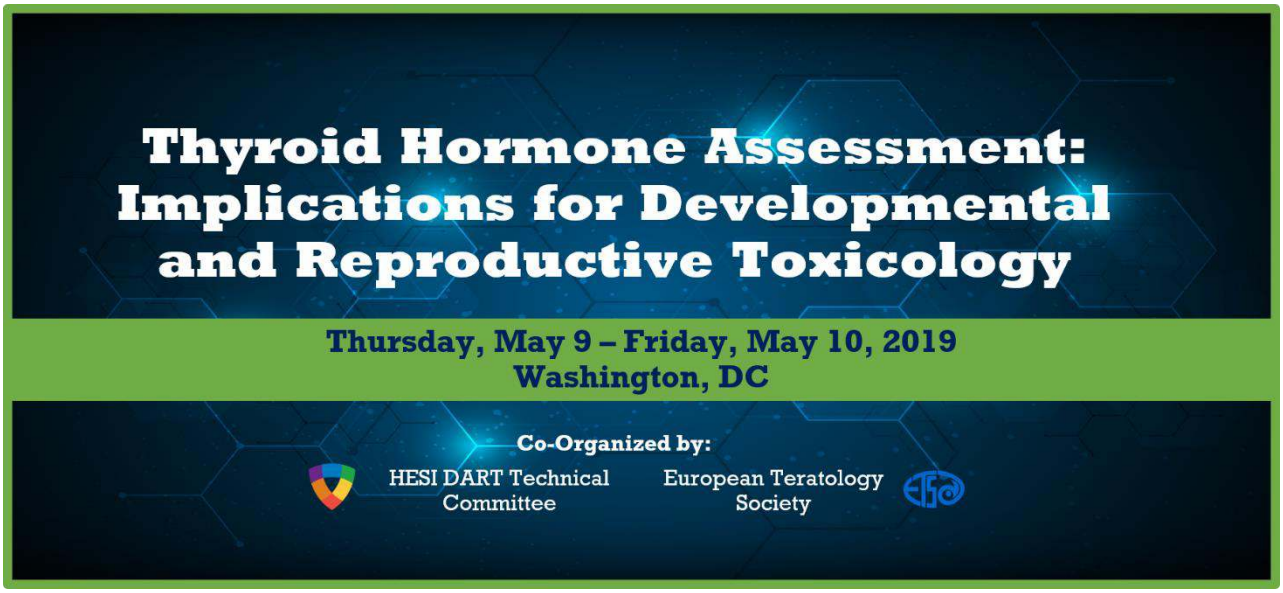

Recent updates to OECD developmental/reproductive toxicology guidelines and other regulatory guidelines and guidance require the measurement of thyroid hormone levels in the blood of mammalian laboratory species during development. Preliminary analyses indicate that there is a wide variability across laboratories in the methods being used to measure thyroid hormones in young rodents, as well as in the success of obtaining reliable data. Even though publicly available regulatory guidelines and guidance address study design, they allow varied approaches to thyroid hormone measurement in rodents, and an optimal study design or logical approach to thyroid hormone testing in young rodents has not yet been established in a regulatory testing context. Validity, accuracy, sensitivity and reproducibility of the assays are issues of concern. It is not clear to what extent variability in the data can be attributed to methodological issues or to innate biological variability.

This workshop aims to:

(1) Present the state-of-the-science on thyroid hormone assessments, specifically as it relates to preclinical methods and data collection, and identify gaps and knowledge as it relates to regulatory DART testing,
(2) Provide clarification and guidance regarding the collection (timing and methods), assessment (standardization and validation), and interpretation of thyroid hormone data (as it relates to adversity) for regulatory toxicology and risk assessment,
(3) Discuss and come to consensus on recommendations on how to improve data interpretation/understanding of thyroid changes and their relationship to adverse outcomes

AGENDA

DAY 1, THURSDAY MAY 9, 2019

7:30am – 8:30am	**Breakfast available**

Session 1: Setting the stage

8:30am – 8:40am	**Welcome & workshop charge** *Susan Makris, US EPA*
8:40am – 9:10am	**The Thyroid Axis – Overview of Anatomy, Physiology, Regulation in Mammalian Systems** *Mary Gilbert, US EPA*
9:10am – 9:40am	**An AOP Network for Thyroid Hormone Disruption and Adverse Outcomes** *Kevin Crofton, R3Fellows, LLC*
9:40am – 10:10am	**Mild thyroid dysfunction during pregnancy; consequences for pregnancy outcome and fetal development** *Robin Peeters, Erasmus University*
10:10am – 10:30am	**Break**

Session 2: Methodologies & Interpretation

10:30am – 11:00am	**Regulatory Requirements for Evaluation of Thyroid Status** *Sue Marty, Dow*
11:00am – 11:30am	**Pathology Endpoints: Evaluation of Thyrotoxicants in Animal Studies** *Brent Walling, Charles River*
11:30am – 12:00pm	**Thyroid hormone perturbation and neurodevelopmental toxicity in animal studies** *Ellen Hessel, RIVM*
12:00pm – 12:30pm	**Overview of in vitro assays to investigate chemicals for thyroid-axis disrupting potential** *Michael Hornung, US EPA*
12:30pm – 1:15pm	**Lunch**

Session 3: Global thyroid activities

1:15pm – 1:35pm	**Overview of ongoing thyroid activities in the European Union and United States** *Manon Beekhuijzen, Charles River*
1:35pm – 2:15pm	**HESI DART- ETS Thyroid Hormone Survey – Results & the Path Forward** *Pragati Coder, Charles River*

Session 4: Breakout Groups

2:15pm – 2:30pm	Breakout group instructions/**break**
2:30pm – 4:45pm	Groups are charged with identifying key data gaps and research needs, recommendations and future directions as it relates to: 1) Specimen collection, assay methodologies, sample analysis and reporting 2) Data interpretation, regulatory aspects and risk assessment
4:45pm	Wrap-up
5:00pm – 6:30pm	**Light Reception**

DAY 2, FRIDAY MAY 10, 2019

7:30am – 8:30am **Breakfast available**

8:30am – 8:35am **Day 1 Recap and Charge for Day 2**

Session 5: Break-out group report-back

8:35am – 10:30am **Break-out groups will report back on their discussions.**

- 20 min per group (15 min presentation, 5 min questions)

10:30am – 10:50am **Break**

Session 6: Perspectives on thyroid testing to improving interpretation

This session will present regional perspectives from both regulators and the regulated. Regulators will provide an overview of their agency's expectations for thyroid testing and outline critical issues regarding interpretation. Regulated industry panelists will address the critical issues encountered during study testing and when results are brought to the regulators and discuss their strategies for responding to regulators.

10:50am – 11:10am **Introduction to Panel**

Facilitators: Susan Makris, US EPA and Pragati Coder, Charles River

European Perspectives

- Niklas Andersson, ECHA
- Nina Hallmark, Bayer

Asian Perspectives

- Hiroaki Aoyama, Institute for Environmental Toxicology (on behalf of Japanese Food Safety Commission)
- Tomoya Yamada, Sumitomo Chemical

North American Perspectives

- Elizabeth Mendez, US EPA
- Bethany Hannas, Corteva
- Jennifer Foreman, ExxonMobil
- Miyun Tsai-Turton, US FDA
- LaRonda Morford, Lilly

11:10am - 12:15pm **Panel Discussion**

Facilitators: Susan Makris, US EPA and Pragati Coder, Charles River

Session 7: Looking ahead

12:15pm – 12:45pm **Identification of research needs and recommendations: A facilitated discussion**

Facilitators: Aldert Piersma (RIVM), Alan Hoberman (Charles River)

12:45pm – 1:00pm **Closing remarks & next steps**

Susan Makris, US EPA and Pragati Coder, Charles River