7-8 May 2026 | Hotel The Standard, Brussels

FROM CONCEPT TO APPLICATION

PRACTICAL IMPLEMENTATION OF ENHANCED 28 DAY STUDIES (SMART STUDIES/TG+) WITHIN A NAM BASED TIERED TESTING APPROACH FOR REPEAT DOSE TOXICITY

This workshop is part of ECETOC's 2026 NEXUS WEEK

Open Workshop on ECETOC's Nexus Week **May 7-8**, 2026, Hotel The Standard Brussels, Belgium. From Concept to Application: Practical implementation of enhanced 28 day studies (Smart studies/TG+) within a NAM based tiered testing approach for repeat dose toxicity

Objectives

The primary objective of this workshop is to review and further develop the concept of a tiered testing framework for hazard characterization and classification of chemicals for repeat dose toxicity testing as required by EU REACH regulations.

The testing framework is consistent with the goals of the EU Commission Roadmap towards phasing out of animal testing for chemical safety assessment, as it provides an opportunity to introduce the use of appropriate non-animal methods and endpoints within and alongside existing 28 day *in vivo* tests and potentially remove the need for studies of longer duration, including 90 day studies. The framework devised by ECETOC includes the use of enhanced *in vivo* studies when they are needed to ensure that the current protection standards provided by CLP classification are maintained. The use of the framework could also act in the short to medium term as a bridge to the regulatory inclusion of *in vitro* tests and new approaches as replacement technologies without compromising safety.

The workshop will bring together industry, CROs, academic and regulatory stakeholders, including representatives from European Agencies, competent national authorities and international organizations.

Background

The long-term investment in the development of NAMs in the EU and other parts of the world is to provide opportunities for the inclusion of new molecular endpoints and non-animal methodologies into chemical safety assessment.

ECETOC has developed a pragmatic and implementable tiered framework incorporating *in silico*, *in vitro* and enhanced *in vivo* methods with the intention of facilitating the introduction of new approach methodologies (NAMs) for regulatory purposes (Ball et al. 2022; Doe et al. 2025). In this step wise approach to information generation and risk assessment, the outputs from each tier (Tier 0 – 3) are classification categories, safe doses, and risk assessments and progress through the tiers depends on the output from previous tiers. The decision to proceed to Tier 3, *in vivo* testing, would depend on previous *in silico* and *in vitro* results. If there is insufficient evidence from early tiers to provide a reliable result, then the assessment moves to the next tier. This would also consider for example the degree of uncertainty in the early tier data for assigning classifications and the use of the data in risk assessment, based on the proposed uses (i.e., the expected margin of exposure).

The *in vivo* studies considered for Tier 3 should serve several objectives. The study design should take into account current regulatory requirements (i.e., OECD test guidelines) and include a more bespoke design, if necessary, based on information obtained in Tier 1 – 2. To ensure that this concept would also help reduce animal testing, ECETOC initiated a project called "smart studies" to evaluate the possibility of minimising animal use by reducing the duration of exposure from 90 days to 28 days (and thus eliminating the need for a 90 day study) while maintaining information requirement levels for risk assessment and classification and labelling.

With the introduction of various 'omics technologies (e.g., transcriptomics and metabolomics) as well as other parameters in a 28 day study, its sensitivity and mode of action information can be enhanced significantly. The smart study design is also intended as a bridge to connect the current *in vivo* testing paradigm with a future "animal free" test strategy. The introduction of 'omics technologies in current short-term OECD test guideline studies would also enable a better understanding of the strengths and potential weaknesses of new technologies and guide their introduction into *in vitro* studies. This would also allow new methods to be incorporated as they develop through continuous selective evolution rather than periodic revolution.

Various initiatives have helped to provide a basis for regulatory use of omics technologies and to gain confidence in their application in regulatory decision making. However, an initiative is needed to increase attention to the concept of smart *in vivo* studies and to facilitate their introduction in current testing.

Conclusion

The workshop will discuss the practical steps that would need to be taken to bring the concept of a tiered approach including the use of enhanced *in vivo* studies into implementation. As well as possibilities to enhance the regulatory acceptance of such a new testing paradigm.

References

Ball N, Bars R, Botham PA, et al. (2022) A framework for chemical safety assessment incorporating new approach methodologies within REACH. Archives of Toxicology 96(3):743-766 doi: https://doi.org/10.1007/s00204-021-03215-9

Doe, J.E., Botham, P., Holland, D. et al. (2025) Framework for classifying chemicals for repeat dose toxicity using NAMs. Archives of Toxicology 1432-0738. doi: https://doi.org/10.1007/s00204-025-04069-1

Workshop programme

Day 1: Repeat Dose Toxicity Testing – 7 May [Onsite]				
Item	**Start**	**End**	**Agenda item**	**Who**
1	9:00 AM	9:30 AM	**Registration – Welcome Coffee and Breakfast**	
2	9:30 AM	9:40 AM	**Welcome and housekeeping rules**	ECETOC Secretariat
3	9:40 AM	10:00 AM	**Setting the Scene: Introduction & objectives of the workshop**	Phil Botham (Syngenta)
4	10:00 AM	10:30 AM	**A tiered testing framework for hazard characterization and classification of chemicals for repeat dose toxicity testing**	John Doe (Liverpool John Moores University)
5	10:30 AM	11:00 AM	**Coffee Break**	
6	11:00 AM	11:15 AM	**Study assessment and data evaluation for Smart Studies**	Barbara Schmitt (Evonik)
7	11:15 AM	11:35 AM	**In vitro technologies, omics, and their application in Smart Studies**	Richard Currie (Syngenta)
8	11:35 AM	12:00 PM	**Closing data gaps with TG+ studies: Combining Test Guidelines with NAMs**	Philip Marx-Stölting (BfR)
9	12:00 PM	1:00 PM	**Lunch**	
10	1:00 PM	1:30 PM	**OECD work towards regulatory confidence and acceptance on NAMs for complex endpoints**	Patience Browne (OECD)
11	1:30 PM	2:00 PM	**IATA for systemic toxicity: Efforts to harmonize approaches and develop a framework for regulatory application**	Kristie Sullivan (IIVS)
12	2:00 PM	2:30 PM	**Update on the omics activities at ECHA**	Ulla Simanainen (ECHA) – Online
13	2:30 PM	3:00 PM	**Application of Omics in Chemical Hazard identification**	Tim Gant (Imperial College London)
14	3:00 PM	3:30 PM	**Results of the LRI Metabolomics Ring-Trial For Chemical Grouping (MATCHING) project: Use of metabolomics and omics signatures within in vivo studies**	Mark Viant (University of Birmingham)
15	3:30 PM	4:00 PM	**Coffee Break**	
16	4:00 PM	4:20 PM	**Transcriptomics applications in *in vivo* studies: Update from the tPOD Working Group**	Connie Mitchell (HESI) – Online

Day 1: Repeat Dose Toxicity Testing – 7 May [Onsite]				
Item	**Start**	**End**	**Agenda item**	**Who**
17	4:20 PM	4:45 PM	Multi-modal cell profiling of chemical potency and mode-of-action	Jessica Ewald (European Molecular Biology Laboratory)
18	4:45 PM	5:00 PM	**First day wrap up and expectations for day two**	
19	5:30 PM	6:30 PM	**Evening Networking Cocktail Event**	All onsite attendees

Day 2: Repeat Dose Toxicity Testing – 8 May [Onsite]				
Item	**Start**	**End**	**Agenda item**	**Who**
1	8:30 AM	9:00 AM	**Welcome Coffee and Breakfast**	
2	9:00 AM	9:20 AM	*Welcome and introduction to day two*	Organising committee
3	9:20 AM	10:20 AM	Panel discussion	Philip Marx-Stölting (BfR) Daniela Holland (Exxonmobil) Katrin Schutte (European Commission) David Rouquie (Bayer)
4	10:20 AM	10:30 AM	**Introduction to the break out groups**	Organising committee
5	10:30 AM	11:00 AM	**Coffee Break**	
6	11:00 AM	11:10 AM	Attendees to proceed to their designated team breakout rooms	Group A, Group B & Group C
7	11:10 AM	12:10 PM	Break-out Session	Group A, Group B & Group C
8	12:10 PM	1:10 PM	**Lunch**	
9	1:10 PM	1:40 PM	**Plenary report from breakout groups**	Rapporteurs
10	1:40 PM	2:10 PM	**Summarize, closing remarks and next steps**	Organising committee
11	2:10 PM	2:40 PM	**End of the event - Closing coffee break**	

Organising Committee

Ben	van Ravenzwaay	Wageningen University
Phil	Botham	Syngenta
John	Doe	Liverpool John Moores University
Sue	Marty	Dow
David	Rouquie	Bayer
Daniela	Holland	ExxonMobil
Sergio	Leon Perez	ECETOC

Venue

The Standard Brussels Hotel

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Contact

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