

Recap of OECD WNT-36 Meeting

ICCVAM Public Forum 5/20/2024

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Overview the OECD WNT

- ▶ Organization for Economic Cooperation and Development (OECD)
 - ▶ Since 1961, the OECD has worked to advise international governments through policy analysis, recommendations, standards, and collaboration that foster prosperity, equality, opportunity and well-being for all.
 - ▶ OECD brings together 38 member countries and other Key Partners to collaborate on global economic, social, and scientific issues including: tax policy, digital transformation, climate change, energy, trade, education, finance, and other.
- ▶ Chemicals and Biotechnology Committee (CBC)
 - ▶ CBC oversees OECD work on chemical safety and biosafety through the activities on eleven Working Parties, which collectively conduct research and develop guidelines on how to test chemicals for hazards to human health and the environment.
 - ▶ Mutual Acceptance of Data (MAD) is built on the OECD Test Guidelines (TG) and Principles of Good Laboratory Practice (GLP). It requires OECD governments to accept non-clinical environment and health safety data developed for regulatory purposes in another country if these data were generated in accordance with the TGs and GLP Principles. These tests are also accepted in non-member countries that adhere to MAD.
- ▶ Working Party of the National Coordinators of Test Guidelines Program (WNT)
 - ▶ National Coordinator from each member and MAD adhering country and the European Commission
 - ▶ Harmonize and approve Test Guidelines and related documents through consensus
 - ▶ <https://www.oecd.org/chemicalsafety/testing/oecd-guidelines-testing-chemicals-related-documents.htm>

Summary of the OECD WNT-36 Meeting

- ▶ Organization for Economic Cooperation and Development (OECD)
 - ▶ Working Party for the Test Guideline Program (WNT) Meeting was held hybrid April 16-19, 2024.
- ▶ Meeting highlights
 - ▶ Approved 9 Items: Test Guidelines and Guidance Documents
 - ▶ Added 18 new Standard Proposal Submission Form (SPSF) for placement on WNT Workplan
 - ▶ US Led/co-Led activities on 5 SPSFs proposals and 1 approved Test Guidelines
- ▶ Other updates and upcoming activities

WNT-36 items approved

- ▶ New Test Guideline on short-term juvenile hormone activity screening assay in *Daphnia magna*
- ▶ New Test Guideline on the Rapid Estrogen Activity In Vitro (REACTIV) assay *
- ▶ New Test Guideline on the *Hyallolela azteca* Bioconcentration Test (HYBIT) assay
- ▶ Updated Test Guideline 442D to add a new Test Method EpiSensA for inclusion in *in vitro* Skin Sensitization *
- ▶ Updated Test Guideline 496 including the Optisafe Macromolecular Test Method for Eye Hazard Potential *+
- ▶ Updated Test Guideline 467 including the Defined Approach for Eye Hazard Identification for solids *
- ▶ New Guidance Document on IATA for phototoxicity testing
- ▶ Updated Guidance Document 75 on Honeybee (*Apis mellifera* L.) Brood Test Under Semi-field Conditions
- ▶ Updated Guidance Document 263 on IATA for eye irritation

WNT-36 items approved - NAMs

- ▶ TG on the Rapid Estrogen Activity In Vitro (REACTIV) assay
 - ▶ Screening assay using transgenic *Oryzias latipes* (Japanese medaka) to detect the potential for endocrine disrupting chemicals with estrogen axis signaling activity using the chgh-gfp genetic construct that contains the medaka choriogenin H gene (required for egg production)
- ▶ Updated TG442D to add a new Test Method EpiSensA for inclusion in *in vitro* Skin Sensitization
 - ▶ Reconstructed human epidermis (RhE) model that demonstrates advantages for testing of lipophilic compounds and pre/pro-haptens and addresses mechanisms described under the second Key Event (KE2) of the Adverse Outcome Pathway (AOP) for skin sensitization.
- ▶ Updated TG467 including the Defined Approach for Eye Hazard Identification for solids
 - ▶ Combination of two *in vitro* validated test methods for the identification of the eye hazard potential for neat solids including the Bovine Corneal Opacity and Permeability using Laser light-based opacitometer (BCOP LLBO in TG437) and the SkinEthic™ Human Corneal Epithelium Eye Irritation Test (HCE EIT in TG492)
- ▶ Updated TG496 including the Optisafe Macromolecular Test Method for Eye Hazard Potential (US)
 - ▶ Describes the Ocular Irritation (OI®) and OptiSafe Eye Irritation Test™ (OS) methods. While both *in vitro* macromolecular test methods can be used to identify chemicals not requiring classification for irritation or serious eye damage, only the OI® can be used to identify chemicals that have potential to induce serious eye damage.

Newly Added Projects

No.	Project Title	Lead /Co-lead
2.76	Mason bees (<i>Osmia</i> sp.), Acute Oral Toxicity Test	FI, CH
2.77	Chronic Oral Toxicity Test for Solitary Bees (<i>Osmia</i> spp.)	SP, IT
2.78	Bumblebee (<i>Bombus</i> supp. L.), Chronic Oral Toxicity Test(10-Day Feeding)	SP
3.2	Revision of OECD Test Guideline 309	UK
4.169	Revision of OECD TG 498 - KeraSkin™ Phototoxicity Assay	KO
4.170	Revision of OECD TG 431 to include a new me-too reconstructed human epidermis test method - KeraSkin™ skin corrosion test	KO
4.171	EASA as a me-too method in TG 442C In Chemico Skin Sensitization	US
4.172	Me-Too validation of the reconstructed human epidermis Epiderm model for the EpiSensA method	FR, JP
4.173	DA for skin sensitizer potency assessment based on quantitative regression models	CH, DE

No.	Project Title	Lead /Co-lead
4.174	Validation of the In Vitro Micronucleus assay for Engineered Nanomaterials	UK, DE, FR, NO, US, LU
4.175	DRP on the application of error-corrected next generation DNA sequencing (ecNGS) for gene mutation evaluation	US
4.176	DRP on specific target organ toxicity (liver) test method using liver organoid	KO
4.177	Revision of in vivo genotoxicity TG: “Evaluation and Interpretation of Results” and “Test Report” language	US, CA
4.178	Revision of OECD TG 443 (EOGRTS) and GD 151	EC, DK, NL
4.179	Colorimetric assessment of deiodinases 1 activity based on Sandell-Kolthoff reaction with human microsomes: DIO1-SK assay	FR, DE
4.180	Fluorometric assessment of transthyretin-binding activity based on the displacement of thyroxine labelled with fluorescein isothiocyanate FITC-T4 TTR binding assay	NL, FR
4.181	New guideline for testing oral, dermal, inhalation and injection toxicity, pathogenicity of microbial pesticides	US, CA
4.182	Adverse Outcome Pathway (AOP) network leading to genotoxicity	BE, FR

Newly Added Projects - US lead/co-lead

- ▶ Update with EASA as a “me-too” method in TG 442C *In Chemico* Skin Sensitization (US)
 - ▶ Evaluate the Electrophilic Allergen Screening Assay (EASA) for inclusion in TG 442C, *In Chemico* Skin Sensitization as an efficient, medium-throughput method for assessing key event (KE) 1 in the skin sensitization adverse outcome pathway (AOP).
- ▶ Validation of the *In Vitro* Micronucleus assay for Engineered Nanomaterials (UK/DE/FR/NO/US/LU)
 - ▶ Address limitations identified in the “Study Report and Preliminary Guidance on the Adaptation of the *In Vitro* micronucleus assay (OECD TG 487) for Testing of Manufactured Nanomaterials” (2022).
- ▶ DRP on the application of error-corrected next generation DNA sequencing (ecNGS) for gene mutation evaluation (US)
 - ▶ Develop a DRP and Retrospective Performance Assessment (RPA) for error-corrected Next Generation Sequencing (ecNGS) methods and outline the performance of ecNGS method for gene mutation evaluation starting with *in vivo* followed by *in vitro* assays.
- ▶ Revision of *in vivo* genotoxicity TG: “Evaluation and Interpretation of Results” and “Test Report” language (US/CA)
 - ▶ Revise the “Evaluating and Interpretation of Results” section language of *in vivo* genotoxicity TGs when assessing whether a response is positive or negative and introduce a new concept that utilizes the historical negative control distributions to provide for assessing biological relevance.
- ▶ New guideline for testing oral, dermal, inhalation and injection toxicity, pathogenicity of microbial pesticides (US)
 - ▶ Adapt the EPA guidelines for mammalian testing (885.3050, 885.3100, 885.3150, 885.3200) with updates into a single OECD guideline that will promote harmonization of mammalian toxicity/pathogenicity/infectivity testing, reduce the redundancy, and promote wider acceptance of data supporting evaluation and authorization of microbial pesticides.

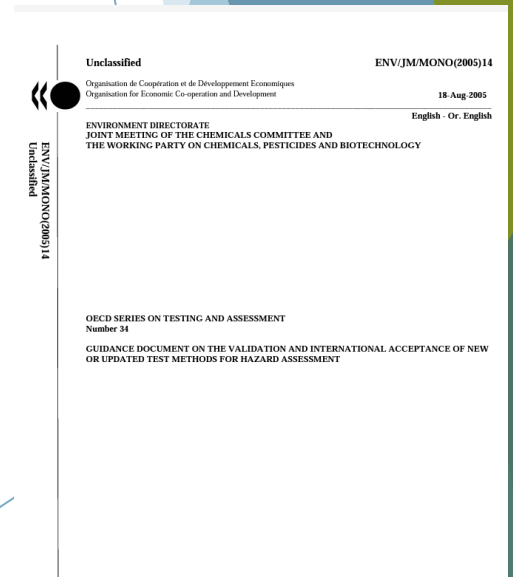
Other updates and activities

Stakeholder Workshop on Operational and Financial aspects of Validation

- ▶ Published a call for mobilization of national and regional resources for the demonstration of reproducibility and reliability of methods developed in single laboratories in January 2023
- ▶ Held pre-workshop webinars in November 2023
 - ▶ Overview on Validation of Methods, Method Readiness, and Case examples of validation studies
 - ▶ <https://www.oecd.org/chemicalsafety/webinars-on-testing-and-assessment-methodologies.htm>
- ▶ Hosted a Stakeholder Workshop in December 2023
 - ▶ Diverse group including researchers, developers, industry, government agencies, and funding organizations to share their lessons learned and identify organizational and financial validation practices to disseminate as good practice
 - ▶ Financial recommendations: Detailed budget planning, announce priority areas for funding, encourage method readiness filter, encourage earmarking budget for validation of NAMs.
 - ▶ Organizational recommendations: Develop an online companion to Guidance Document 34 (preparing SOPs, identifying partner labs, etc.), connect method developers with available resources, filling communication, training, and education gaps.
 - ▶ Workshop report (expected June 2024) <https://www.oecd.org/chemicalsafety/testing/resources-validation-testing-methods-chemicals.htm>
 - ▶ US participation influenced by the ICCVAM's published *Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies*

Project to Revise Guidance Document 34

- ▶ 2022: WNT initiated activities to modernize the processes to validate and develop Test Guidelines to keep pace with emerging science and technologies that provide alternatives to animal testing for chemical safety
 - ▶ Webinars <https://www.oecd.org/chemicalsafety/testing/webinars-on-emerging-science.htm>
- ▶ 2023: WNT formally approved the project to revise GD34 (EU-JRC, NL, US)
 - ▶ Developed an expert group, participated in meeting with ICATM at 12th World Congress, and held meeting with National Coordinators to discuss the intent of GD34 and provide an opportunity for feedback on GD34 revision direction, topics to revise, and prioritize issues
- ▶ 2024: WNT held working meeting to discuss proposed revisions
 - ▶ Working on revisions to Section 4: Design and Conduct of Validation Studies
 - ▶ Scoping topics Readiness Criteria, Defined Approaches, and Transferability
 - ▶ Planning another working meeting for later in 2024



OECD TG/GD Process Mentor

- ▶ The NanoHarmony project, funded through Horizon 2020, to support the development of Test Guidelines and Guidance Documents where nanomaterial-adapted test methods have been identified as a regulatory priority.
- ▶ Coordinates the collection and use of available data and information to support the finalization of the test method development and organize a sustainable network
- ▶ The **NanoHarmony Process Mentor** provides guidance and understanding on developing OECD Test Guidelines and Guidance Documents
- ▶ Outlines when and how to prepare for required activities, highlights key start and finish dates of the development process, and identifies who to involve in which activities and when.
- ▶ www.testguideline-development.org



Upcoming Dates

- ▶ SPSF submission deadline October 11, 2024
- ▶ WNT - 37 March 31 - April 4, 2025