Updates to OECD Guidance Document 34 on Validation of new and updated Test Methods

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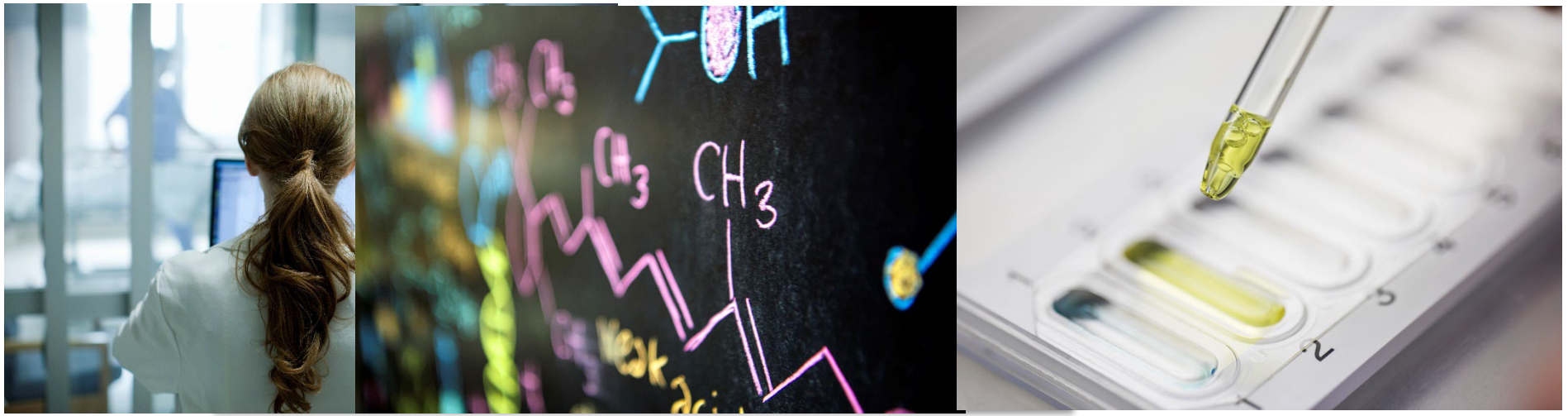
U.S. National Coordinator to the OECD Test Guidelines Program (WNT)

SACATM September 17, 2024



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Background from SACATM 2023

- OECD WNT adopted the proposal to update GD34
  - U.S. members: Warren Casey, Alison Harrill, Nicole Kleinstreuer, Charles Kovatch
- Anne Gourmelon OECD presented on Organizational and Financial Aspects of Validation and International Harmonization
- Valerie Zuang EC-JRC presented an on Update GD34 and major topics to address
  - Long WNT review and approval process, method reliability, clarity on some guidance, doesn’t describe defined approaches or new and emerging technologies
- WNT held an in-person Stakeholder Workshop on Validation and a virtual GD34 meeting in December 2023
- Review of ICCVAM Strategic Roadmap 5 Years
- ICCVAM Validation Work Group Report

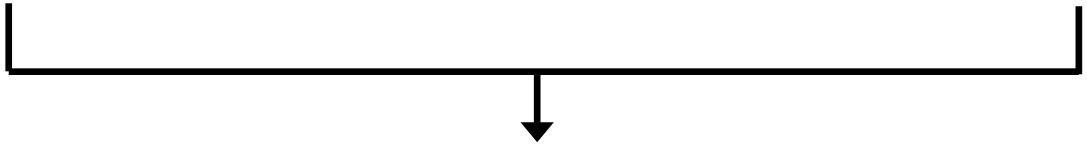
Mutual Acceptance of Data (MAD)

- 1981 Council Decision on MAD
  - *"Test data generated in any member country in accordance with OECD Test Guidelines and Principles of Good Laboratory Practice (GLP) shall be accepted in other member countries for assessment purposes and other uses relating to the protection of human health and the environment"*
- Under MAD:
  - Council Decision **is legally binding** on OECD Member countries
  - Countries can set their own data requirements and make their own assessment of the information provided by the tests
  - Countries **cannot** ask industry in an OECD country to do a test using a different method for which an agreed OECD TG exists
  - *"Tested once, accepted everywhere"*

Countries go MAD for Reliable Data

Test Guidelines

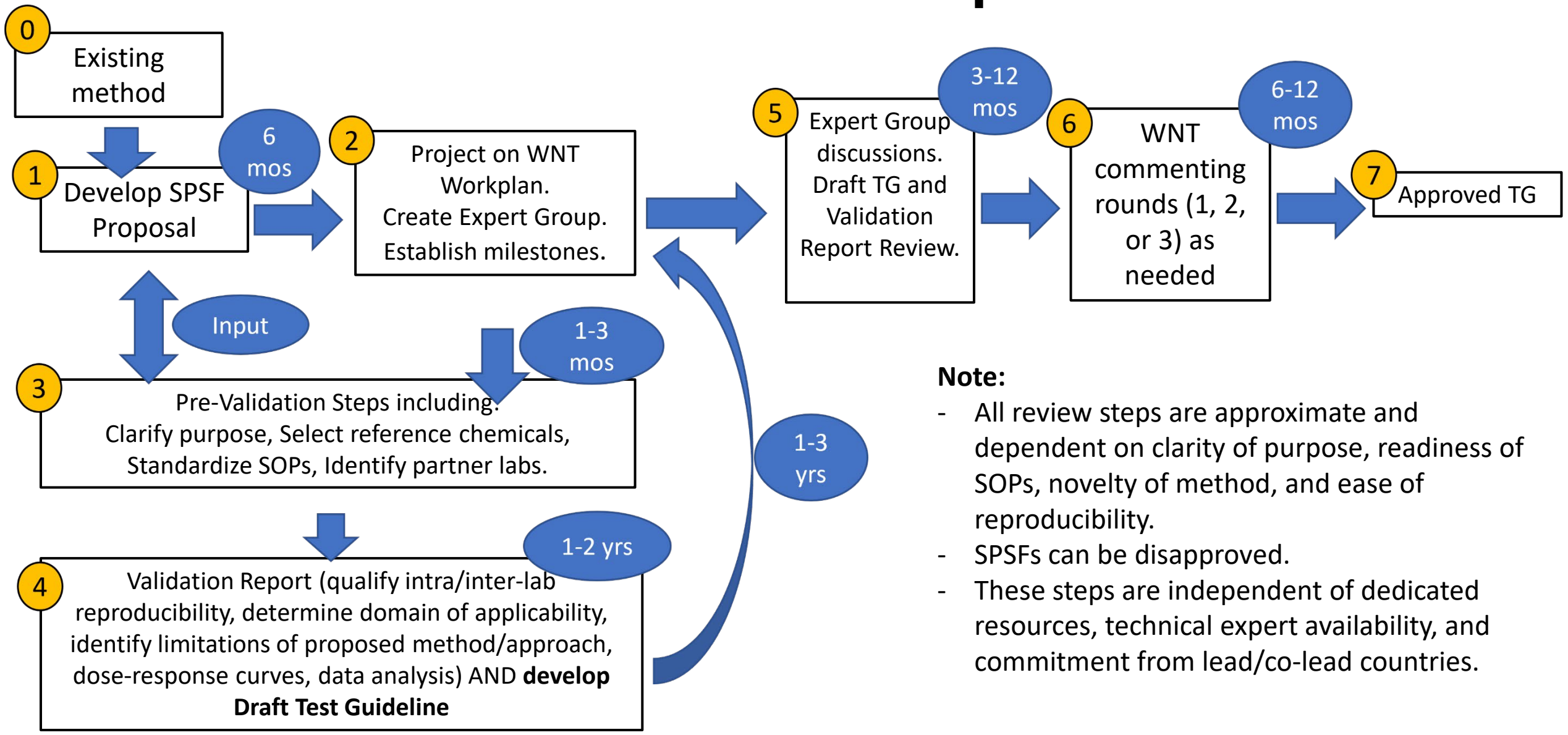
Good Laboratory Practice



Mutual Acceptance of Data

- Reduce trade barriers
- Avoid duplication
- Save time and money
- Reduce animal use
- Increase chemical safety

OECD Test Guideline Development Process



Note:

- All review steps are approximate and dependent on clarity of purpose, readiness of SOPs, novelty of method, and ease of reproducibility.
- SPSFs can be disapproved.
- These steps are independent of dedicated resources, technical expert availability, and commitment from lead/co-lead countries.

OECD GD 34

Unclassified

ENV/JM/MONO(2005)14

Organisation de Coopération et de Développement Economiques
Organisation for Economic Co-operation and Development

18-Aug-2005

English - Or. English

ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND
THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY

ENV/JM/MONO(2005)14
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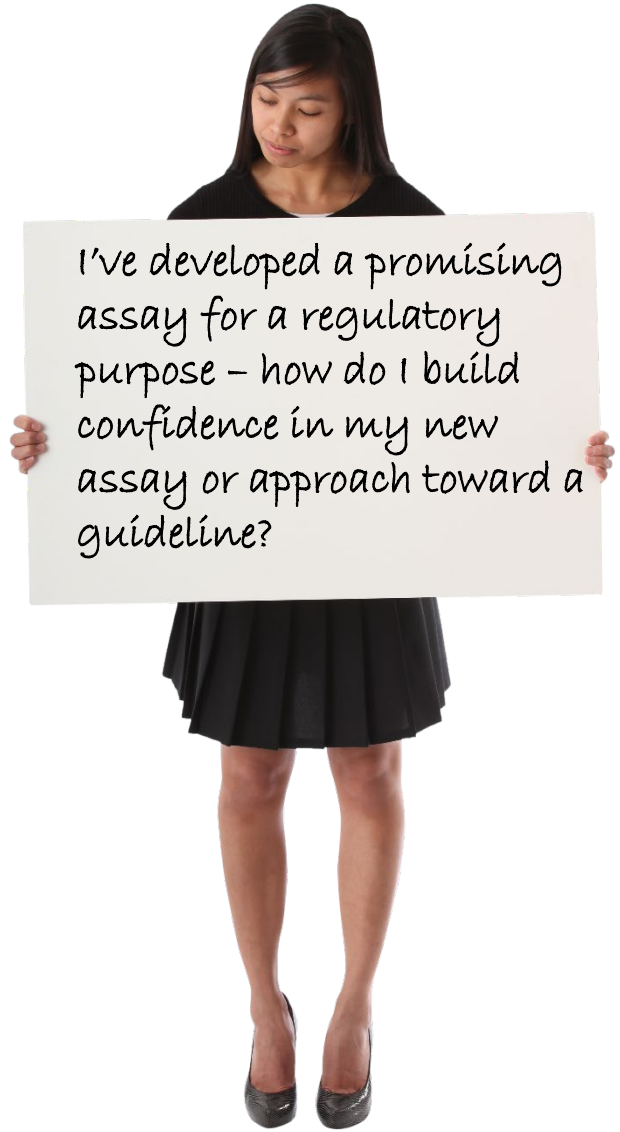
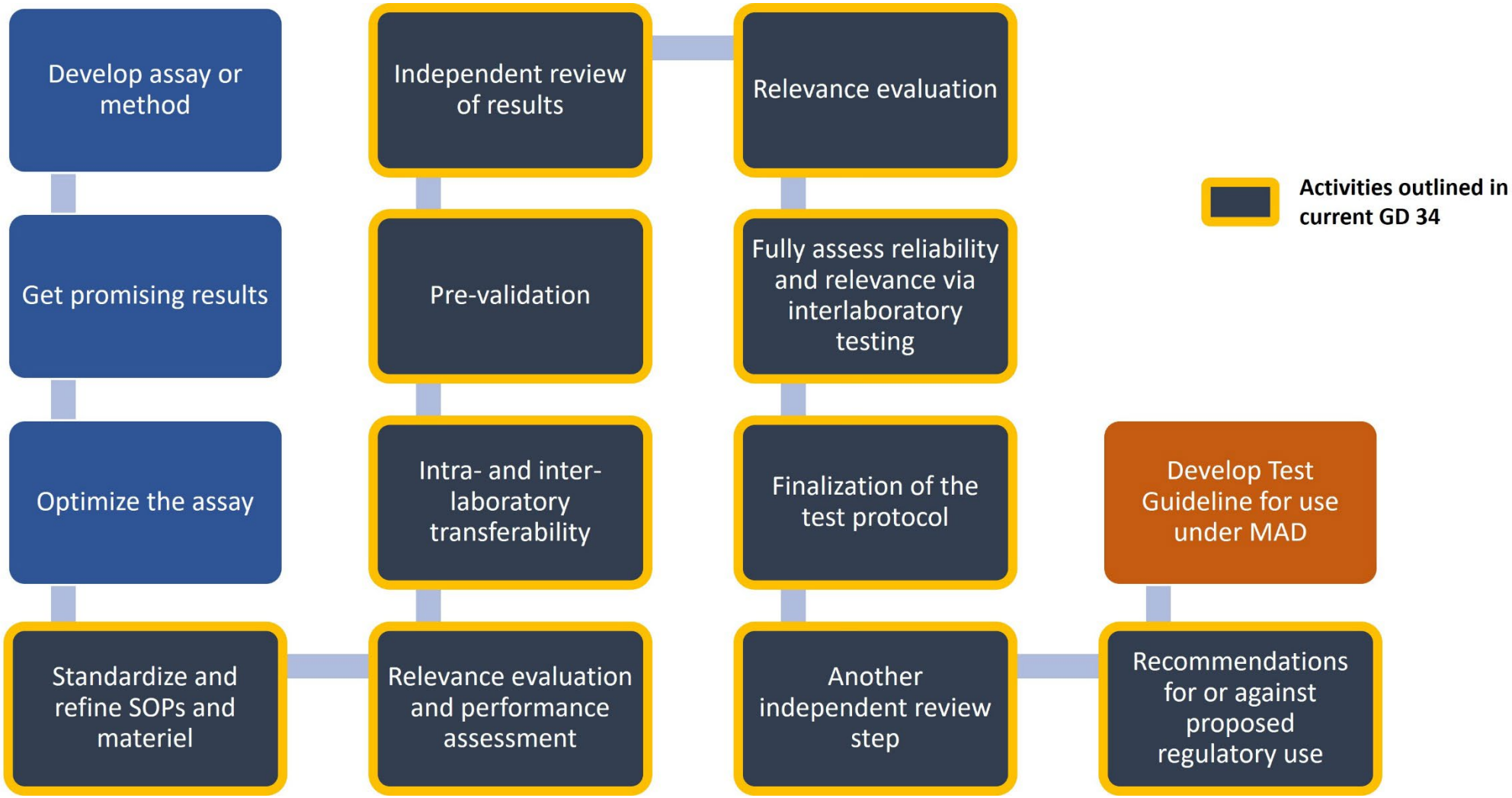
OECD SERIES ON TESTING AND ASSESSMENT
Number 34

GUIDANCE DOCUMENT ON THE VALIDATION AND INTERNATIONAL ACCEPTANCE OF NEW OR UPDATED TEST METHODS FOR HAZARD ASSESSMENT

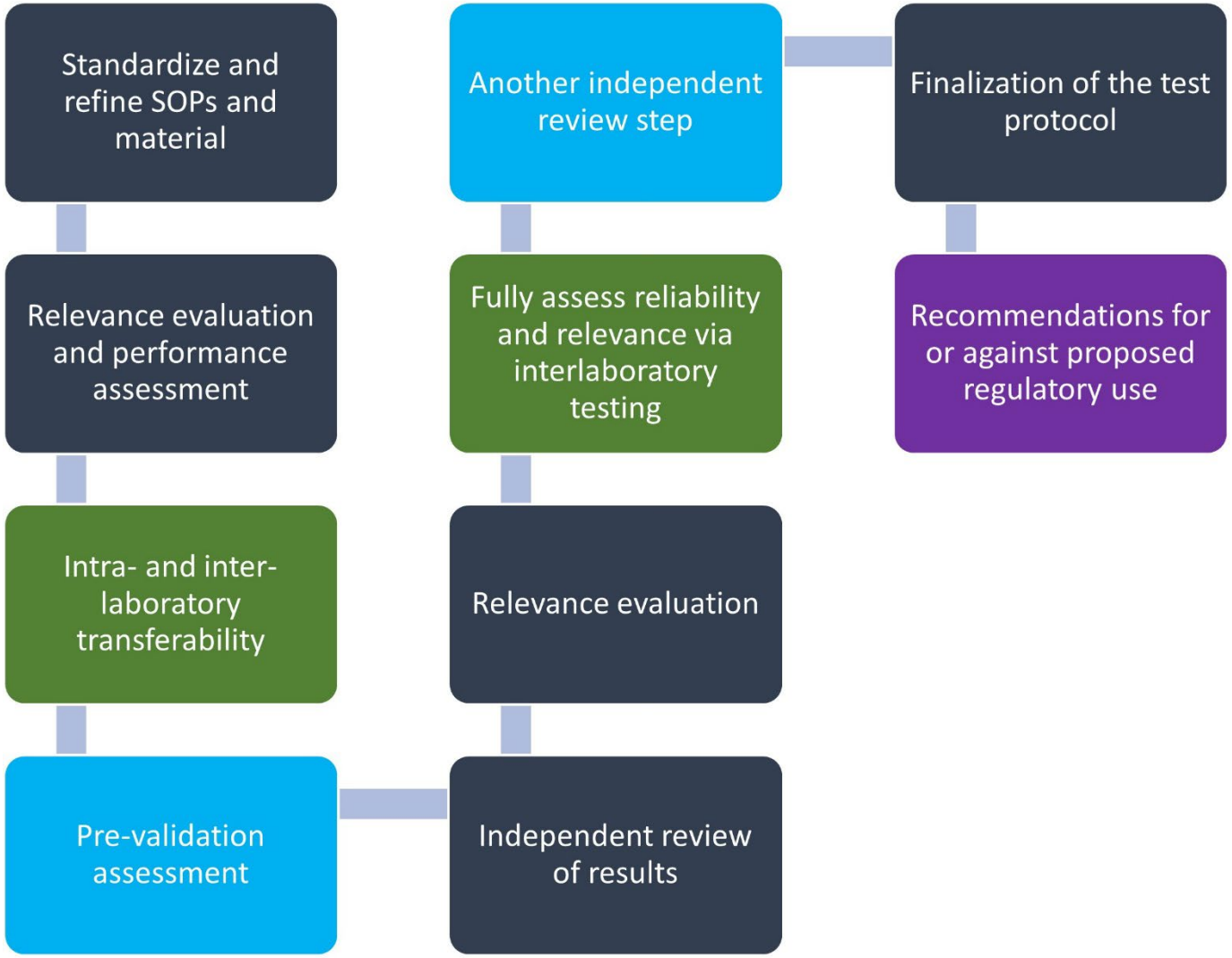


GD34 Process for Review and Acceptance of New or Revised Approaches for Regulatory Decisions



Considerations for Revising GD 34

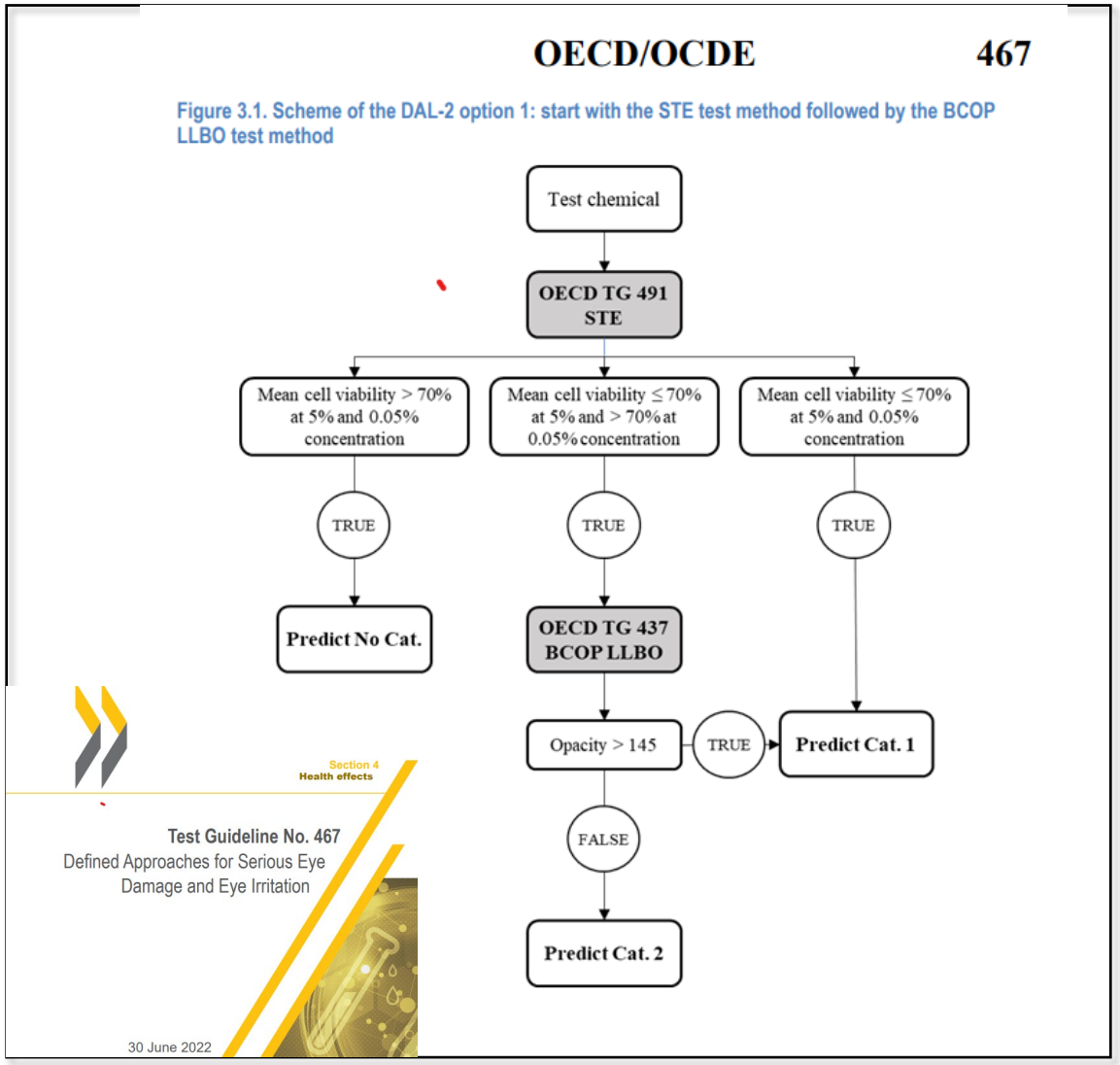
- How and when should relevance of a method be established?
- Is there value in conducting transferability studies in both “pre-validation” and validation phases?
- A frequent difficulty encountered in validation studies is a lack of readiness criteria – could defining and verifying readiness replace pre-validation steps?
- What should interlaboratory transferability studies look like and can the process be streamlined?
- What should be considered in the final step on utility of the method for regulatory decision making?
- How to make the process more practical without compromising confidence building?
- How to best position methods for consideration as an OECD test guideline?



Top Priorities Identified for GD34 Revision

- Develop guidance for validation of DAs and building blocks
- Include more practical guidance
- Define concept of technical validation
- Define assessment of relevance beyond accuracy
- Develop guidance for validation of new technologies
- Transferability and between-laboratory reproducibility
  - Is a ring-trial with 3 or more laboratories testing a large set of chemicals was always necessary
- Address emerging technologies, especially those that may be challenging to transfer between laboratories
  - How to determine whether there is a path to TG development

Defined Approaches and Test Batteries



- Could/Should methods intended to be utilized in a Defined Approaches (DAs) or a test battery be validated together?
- If so, how to document performance for each method?
- May require use of labs with differing expertise and capabilities.

What would we need to add to GD 34 to cover DAs?

- Assessment of readiness and technical characterization of each information source, and how that translates to DA assessment
- Protocol optimization and transferability studies to facilitate method standardization (need for “naïve” labs? all methods sent to same labs or different ones, depending on capabilities & expertise?)
- Performance assessment of methods (i.e. mechanistic/KE-based reference chemicals) vs. DA (i.e. adverse outcome-based reference chemicals)?
- Transferability of the data interpretation procedure (DIP)
  - Does the DIP for the DA need transferability in the case of more complicated computational strategies (computer code, QSAR, machine learning, AI)? If the DIP is more straightforward (like a decision tree), may not need transferability but needs a level of expert review to be described in GD 34

OECD Stakeholder Workshop on Financial and Operational Aspects of Validation

- January 2023: WNT published an announcement that called for the mobilization of resources to assist in accelerating the pace of new emerging technologies for chemical safety testing and assessment.
- December 2023: WNT hosted a Stakeholder Workshop on the Operational and Financial Aspects of Validation.
  - As part of Workshop preparation, WNT conducted a stakeholder survey, held two webinars, and compiled twelve case studies on validation from the community.
  - Leveraged expertise across the diverse stakeholder community to share experiences and lessons learned and successes in validation
- Activities from Workshop Recommendations:
  - Develop a good practice guide on operational aspects of validation
  - Promote method readiness tools
  - Make existing validation resources better known and accessible
  - Announce, share, and promote funding opportunities
  - Evolution of the concept of performance standard and guidance for batteries of assays

What progress has been made so far on the GD 34 revision effort?

WNT Discussions, Workshops, Related Activities

2022

- WNT workshop on considerations for updating GD 34
- Scoping of GD 34 revision proposal

2023

- GD 34 revision project accepted and expert group formed
- 1st GD 34 expert group meeting (virtual)
- ICATM working group discussion at WC12 on international perspectives
- WNT Stakeholder Workshop on Financial and Operational Aspects of Validation

2024

- ICCVAM publishes NAMs validation report
- 2nd GD 34 expert group meeting (in person)
- Ongoing GD 34 discussions and text revisions
- Developed sub-groups
- 3rd GD 34 expert group working meeting (in person)

Project Leads

United States
Warren Casey
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Nicole Kleinstreuer
Charles Kovatch

EURL-ECVAM
João Barroso
Valerie Zuang

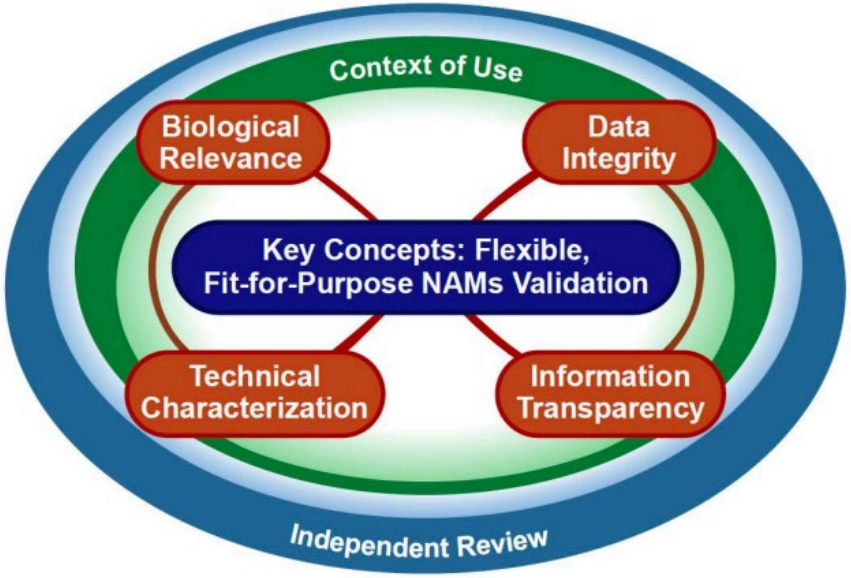
Netherlands
Betty Hakkert
Jelle Vriend
Damien van Berlo

WNT Secretariat
Anne Gourmelon

WNT: National Coordinators of the Test Guideline Programme

Relevance to ICCVAM / SACATM

- ICCVAM Roadmap 2022-2023
- ICCVAM Activities 2024
  - Validation Document
  - Developers Forum
  - Lead/co-lead on 15 OECD WNT projects
  - Ongoing research projects
  - Agency NAMs workplans
  - EPA scheduled NAMs Conference October



NICEATM 2024, van der Zalm 2022

- Looking forward to 2025
  - Leverage ICCVAM to quantify validation processes and steps in support of GD34
  - Engage ICCVAM more strategically to communicate interagency methods development, research, and validation
  - Identify shared communication and training opportunities

Questions