OPERATIONAL AND FINANCIAL ASPECTS OF VALIDATION:

A SURVEY TO COLLECT STAKEHOLDERS INPUT IN PREPARATION FOR A WORKSHOP

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SACATM Meeting , 21 September 2023

BETTER POLICIES FOR BETTER LIVES

RECAP OF RECENT DISCUSSIONS AT THE OECD - CHEMICAL SAFETY PROGRAMME

- In 2022, Chemicals and Biotechnology Committee:
  - discussed the future of chemicals assessment
  - supported evolutions proposed, incl.
    - Having a framework/guidance for the validation of New Approach Methods (NAMs)
    - Standardised reporting templates to facilitate regulatory use (QSAR models and predictions, IATAs, omics, etc.)
    - Emphasis on new methods for exposure assessment
    - Considerations of the technical readiness of NAMs

CURRENT STATE-OF-PLAY ON VALIDATION

Years reflecting on validation practices and principles

- Consensus today seems to be:
  - Validation principles are universal (i.e. demonstrating relevance and reliability, including transferability)
  - Validation practices should evolve as:
    - it is not realistic to expect an individual/mechanism-based method to predict an adverse effect in an animal, nor to be a replacement of an animal test;
    - reproducibility demonstration needs to be done thoroughly in each lab implementing a new method; ring-trials across many labs are not a practical solution:
      - logistics are cumbersome, the added value is questionable,
      - important aspects of the method implementation and how they impact reproducibility are often not well reflected
- Meanwhile, validation practitioners have evolved and new issues have emerged

WHO ARE THE VALIDATION PRACTITIONERS TODAY?

- In Europe:
  - method developers from private sector increasingly coordinate validation studies;
  - H2020 academic projects hardly coordinate validation;
  - National agencies sometimes get involved in methods validation;
  - EURL-ECVAM can provide support/advice but no longer coordinates validation studies;
  - EU-NETVAL labs play a role in validation but funding can be an issue;
- In Japan:
  - JaCVAM continues to coordinate most methods validation for new and me-too methods;
- Korea:
  - KoCVAM operates similarly to Japan;
- In the United States:
  - ICCVAM does not coordinate validation studies;
  - Methods validation seems decentralised or delegated to agencies/national centres for purpose-specific validation studies;
  - Private sector contribution to methods validation (?)

- Overall, very diverse range of practitioners
- Growing number of small companies

2023: ENGAGING TOGETHER IN CONCRETE ACTIONS

- 2023:
  - Jan: Call for increased public funding into methods validation to allow new standard methods based on emerging science and technologies and allow broad accessibility and use in countries

  - Project started to update OECD Guidance Document 34 on Validation (collaboration EC-JRC, US, NL)
  - Survey of validation practitioners on-going on practical and financial aspects of validation (closure 15 September)
    - collect insight on specific issues and identify opportunities to work more cost efficiently on methods validation

  - Workshop with validation practitioners in Dec. 2023 to explore options and solutions to the TG Programme

WNT SUPPORTED THE IDEA OF A STAKEHOLDERS WORKSHOP IN DECEMBER 2023

- Objectives:
  - Collect feedback on recent and relevant experience with validation of new methods
  - Identify and understand drivers of validation, sources of funding
  - Identify issues and challenges in operational aspects of validation and potential solutions
  - Propose pragmatic, example-based, good practices, to illustrate the updated GD 34, focussing on operational and financial aspects

OECD SURVEY QUESTIONNAIRE LAUNCHED (JULY 2023 >>> 15 SEPTEMBER 2023)

- **Objective:** develop an overview of the validation landscape, document experience, identify challenges and what solutions may come from practitioners;

- 35 questions to collect feedback in the following areas:
  - Understanding of “validation for regulatory purpose”
  - Practical experience with validation
  - Level of interaction with other stakeholders in the field
  - Perspectives on practices and processes and where efficiency gains might be
  - Interest and incentives to take part in validation studies in future
  - Financial aspects of validation: collect cost figures, who funds? who should fund? what is costly and where efficiency gains are possible
  - Organisational support for funding (parts of) validation?
  - Good practices that should be promoted (funding and operational aspects)
  - Different models for organising and funding validation studies?

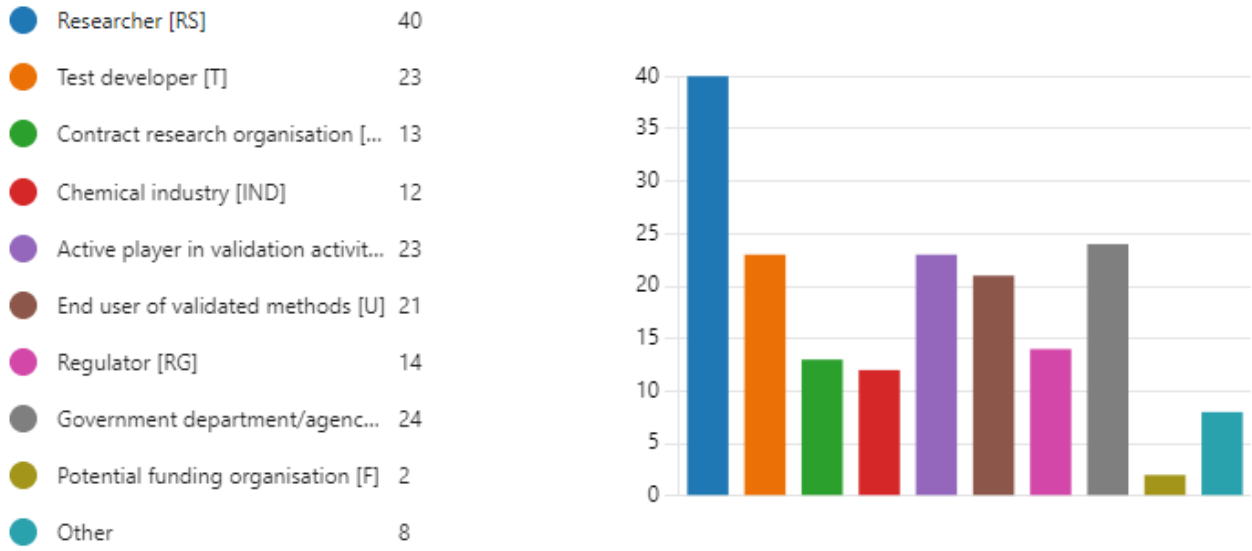
WHAT WILL WE DO WITH THE RESPONSES TO THE SURVEY?

- 15 September: survey closure
  - >75 responses (9 Sept), more responses expected.
- by end September:
  - compilation of responses and presentation to WS steering group; discuss feasibility of improvements suggested;
  - prepare WS agenda and invitation letter to the WS;
  - work with WS steering group on WS material.
- In November:
  - Proposal for a prep. webinar on recent experience from method developers (private, gov.agencies, academia…)
- 14-15 December:
  - Workshop at OECD

WHAT DO RESPONSES RECEIVED SO FAR TELL US?

Country	Number of responses
Austalia	1
Austria	2
Belgium	2
Brazil	3
Canada	1
Czech Republic	1
Denmark	3
France	4
Germany	16
Italy	3
Japan	10
Netherlands	4
South Korea	2
Spain	3
Sweden	1
Switzerland	4
United Kingdom	4
United States	11
Other	1
TOTAL	76

Who are the respondents?



(As of 9 September)

WHAT DO RESPONSES RECEIVED SO FAR TELL US?

- **Evolution of practical/organisational/managerial aspects of validation**
  - "Validation as an integral part of assay development"
  - "Validation should be funded by a consortium of industry, CRO, agencies that have an interest in the method(s)"
  - "Repository of reference chemicals for each toxicological endpoints"
  - "Provide guidance at an early stage on test method standardisation to methods developers"

WHAT DO RESPONSES RECEIVED SO FAR TELL US?

- **Efficiency gains in practical aspects of validation**
  - "Education of academic partners on what regulators expect: clear and reproducible protocol, test results for a range of active and inactive substances"
  - "Standardised format for SOPs",
  - "Establishment of fully externally funded validation projects would speed up process"
  - "Availability of on-line training material for a method entering validation"
  - "Method development needs to be standardised, systematic, and transparent. All data should immediately be published under FAIR data principles. This will enable faster validation"
  - "Only methods with a high readiness and clear use case (defined by an independent panel of potential users) should be validated."
  - "Focus on aspects that are truly essential (e.g., good reference chemicals and reproducibility), ensure proper funding, dedicated projects."
  - "Limit the number of labs needed to demonstrate transferability."
  - "Improve the initial organizational aspect before proposing the method to the validating laboratory. Certain data should already be present from which to start, to avoid useless tests that do not lead to reproducibility of the data."
  - "Provide or facilitate procurement", "Provide (chemical/test material) repositories"

WHAT DO RESPONSES RECEIVED SO FAR TELL US?

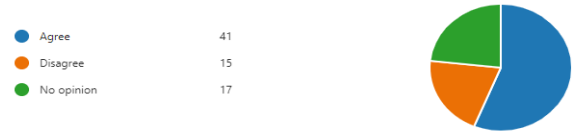
- **Costs:**
  - "Between 100 kEUR (cell-based assay with ELISA read-out) and 600 kEUR (cell-based assay with genomic readout)"
  - "The main drivers of the costs include technology transfer and training, between laboratory reproducibility, chemicals procurement, coding, blinding and shipment."
  - "Participation in a phase 1 (5 compounds) and phase 2 validations (15 compounds) costs approx 150kEUR. When new equipment needs to be qualified/validated at a GLP labs costs can rise up to 200kEUR."
  - "Preparation, coordination, data analysis, report preparation: 50 000 - 75 000 € Execution of the validation (3 labs, 20 chemicals): 60 000 - 90 000 € Analytical chemistry: 35 000 - 80 000 € Test chemical procurement: 20 000 - 40 000 € Total: 175 000 - 275 000 €."
  - "According to our experience, 300 -400 k€/year for the developer (who would provide cells + training/transfer), 200 k€ for the naive labs. A validation of an already dveloped test study should be completed within 2 years."

WHAT DO RESPONSES RECEIVED SO FAR TELL US?

- **Ideas for ways of organizing and funding validation activities?**
  - Agencies? EFSA has started funding projects on NAMs, including lab transferability of US EPA DNT assays for 500 kEUR
  - Consortia of government agencies, industries, CROs?
  - International grants (EU, US…)?
  - Certain aspects of validation might be funded and organized via grants and tender agreements (chemicals procurement and blinding/coding/distribution, reagents, developing on-line and re-usable training material, statistical analysis and reporting)?

WHAT DO RESPONSES RECEIVED SO FAR TELL US?

Should validation be organised by a public-funded body?



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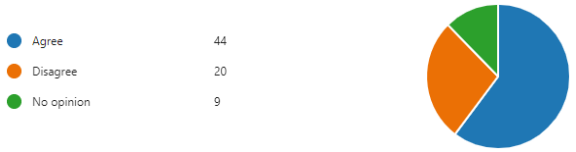
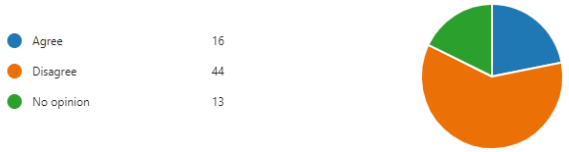
The validation can be organized by the test method developer.



Laboratories participating in a validation study should not have a commercial interest in the method.

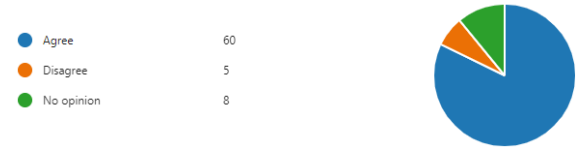


The validation should be financed by the test method developer.

The laboratory(ies) participating in the validation should self-support most of the costs.

Validation is a common good and should be sponsored by all the stakeholders.

Organisational aspects of the validation should be standardised by the OECD as much as possible.



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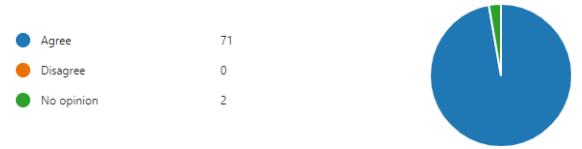
Having multiple models for organising and funding validation studies is advantageous as it reflects the diversity of possible situations and needs.

In the case where a validation study is organized or funded by the test developer or a company/individual with vested interest, good practices should be promoted to ensure data integrity and transparency.



Challenges at the workshop and beyond

- Parse out responses contributing to potential solutions
- Identify economic models that are fair and possible to implement;
- Discuss operational and financial responsibilities in a prior-informed way and openness to contribute to the efforts needed;
- Find a balance between public and private investments and interests;
- Find support from all stakeholders (member countries, , agencies, donors, method developers, CROs…) for shared responsibilities that transform into real commitment and concrete actions.

Ultimately, what we all want is to have a minimum set of common new approach methods trusted by all to generate chemicals safety data. It should be possible to achieve this goal with less than 50 million EUR.

THANK YOU FOR LISTENING!

Stay connected and learn more about OECD:

- https://www.oecd.org/chemicalsafety/
- Contact: ehs.contact@oecd.org

Dec. 2022 WNT workshop: "How to adapt the Test Guidelines Programme for the uptake of emerging technologies?"

>> July 2023 report:

>> Preparatory webinars


OECD Home › Chemical safety and biosafety › Testing of chemicals › Webinar Series on Emerging Science to Improve Chemical Safety

Webinar Series on Emerging Science to Improve Chemical Safety

*The **OECD webinars on Emerging Science** provide an opportunity to chemical safety professionals to learn and discuss new methodologies developed by research globally. These new approaches might make their way into future regulatory applications, but a dialogue will help scientists understand the needs of the regulatory community, and allow regulators to ask the relevant questions early on. Video recordings of our webinars are made available online afterwards.*

OECD WORKSHOP ON HOW TO PREPARE FOR EMERGING TECHNOLOGIES - WATCH THE SERIES OF WEBINARS

This series of six webinars was organised by the OECD Secretariat and the steering group in preparation of a workshop of the OECD Working Party of the National Coordinators of the Test Guidelines Programme (WNT) in December 2022. The focus of the workshop was on how to prepare for emerging technologies. Biotechnologies and data engineering are rapidly evolving, and some applications very well address the demand of alternatives to animal testing for chemical safety. The WNT is receptive to the new opportunities these fields of science can bring to the Test Guidelines Programme. This workshop was an excellent occasion to start discussing priority issues, such as method readiness criteria, validation practices, validation for batteries of assays, performance standards, in light of emerging science and technologies.

The webinars were held from June to November 2022, with invited speakers mostly outside the WNT. Presentations in the webinars were for information purposes, and do not reflect consensus views of the WNT. The topics of each webinar were identified and prioritised by the WNT. Speakers were then identified by the OECD Secretariat and the workshop steering group. Key points and messages were used as preparatory material for the workshop, mostly as sources of inspiration for the workshop discussions.

Access the webinar recordings below:

- Webinar No. 1 - Extracting the essential principles of validation and good in vitro method practices for NAMs (i.e. NAMs intended to become Test Guidelines)
- Webinar No. 2 - Ecotoxicology: new methods and approaches for cross-species extrapolation tools
- Webinar No. 3 - Scientific and test method readiness of emerging technologies: criteria, examples and experience
- Webinar No. 4.1 - Reproducibility issues (from a technical perspective) in toxicological studies (in vitro) and how they affect emergence of new approach methods
- Webinar No. 4.2 - Probabilistic modelling (making better use of quantitative information from in vitro assays and taking into account uncertainty): example of applications and where they might fit in data interpretation
- Webinar No. 5 - Identifying reference chemicals and building curated datasets: what are the approaches, issues and learnings for the future
- Webinar No. 6 - Current practices and challenges encountered in other standard-setting organisations