EURL ECVAM contribution to validation and regulatory acceptance of test methods/approaches

Valérie Zuang

Joint online Workshop: Harmonisation & Standardisation of Test Methods for Nano- and Advanced Materials (22-23 November 2023)

European Union Reference Laboratory for Alternatives to Animal Testing

Established under the Directive 2010/63/EU on the protection of animals used for scientific purposes

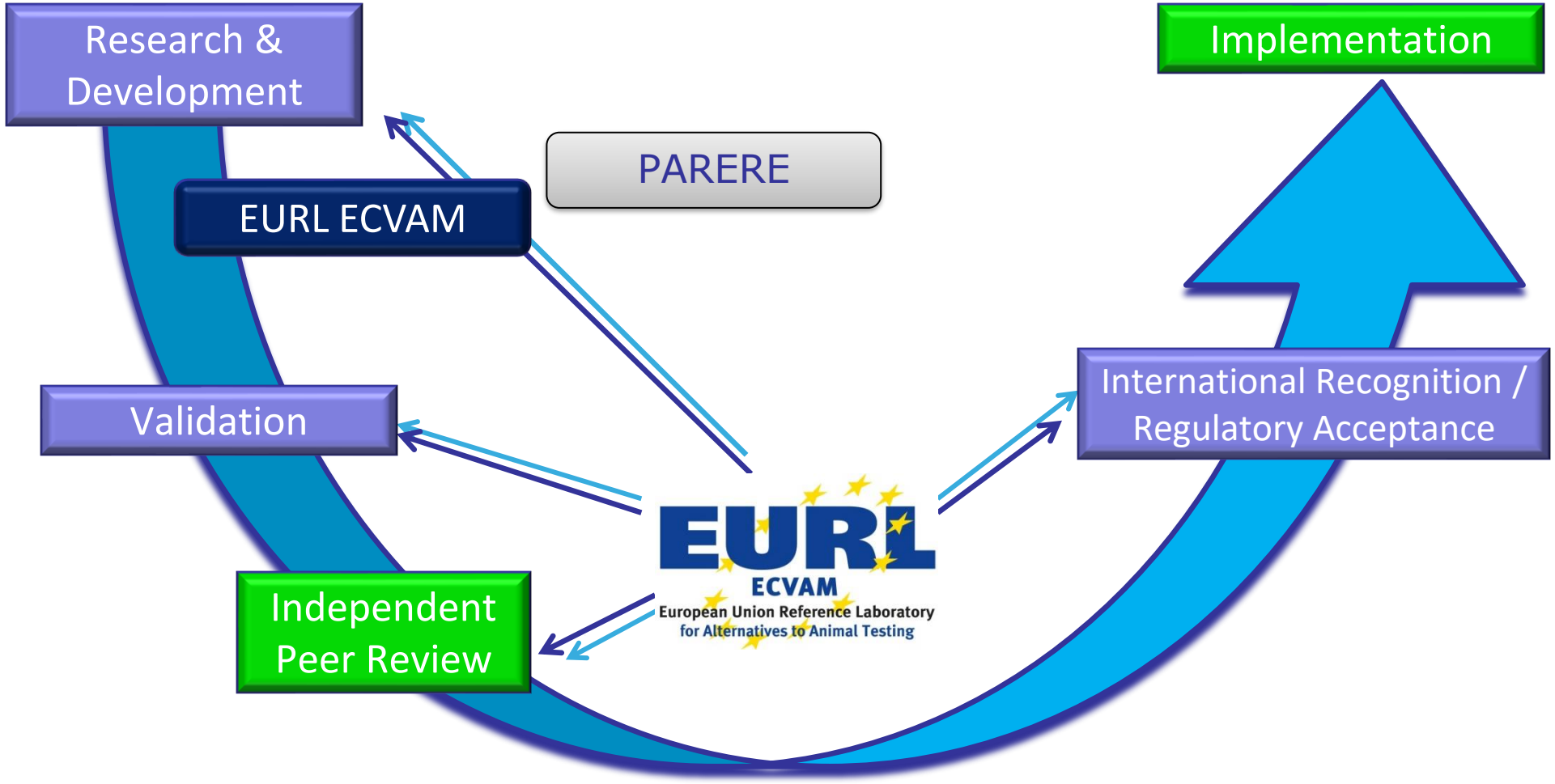
Duties and tasks*

- Guide & promote **research** on alternative methods
- Coordinate **validation** within the EU
- **Disseminate** information on the 3Rs
- **Promote** stakeholder dialogue
- **Promote** international acceptance

** Article 48 of the Directive, Annex VII*

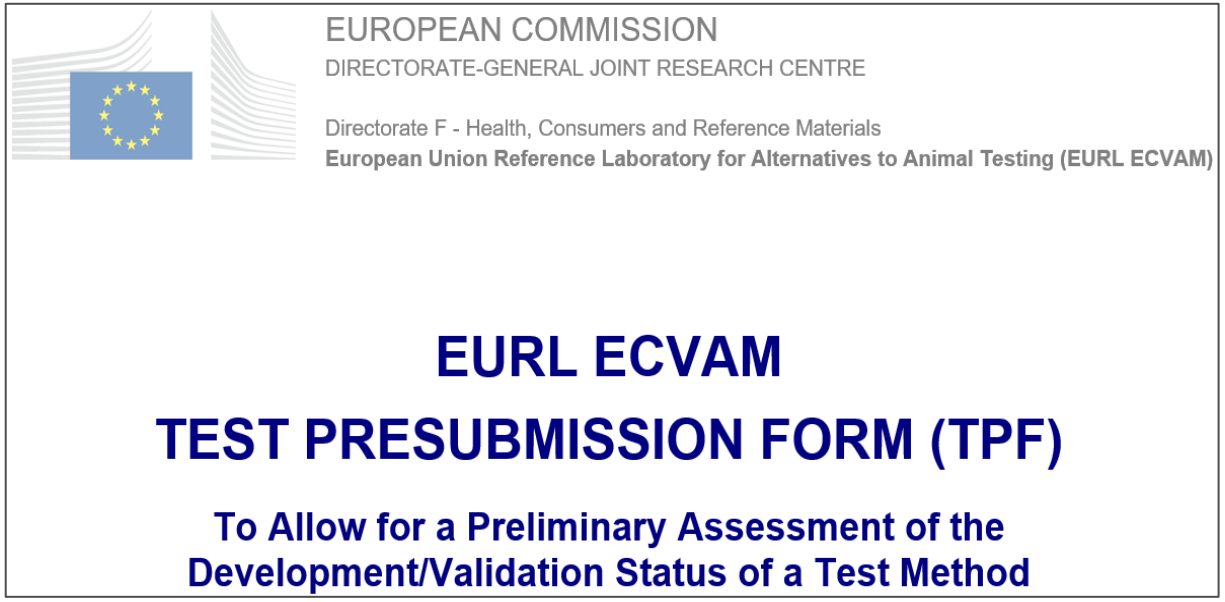
European Commission

Life cycle of a new regulatory test method or approach



European Commission

Two-step submission assessment
Step 1 - Presubmission



EUROPEAN COMMISSION
DIRECTORATE-GENERAL JOINT RESEARCH CENTRE

Directorate F - Health, Consumers and Reference Materials
European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM)

EURL ECVAM

TEST PRESUBMISSION FORM (TPF)

To Allow for a Preliminary Assessment of the Development/Validation Status of a Test Method

Preliminary assessment of

the status of

- development
- optimisation
- validation of the test method
- its potential relevance

If positive outcome, invitation to fill in a full submission (step 2)

https://joint-research-centre.ec.europa.eu/eu-reference-laboratory-alternatives-animal-testing-eurl-ecvam/alternative-methods-toxicity-testing/validation-and-submission-process/eurl-ecvam-test-method-submission_en

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Two-step submission assessment
Step 2 - full submission


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EURL ECVAM
Test Submission Template (TST)

- Comprehensive information
- To allow to assess if test is ready to enter EURL ECVAM process &
- To select the appropriate sub-process (e.g. prospective validation, val. based on performance standards, peer review)

European Commission

TSAR - Example

TSAR - Tracking System for Alternative methods towards Regulatory acceptance

European Commission > EU Science Hub > EURL ECVAM > TSAR

TRACKING SYSTEM FOR ALTERNATIVE METHODS TOWARDS REGULATORY ACCEPTANCE

TSAR tracks the progress of alternative, non-animal methods, for testing chemicals or biological agents such as vaccines towards acceptance as a recognised test method for use in various sectors

TSAR

TSAR indicates the stages methods have reached in terms of acceptance as a recognised test method for use in various sectors together with a summary description. Where available, TSAR also includes relevant records and documents associated with a method linked to the different steps of the entire process: submission, validation, peer-review, recommendations and regulatory acceptance including international standards represented in the tracking system.

Show Filters

Results 1 - 2 of 2

Download (Excel compatible) All methods

3D Reconstructed Human Skin Comet assay

TM Status:	Open	**Topic(s):**	Genotoxicity/Mutagenicity
Test Method Number:	TM2020-01 (EU)		
Short Name of TM:	RS Comet assay		
Responsible Organisation:	EURL ECVAM - European Union		

SUBMISSION Finalised | VALIDATION Finalised | PEER-REVIEW Ongoing | RECOMMENDATION Step not reached | REGULATORY ACCEPTANCE/STANDARDS Step not reached

https://tsar.jrc.ec.europa.eu/

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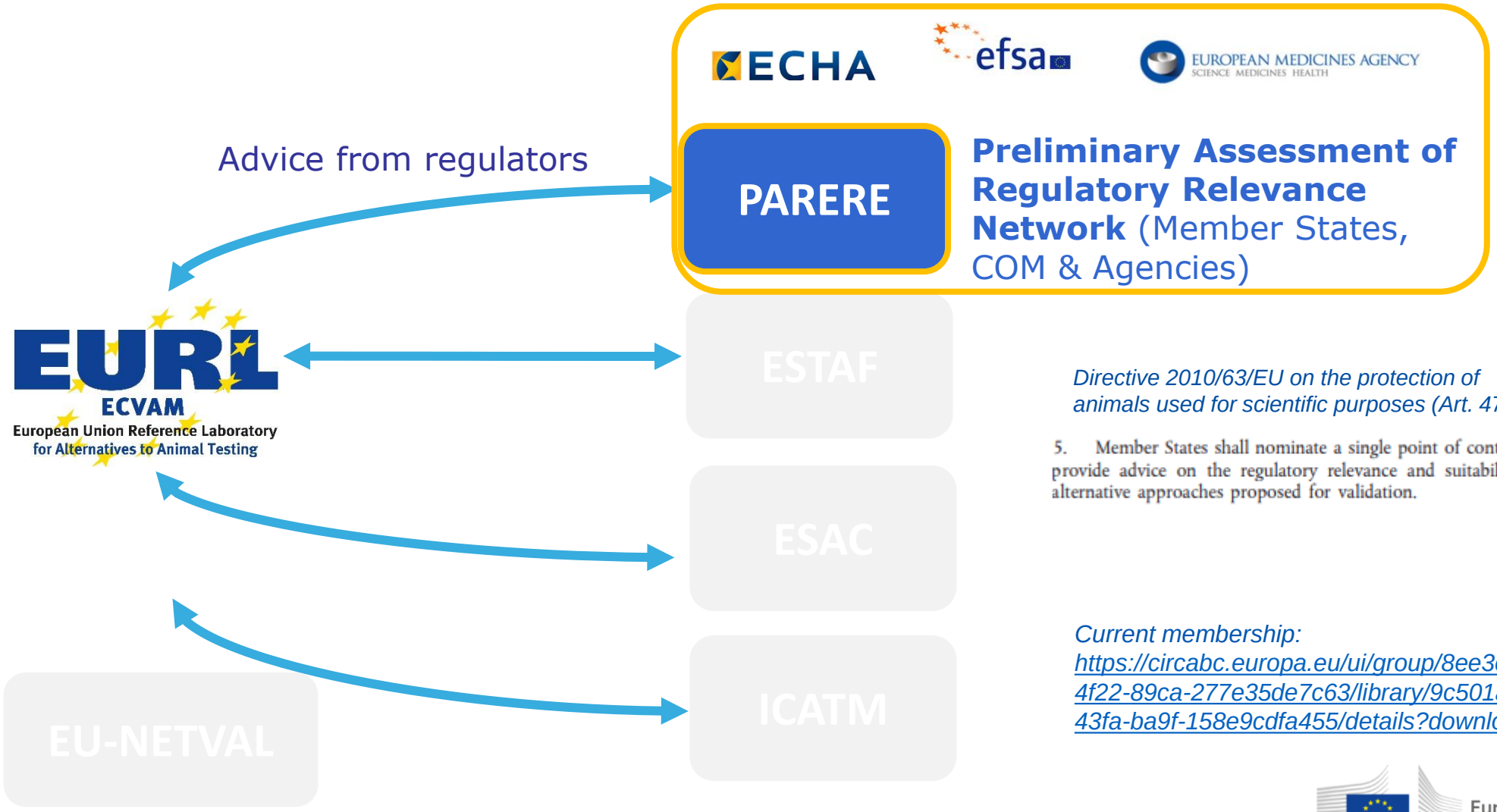
Staying connected



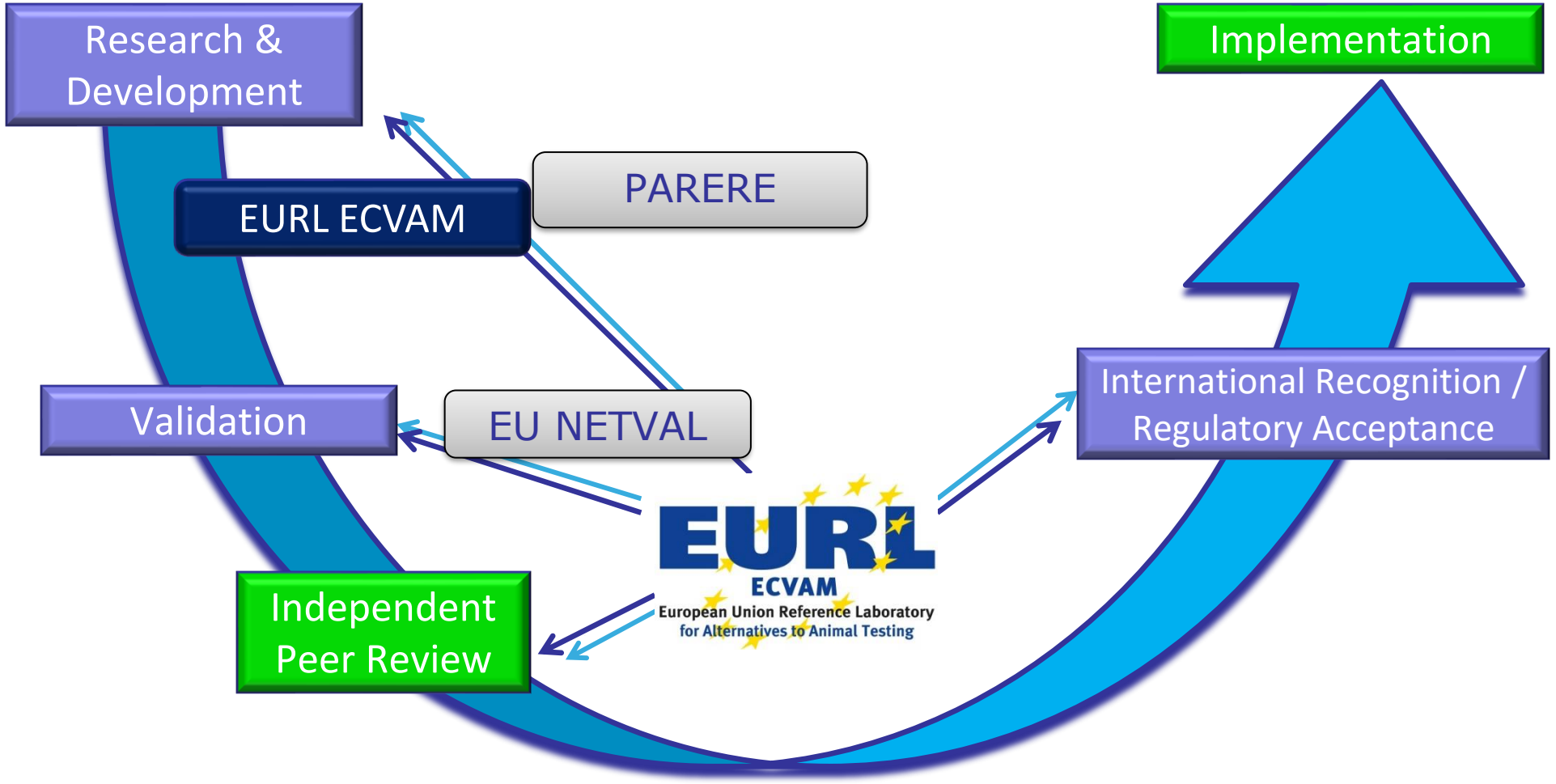
Directive 2010/63/EU on the protection of animals used for scientific purposes (Art. 47)

5. Member States shall nominate a single point of contact to provide advice on the regulatory relevance and suitability of alternative approaches proposed for validation.

Current membership:
https://circabc.europa.eu/ui/group/8ee3c69a-bccb-4f22-89ca-277e35de7c63/library/9c501a15-e53c-43fa-ba9f-158e9cdfa455/details?download=true

European Commission

Life cycle of a new regulatory test method or approach



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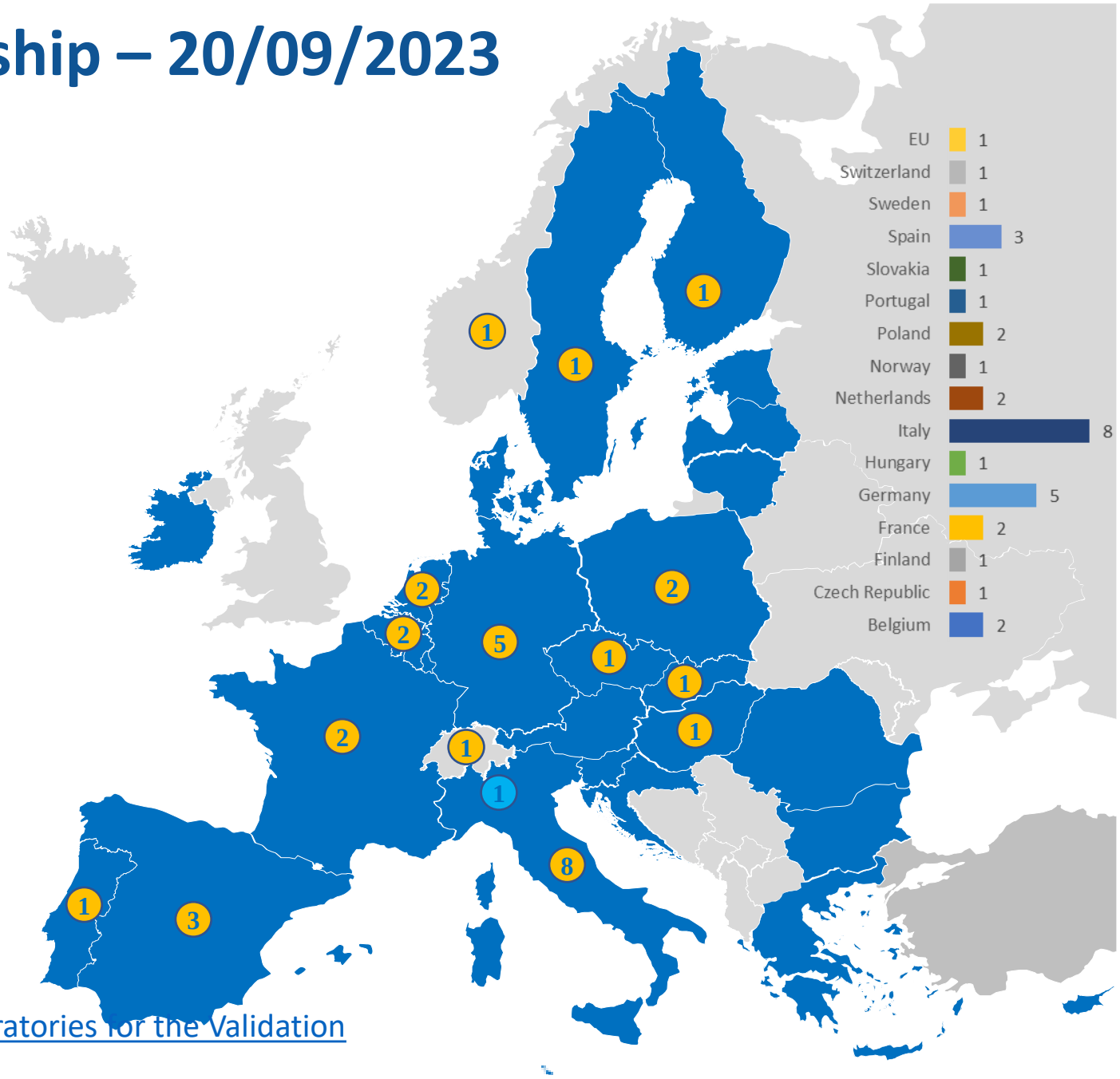
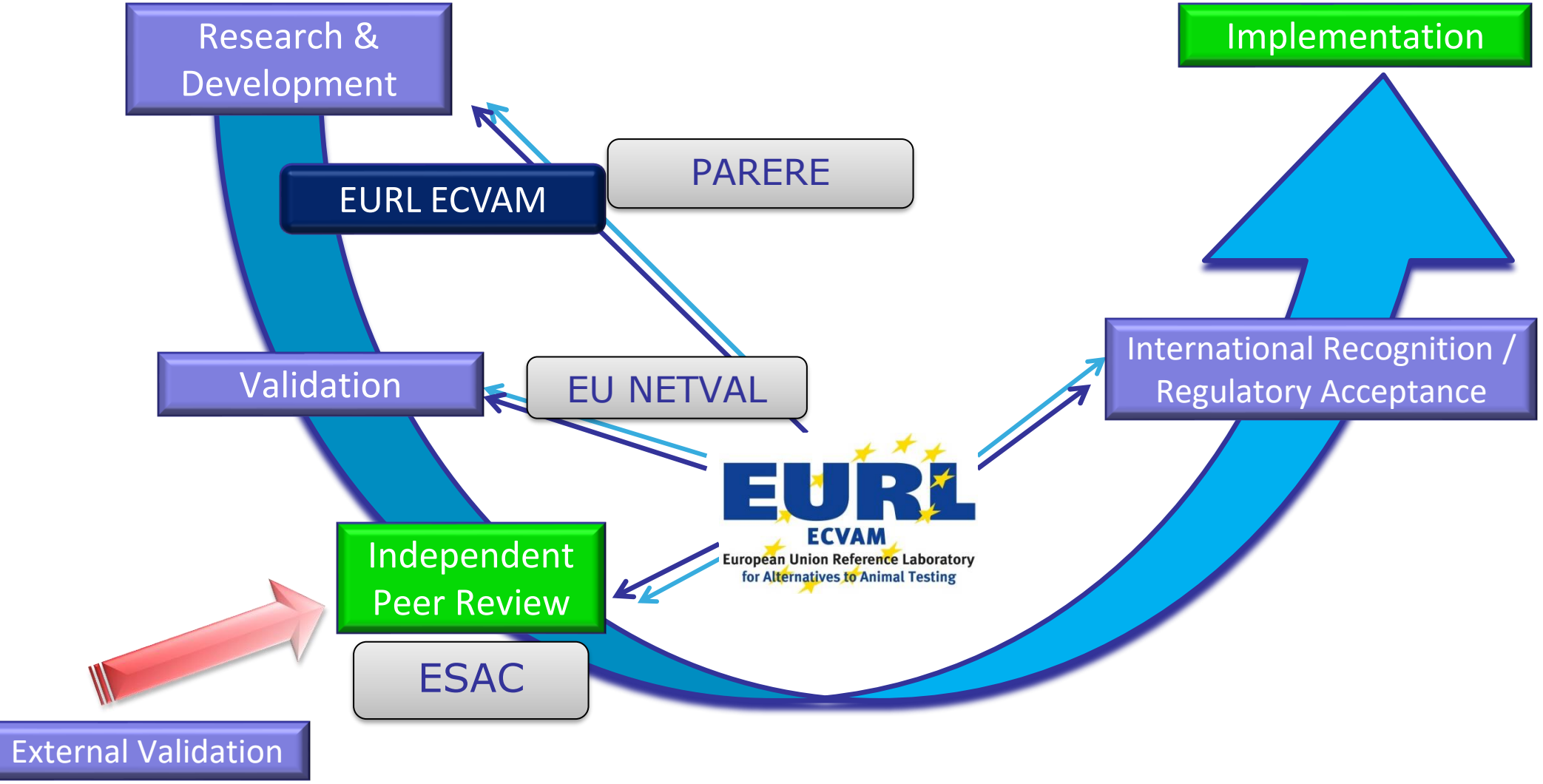
EU-NETVAL Membership – 20/09/2023

Belgium	2
Czech Republic	1
Finland	1
France	2
Germany	5
Hungary	1
Italy	8
Netherlands	2
Norway	1
Poland	2
Portugal	1
Slovakia	1
Spain	3
Sweden	1
Switzerland	1
EU	1
Total	**33**



[EU-NETVAL (European Union Network of Laboratories for the Validation of Alternative Methods) (europa.eu)]

Life cycle of a new regulatory test method or approach

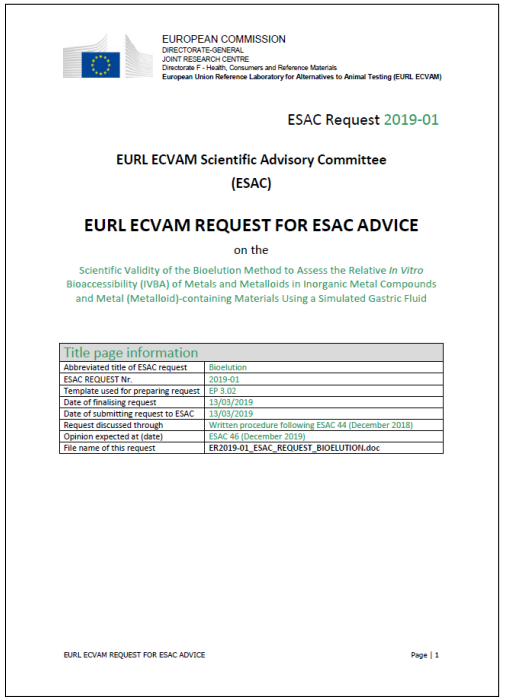


ESAC (5 year mandate)

Selection via Public Call for Applications

ESAC advice

- **Peer review of validation studies**
  - Coordinated by EURL ECVAM
  - Submitted to EURL ECVAM
- **Any other advice**
  - Non-animal-derived antibodies
  - …



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ESAC Request 2019-01

EURL ECVAM Scientific Advisory Committee (ESAC)

EURL ECVAM REQUEST FOR ESAC ADVICE

on the

Scientific Validity of the Bioelution Method to Assess the Relative *In Vitro* Bioaccessibility (IVBA) of Metals and Metalloids in Inorganic Metal Compounds and Metal (Metalloid)-containing Materials Using a Simulated Gastric Fluid

Title page information	
Abbreviated title of ESAC request	Bioelution
ESAC REQUEST Nr.	2019-01
Template used for preparing request	EP 3.02
Date of finalising request	13/03/2019
Date of submitting request to ESAC	13/03/2019
Request discussed through	Written procedure following ESAC 44 (December 2018)
Opinion expected at (date)	ESAC 46 (December 2019)
File name of this request	ER2019-01_ESAC_REQUEST_BIOELUTION.doc

EURL ECVAM REQUEST FOR ESAC ADVICE Page | 1

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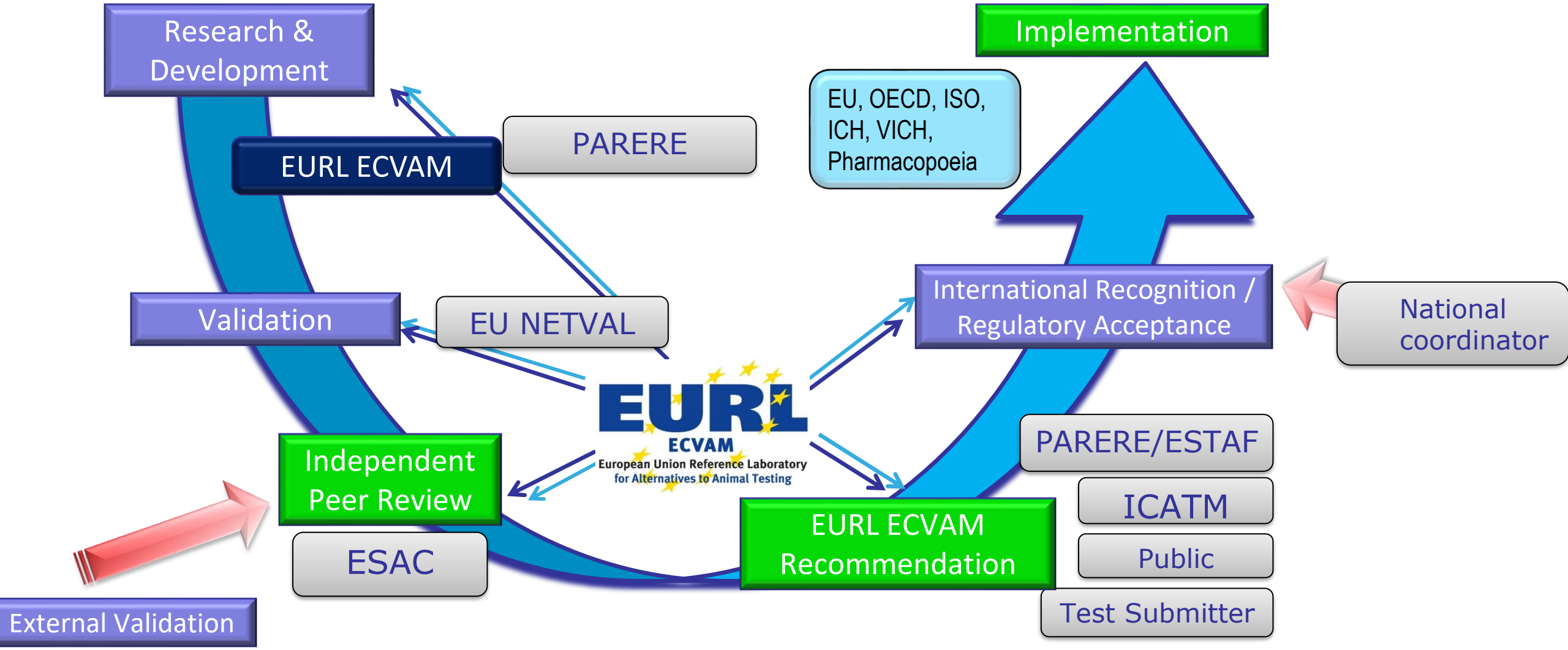
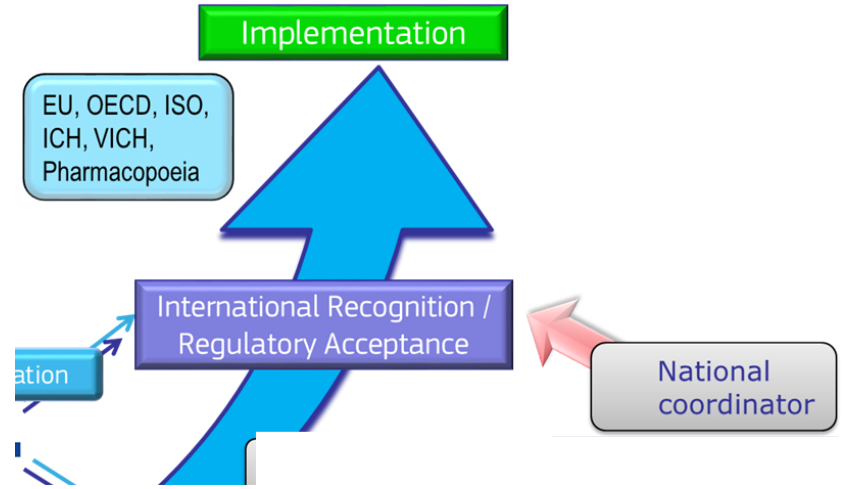
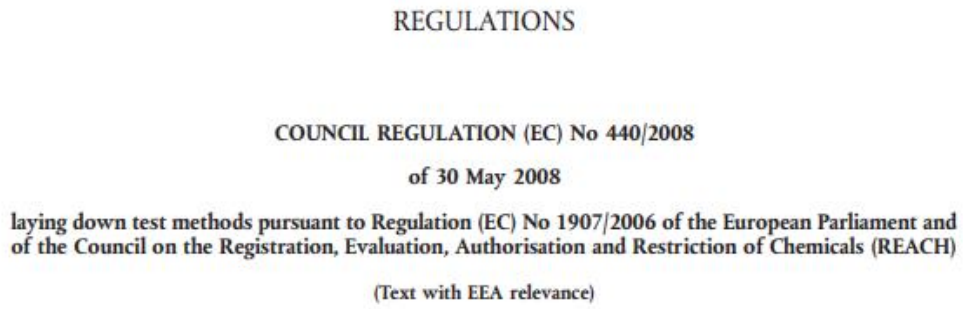


International recognition



- **New project proposal submitted to OECD**
  - Validation outcome and draft **Test Guideline** discussed at expert groups level and Test Guideline is approved by Working Party of the National Coordinators of the Test Guidelines Programme (WNT)



REGULATIONS

COUNCIL REGULATION (EC) No 440/2008

of 30 May 2008

laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

(Text with EEA relevance)

- **Regulatory acceptance in the EU**
  - TG taken up at EU level in EU Test Method Regulation and becomes an official test method to be used for chemical safety testing under REACH and various other EU legislation.

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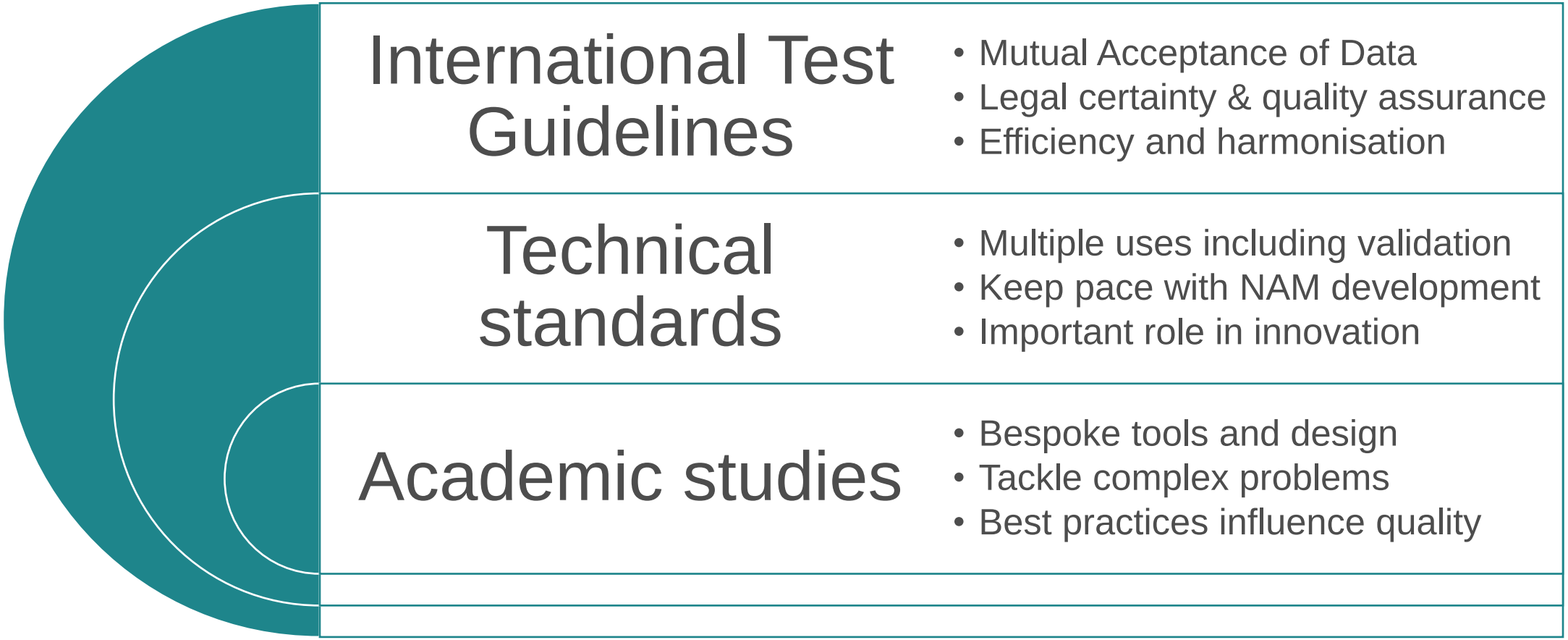
Levels of standardisation



Establishment of a European coordination platform to advance standardisation for Organ on Chip

Analysis of standards for OoC

EUROOCS EUROPEAN ORGAN-ON-CHIP SOCIETY

PSIS workshop

OUTCOME

CEN CENELEC

CEN-CENELEC Focus Group

Lab on a Chip

ROYAL SOCIETY OF CHEMISTRY

PERSPECTIVE

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Cite this: *Lab Chip*, 2021, **21**, 2857

Standardisation needs for organ on chip devices†

Monica Piergiovanni, * Sofia B. Leite, Raffaella Corvi and Maurice Whelan

Organ on chip (OoC) devices represent the cutting edge of biotechnologies, combining advanced cell and tissue culture with microengineering. OoC is accelerating innovation in the life sciences and has the potential to revolutionise many fields including biomedical research, drug development and chemical risk assessment. In order to gain acceptance by end-users of OoC based methods and the data derived from them, and to establish OoC approaches as credible alternatives to animal testing, OoC devices need to go through an extensive qualification process. In this context, standardisation can play a key role in ensuring proper characterisation of individual devices, benchmarking against appropriate reference elements and aiding efficient communication among stakeholders. The development of standards for OoC will address several important issues such as basic terminology, device classification, and technical and biological performance. An analysis of technical and biological aspects related to OoC is presented here to identify standardisation areas specific for OoC, focusing on needs and opportunities. About 90 standards are already available from related fields including microtechnologies, medical devices and *in vitro* cell culture, laying the basis for future work in the OoC domain. Finally, two priority areas for OoC are identified that could be addressed with standards, namely, characterisation of small molecule absorption and measurement of microfluidic parameters.

Received 25th March 2021,
Accepted 17th June 2021

DOI: 10.1039/d1lc00241d

rsc.li/loc

Stem Cell Reports

ISSCR

Meeting Report

OPEN ACCESS

Putting Science into Standards workshop on standards for organ-on-chip

Monica Piergiovanni,[1,*] Ozlem Cangar,[2] Sofia B. Leite,[1] Livia Mian,[3] Andreas Jenet,[4] Raffaella Corvi,[1] Maurice Whelan,[1] Fabio Taucer,[4] and Ashok Ganesh[3]

[1]European Commission, Joint Research Centre (JRC), Ispra, Italy
[2]European Health and Digital Executive Agency (HaDEA), Brussels, Belgium
[3]CEN-CENELEC, Market Perspective and Innovation, Brussels, Belgium
[4]European Commission, Joint Research Centre (JRC), Brussels, Belgium
*Correspondence: monica.piergiovanni@ec.europa.eu

https://doi.org/10.1016/j.stemcr.2021.07.010

The European Commission Joint Research Centre and the European Standardization Organizations CEN and CENELEC organized the "Putting Science into Standards" workshop, focusing on organ-on-chip technologies. The workshop, held online on 28–29 April, 2021, aimed at identifying needs and priorities for standards development and suggesting possible ways forward.

European Commission

JRC CONFERENCE AND WORKSHOP REPORT

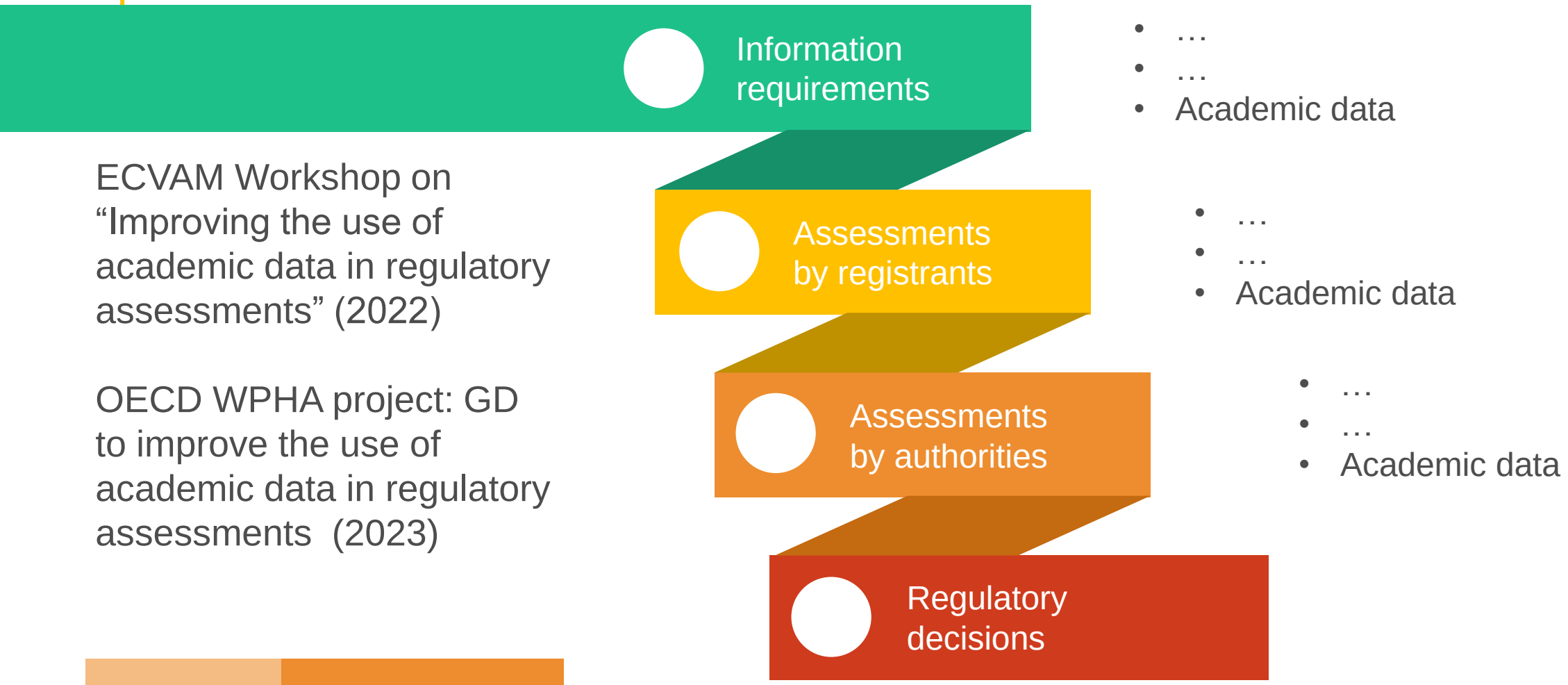
Organ on chip: building a roadmap towards standardisation

Putting Science into Standards

Piergiovanni, M.; Jenet, A.; Batista Leite, S.; Cangar, O.; Mian, L.; Maurer, P.; Ganesh, A.; Whelan, M.; Taucer, F.

2021

Non-standard data in regulatory assessments



ECVAM Workshop on "Improving the use of academic data in regulatory assessments" (2022)

OECD WPHA project: GD to improve the use of academic data in regulatory assessments (2023)

58% Non-standard key studies in REACH restrictions

Borchert et al 2022

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EURL ECVAM STATUS REPORT 2022

https://publications.jrc.ec.europa.eu/repository/handle/JRC132525

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Thank you

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