The future of validation: Update of OECD GD 34

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The principles and process of validation OECD Guidance Document 34

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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

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Top priorities for the update

1. Validation of Defined Approaches (DAs) and their building blocks
2. Including more practical guidance on validation, such as chemicals selection, data integrity, quality assurance, study design
3. Defining the concept of Technical Validation
4. Assessment of relevance beyond accuracy to predict animal data
5. Validation of new technologies such as Organ-on-Chip and Artificial Intelligence
6. Revise the process to assess reproducibility and transferability
7. Evolution of Performance Standards

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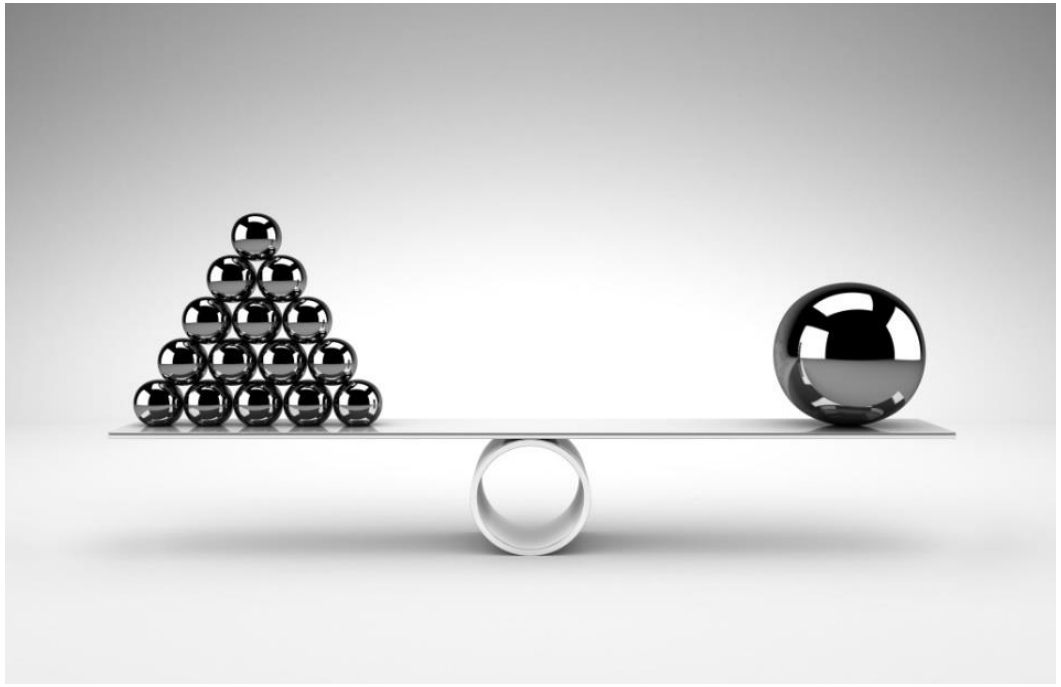
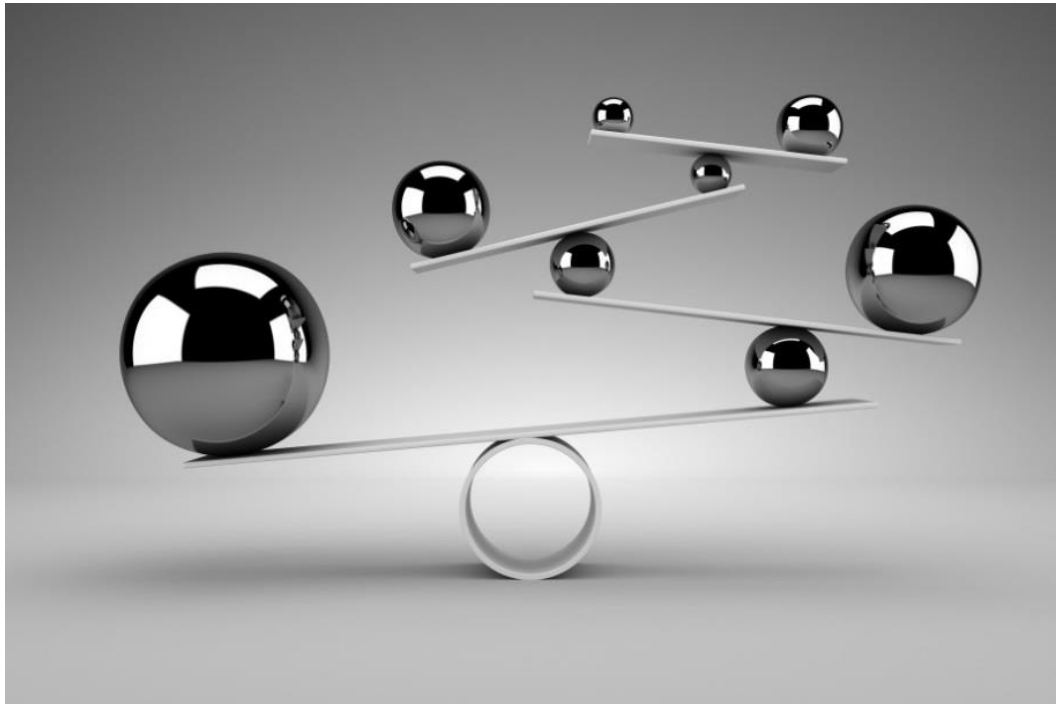
Concept and validation of Defined Approaches and IATA

Defined Approach

- Fixed information sources
- Fixed Data Interpretation Procedure

↳ **Can be validated and falls under MAD**





Integrated Approach to Testing and Assessment

- Flexible approach
- Weight of evidence/expert judgement

➢ Need for a confidence building framework

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How to validate and accept mechanistic methods that are part of a Defined Approach?

- What level of validation and approval for individual methods is required prior to DA consideration and adoption?
- Expedite TG development and approval for individual methods during or immediately after DA approval

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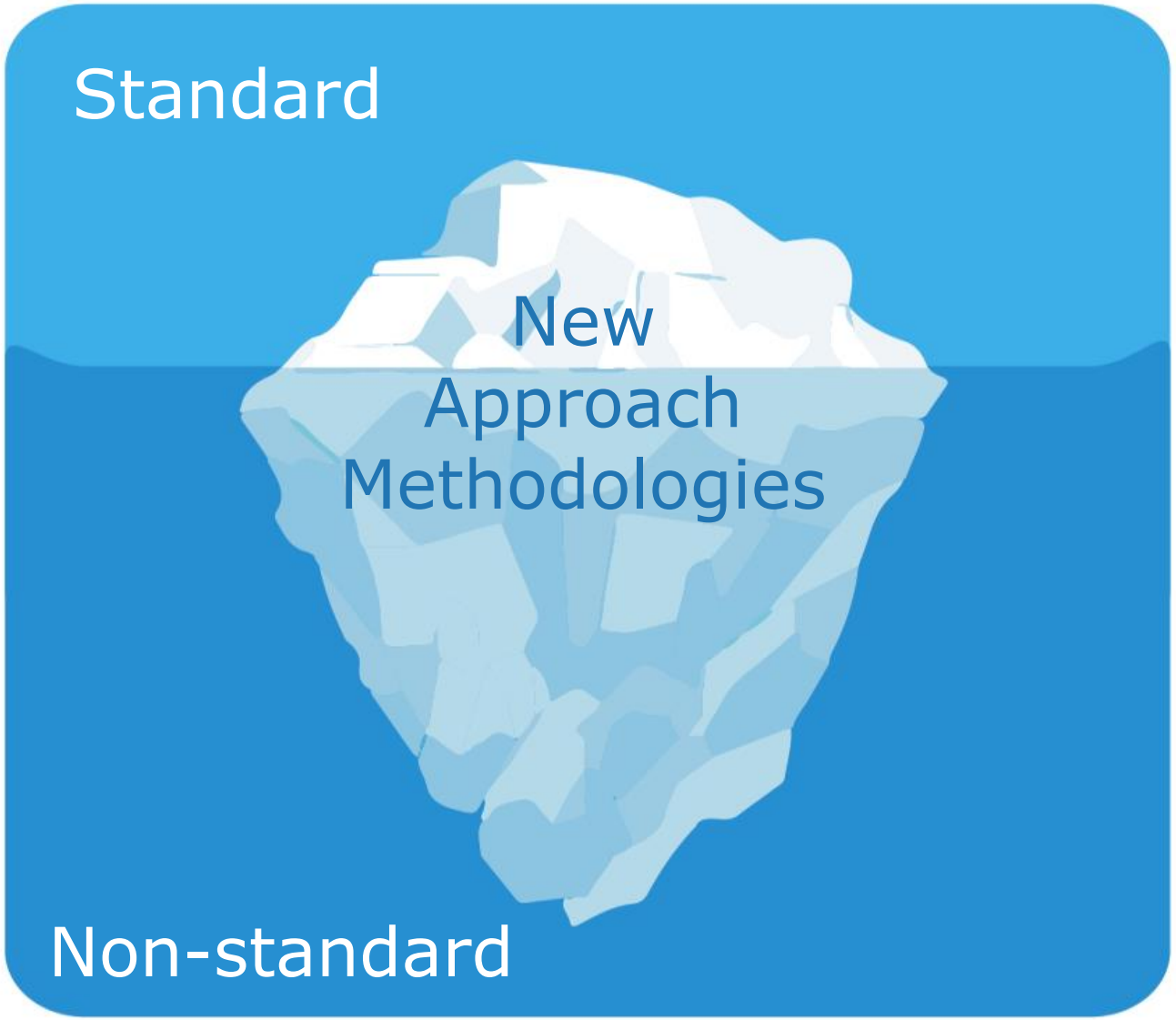
Facilitating acceptance of mechanistic NAMs



- Technical characterisation, including reproducibility, biological relevance and regulatory usefulness, without having to establish regulatory application
- Acceptance of mechanistic NAMs that are not stand-alone and/or for which regulatory application is not yet clear

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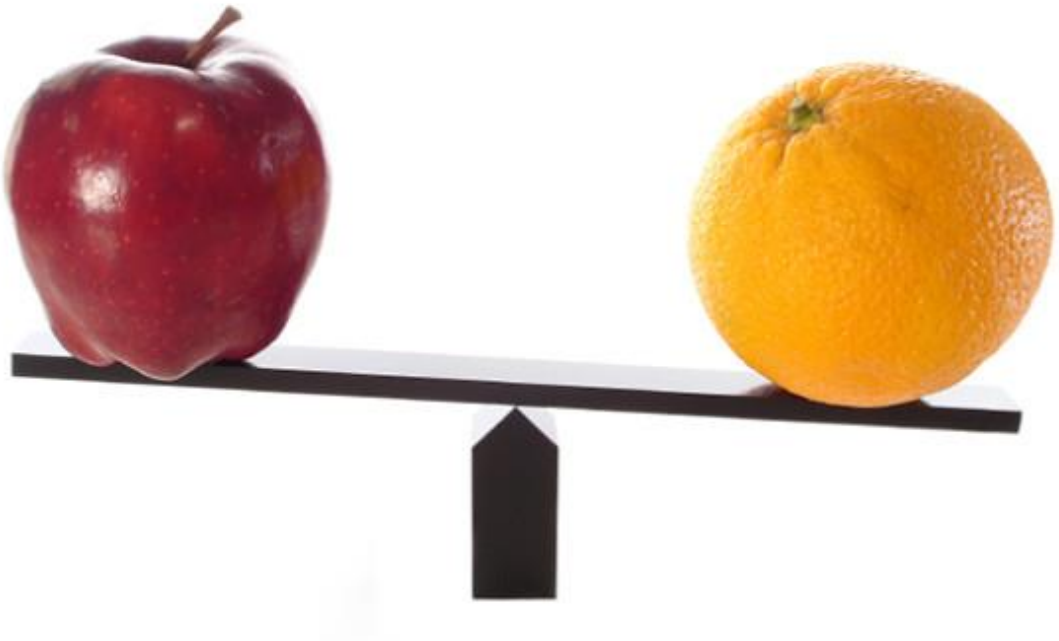
Relevance versus predictive capacity



- Value of empirical data versus biological/mechanistic knowledge
- Value of Predictive Capacity and comparison with existing animal data versus mechanistic/biological understanding and consistency across methods/approaches
- Use biological relevance of a method/approach to benchmark its performance

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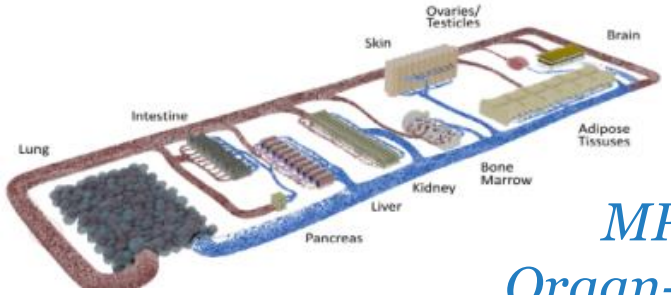
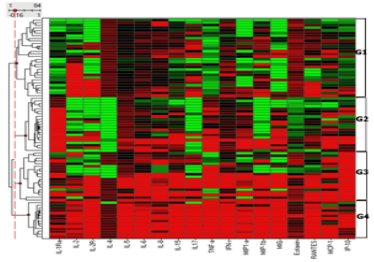
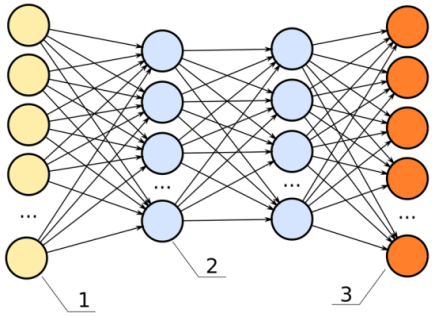
Validation of new technologies



MPS & Organ-on-Chip

'omics





machine learning & AI

Organ-on-chip

- Assembly of chips, flow and operation, chemical binding to devices, complexity of implementation and handling
- Physiological and biological relevance

Machine learning & AI

- Transparency, interpretability, explainability
- Robustness (dependence on training set), feature importance, overfitting, complexity

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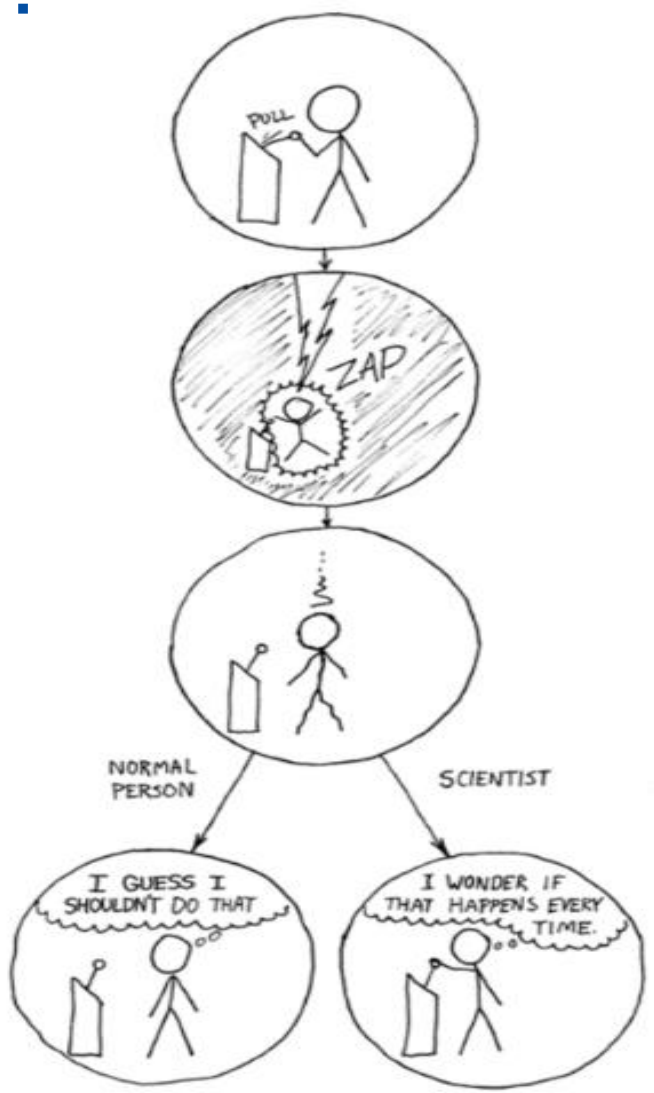
Need for multi-laboratory ring trials?

- Demonstrating reproducibility is essential
- Ring trials are the most time-consuming and expensive part of a validation study
- Properly designed training and transfer studies are essential and informative
- Proficiency testing adds confidence on capacity of a laboratory to perform test



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Evolving Performance Standards

- PS = Essential Test Method Components; Reference Chemicals; Targets of reproducibility and Predictive Capacity
- Worked well for very similar, stand-alone methods, but evolution needed!
- Standards that can be used as benchmark for various non-similar methods/approaches that provide equivalent information

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Thank you

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