Session 4: Enhancing the translation of non-animal approachess into regulation

Introduction

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Workshop on the Commission roadmap towards phasing out animal testing for chemical safety assessments, 11-12 December 2023

We all agree the translation is too slow – but what's needed to accept a method for regulatory use?

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Session topics

- Part 1 – what is validation and what do we need from it?
- Part 2 – how can validation be accelerated?

  how can operational and financial needs of validation be met?
- Part 3 – what other factors do we need to address in addition to achieve regulatory acceptance faster?

Validation and Regulatory Acceptance

Validation –

a scientifically anchored process that serves to demonstrate the **reliability and relevance** of a method for a particular purpose, building trust and confidence, within a **regulatory context of use.**

Regulatory Acceptance –

uptake of a method and **reliance** on data obtained from it in different decision-making contexts

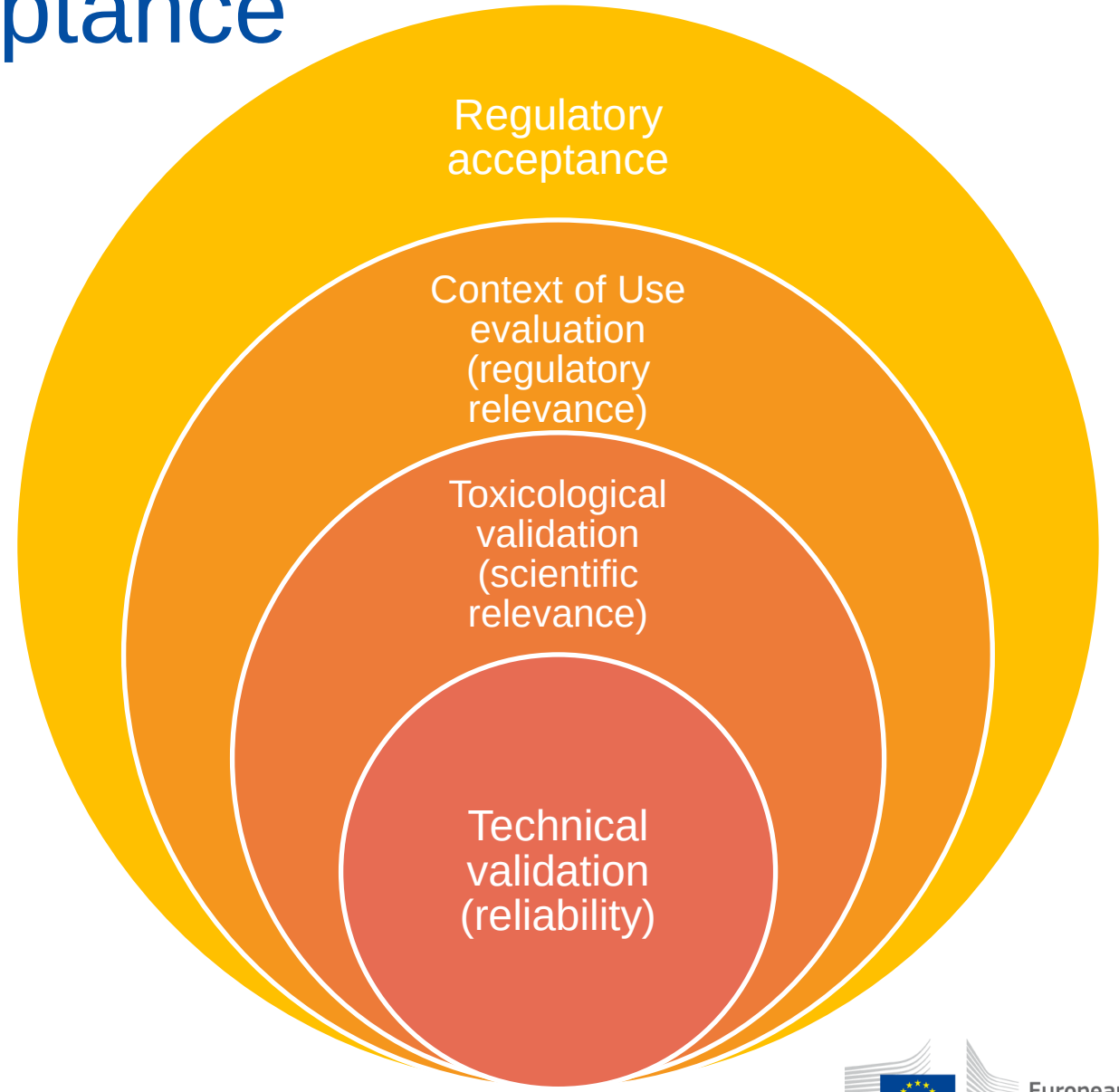
From validation to acceptance

Broad acceptance among regulators

Fitness for purpose. Building trust and confidence, within a regulatory context of use

Relevance for a particular scientific purpose

Method is sufficiently robust and reproducible = reliable



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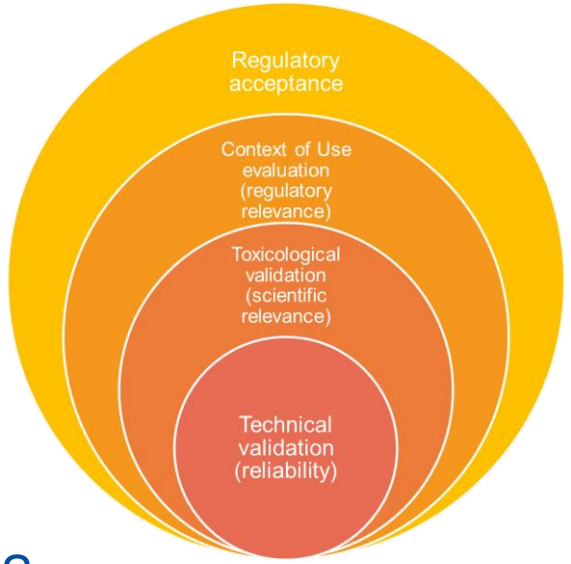
Different needs from validation depending on NAM use:

- for initial screening and priority setting
- for (additional) mechanistic understanding in a testing strategy
- for full replacement of existing in vivo approaches
- as a component in a defined approach
- for risk assessment of substances within known (limited) exposure
- mutual acceptance of data in an international context (MAD)
- for hazard assessment and comparison to classification criteria

A lengthy process today – how can we accelerate?



What outcomes are needed from the 4 parts of the process?

- Technical validation (reliability): what degree of **reproducibility** do we need?
- Toxicological validation (scientific relevance): what are key requirements?
  what **reference data** do we compare to?
  how many **reference substances** are needed?
- Context of Use evaluation (regulatory relevance): **how is the NAM used** in decision making?
  what **additional evidence** is used?
- Regulatory acceptance: what really is the key driver for **global regulators** to accept a method?

What served us well so far?

Quality data obtained from OECD-accepted methods, carried out under GLP:

- are considered reliable, comparable and re-usable
- allow mutual acceptance of data (**MAD**) between different EU legislations and at international level (avoiding duplicate testing)
- lead to legal certainty for industry as well as demonstrability of compliance and enforcement

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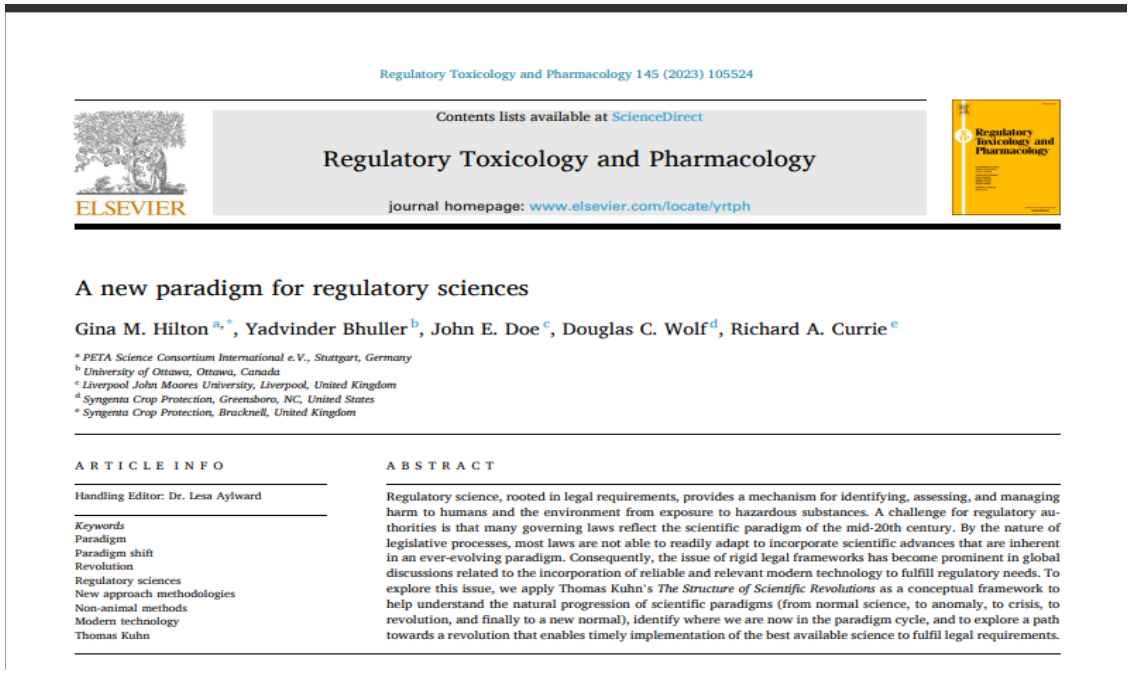
Do we need a paradigm shift? How do we achieve it?

“The scientific community is currently in the ‘crisis’ phase of the paradigm cycle – caught in a paradox of modern science that can fulfill regulatory requirements coupled with outdated legal mandates not reflecting the current state of knowledge and technology.”



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A new paradigm for regulatory sciences

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ABSTRACT

Regulatory science, rooted in legal requirements, provides a mechanism for identifying, assessing, and managing harm to humans and the environment from exposure to hazardous substances. A challenge for regulatory authorities is that many governing laws reflect the scientific paradigm of the mid-20th century. By the nature of legislative processes, most laws are not able to readily adapt to incorporate scientific advances that are inherent in an ever-evolving paradigm. Consequently, the issue of rigid legal frameworks has become prominent in global discussions related to the incorporation of reliable and relevant modern technology to fulfill regulatory needs. To explore this issue, we apply Thomas Kuhn's *The Structure of Scientific Revolutions* as a conceptual framework to help understand the natural progression of scientific paradigms (from normal science, to anomaly, to crisis, to revolution, and finally to a new normal), identify where we are now in the paradigm cycle, and to explore a path towards a revolution that enables timely implementation of the best available science to fulfil legal requirements.

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Milestones on the road to faster regulatory acceptance:

Need to define them together!

1.

2.

3.

4.

5.

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Thank you

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