Pepper

Public-private platform for the pre-validation of endocrine disruptors characterization methods

Cécile Michel-Caillet
CEO



Validation of test methods to identify endocrine disruptors:

Example of a functional and effective model

Which assessment areas to prioritise for early implementation in pesticides and biocides?

Pepper answer: EDCs

Answer based on:

- Regulatory need
- Scientific readiness
- Not a replacement so a priori no potential reduction in animal use

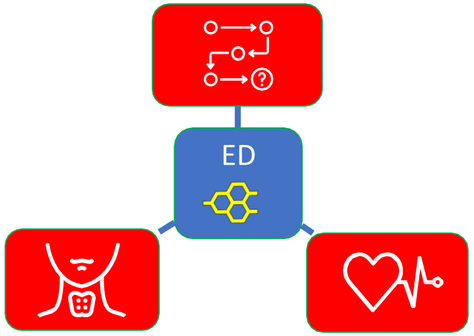
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Why to focus on EDCs:

- Pragmatism:
  - Cannot do all at the same time
  - Proof of concept
- Regulatory needs: In France, Pepper to build innovative tests methods for assessment tools currently lacking

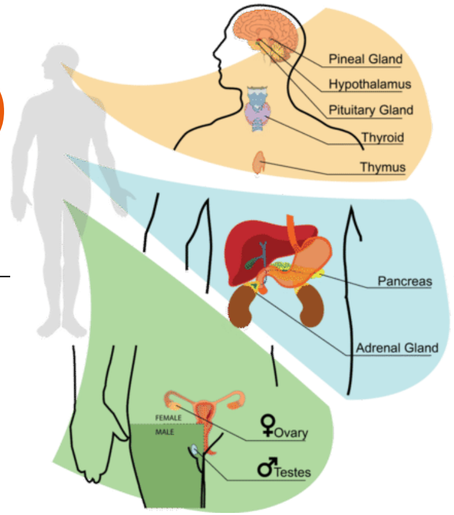
Improving identification

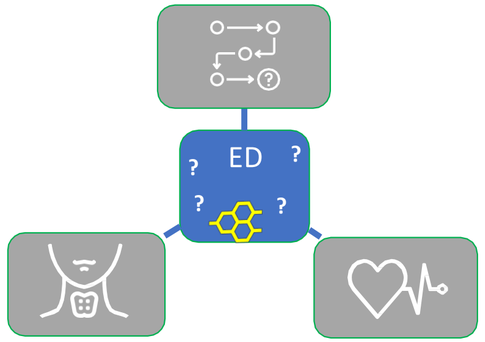
- Numerous studies have confirmed that EDs can have a wide range of effects on humans and fauna
- Few data for many chemicals/ source of EDCs
- Lack of tests methods to assess



SMALL NUMBERS OF EDs IN LEGISLATION E.G EDLISTS.ORG (2026):

substances and groups of substances **135**





HIGH NUMBERS OF SUBSTANCES UNDER SCRUTINY E.G. ANSES (2021):

906 « substances of interest » with regards to ED characterisation

? Many endpoints not covered by the test methods available

→ Identifying these gaps, and methods developed properly to fill them => challenging

What concrete measures for the greatest impact in overcoming current implementation barriers?

Pepper answer: validation

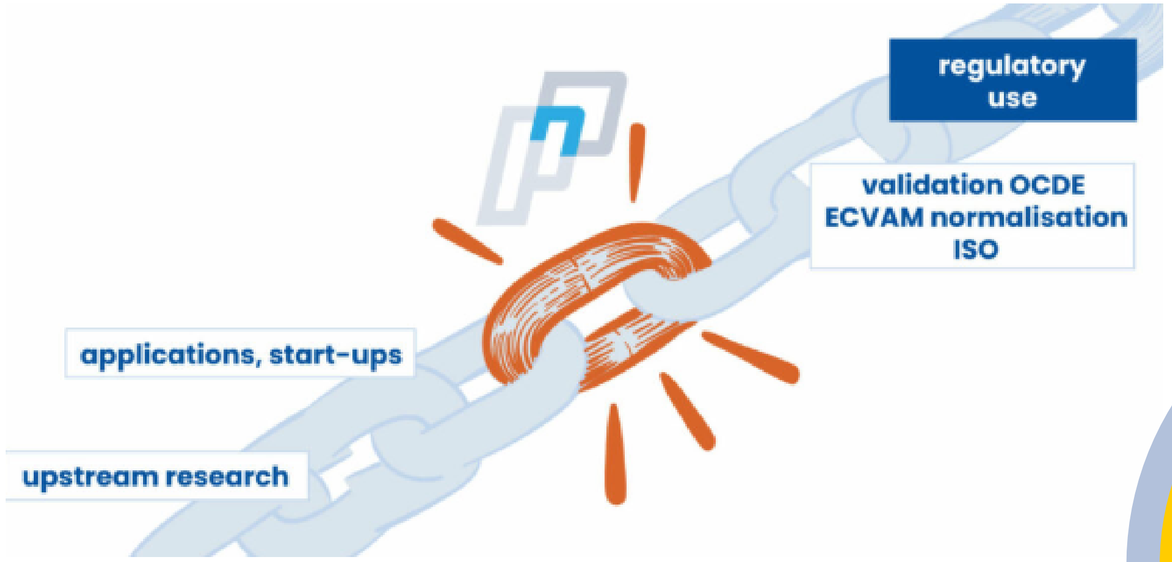
Validated methods help build trust, allow MAD* and regulatory acceptance :

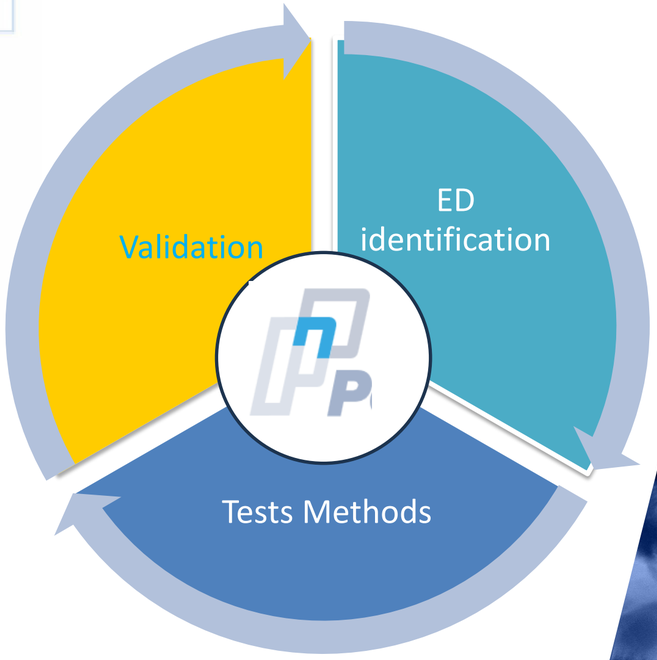
- Updating guidance,
- Training: skills development
- Provision of tools tailored to regulatory needs
- Have concrete proposals : analysis of use cases, challenges encountered, etc.

Validation = the most effective way to reduce reliance on animals while implementing tools that ensure health and safety.

*Best tool to reduce animal testing

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Validation: what, why difficulties encountered

Process by which the reliability and relevance of a particular approach, method, process or assessment is established for a defined purpose.
(OECD GD34; 2005)

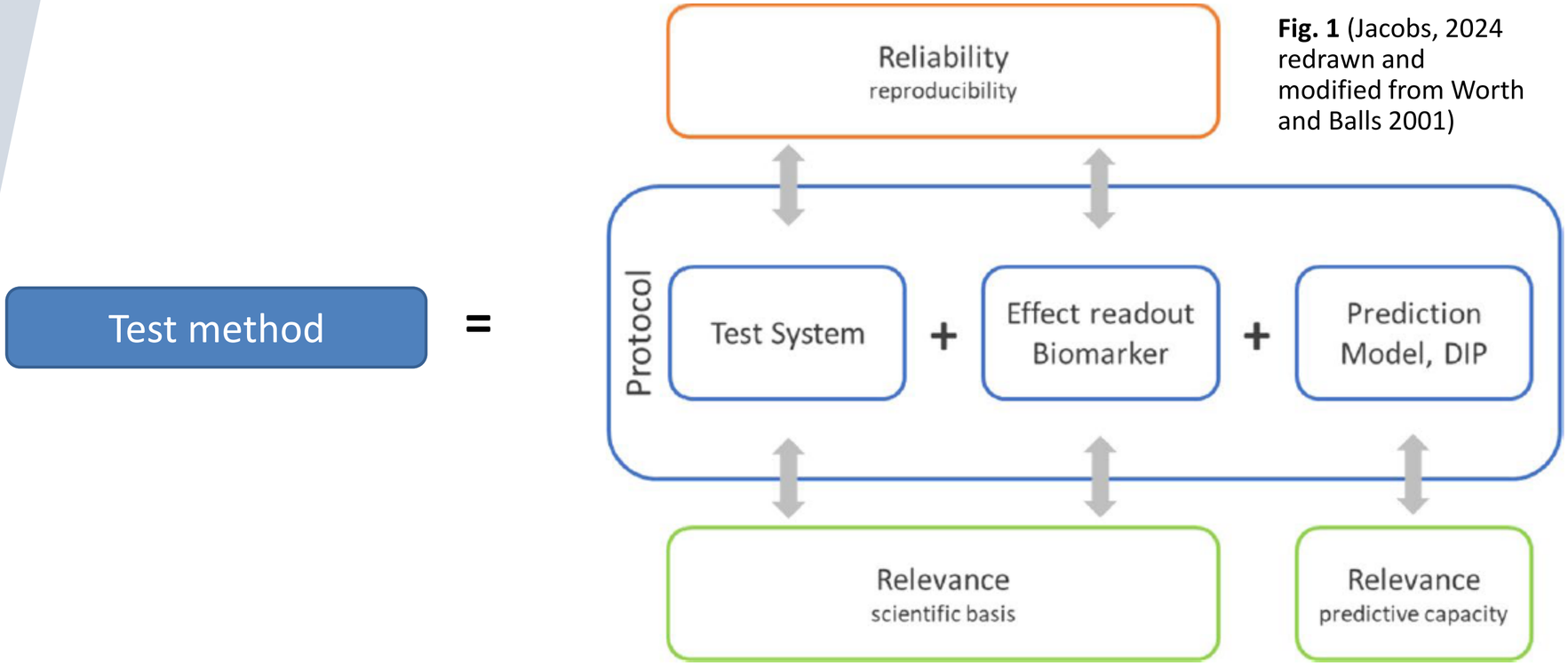


Fig. 1 (Jacobs, 2024 redrawn and modified from Worth and Balls 2001)

Work on the bottlenecks of validation:

- Gathering enough funding
- Work to
  - Build models that are biologically & economically sustainable
  - Identify clearly their strength, limits (applicability domain) to include them into DA/IATA/integrated approaches

Sector-specific considerations for pesticides and biocides that need particular attention during implementation of the roadmap

Do not get lost in translation: Qualification versus validation

Qualification as a step toward broader validation and regulatory acceptance.

- Qualification of methods in defined regulatory contexts can build confidence before full validation is achieved.
- Case studies and context-of-use approaches can accelerate acceptance.
- Cost of qualification may be covered by the user within their specific context.

BUT

- Qualification does not account for the time required for evaluation by the authorities for each specific context of use—a process that can quickly become quite costly (in terms of the authorities' resources, rather than those of the developer or a dedicated organization).
- Most significant resource savings—whether through animal-based testing, non-animal testing, or *in silico* simulations—are achieved via OSOA & MAD .

➢ Ultimately, validation is still required.

Who will fund broader validation?

Is validation the end goal?

Seems necessary to provide for retrospective validation of the methods to refine their appropriate use and acceptability criteria. Who will bear the cost?

Conclusions: a set of points that could not be addressed through the questions sent

E: cecile.michel-caillet@ed-pepper.eu

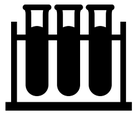
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Issue of leadership: for each point of the roadmap, identify the institutional leader.

- Quantify the resources,
- Identify where available expertise and coordination
- Organize, set up leadership



Optimization of validation, standardization and regulatory qualification :

- Set up reference chemical databases
- Identify incentives that experience from cosmetics, pharmaceuticals and other sectors could be leveraged more effectively.



Acceptance of NAM or integrated approach is a political decision: historically, sat up by scientists. Who to define the level of uncertainty acceptable?