Level of validation of NAMs: expectations for methods used under REACH

REACH Article 13 ***General requirements for generation of information on intrinsic properties of substances*** provides:

> Tests shall be conducted according to the methods described in Commission Regulation **(EC) No 440/2008 laying down test methods pursuant to REACH** ('Test Method Regulation').
>
> *or*
>
> in accordance with **other international test methods recognised by the Commission or the Agency as being appropriate.**
>
> *or*
>
> Information on intrinsic properties of substances may be generated **in accordance with other test methods provided that the conditions set out in Annex XI are met**.

Level of validation of NAMs: expectations for methods used under REACH

Other test methods provided that the conditions set out in Annex XI

- sufficiently well developed according to **internationally agreed test development criteria** (e.g. the ECVAM criteria for the entry of a test into the pre-validation process).

- method whose scientific validity has been established by a validation study, according to **internationally agreed validation principles**.

Level of validation of NAMs : expectations for Plant Protection Products (PPPs)

- Communications on data requirements*: “Only test methods that have been **validated** (e.g. ring-tested by **OECD or equivalent international organisations**) are listed.
  Test methods only described in scientific publications have not been included.”

- Data Requirements for active substances and PPPs: ..In the absence of suitable internationally or nationally validated test guidelines, **test guidelines accepted by the European competent authority** shall be used. ….”

- Use of NAMs is considered by EFSA (EFSA strategy 2027, Roadmap https://www.efsa.europa.eu/en/supporting/pub/en-7341))

-> DG SANTE is interested in the further development and follows it up with EFSA, and JRC
-> it has to be proven to be robust and fit for purpose

* Commission Communications **2023/C 344/02** and **2023/C 344/01** (chemical active substances and ppps),
Commission Communications **2023/C 202/03** and **2023/C 202/02** (microbiological active substances and ppps).

Level of validation of NAMs: expectations for Biocidal Products

- Information requirements on active substances and biocidal products laid down in Annexes II and III of the BPR

  Tests shall be conducted according to the methods described in Commission Regulation **(EC) No 440/2008 laying down test methods pursuant to REACH**.
  Other internationally recognised (if possible) methods can be used but need to be justified in the application.
- **Internationally recognised test methods** shall be available.
- Training on NAMs are needed for Member States and all stakeholder groups

- ECHA is committed to support the transition towards an animal-free regulatory environment for chemicals:
  - ECHA workshop on NAMs - 31.05 to 01.06.2023

Cosmetics – SCCS
ACCEPTANCE OF NEW ALTERNATIVE METHODS

(1) OFFICIALLY VALIDATED REPLACEMENT METHODS/STRATEGIES (OECD TGs)

(2) VALID REPLACEMENT METHODS WITH POSITIVE & NEGATIVE CONTROLS, SHOWING FULL PROTOCOLS & ALL PUBLICATION(S); IF HISTORICAL CONTROLS ARE USE → UPDATED CASE-BY-CASE, INCLUDING EXPERT JUDGEMENT
ADDITION OF RELATED NAMs TO BUILD WoE; CASE STUDIES TO CREATE TRUST

(3) MECHANISTIC METHOD FOR WHICH DEVELOPMENT IS BASED ON BUILDING BLOCKS OF AOP PREFERABLY BASED ON HUMAN CELLS or TISSUES, ALL PUBLICATIONS, INCLUDING EXPERT JUDGEMENT

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(4) PBPK MODELS FOR QUANTITATIVE SAFETY EVALUATION: criteria
→WHEN COMMERCIAL MODEL IS USED → SECOND 'FREE ACCESS MODEL' (comparable results)
→ SENSITIVITY & UNCERTAINTY ANALYSIS FOR ALL PARAMETERS
→ RATIO OF SIMULATED & OBSERVED DATA WITHIN FACTOR 2
→ CORRECT PREDICTION: NO USE OF THE SAME EXPERIMENTAL DATA AS USED TO BUILD THE MODEL
→ ADDING RESULTS OF SUITABLE READ-ACROSS EXERCISE
→ TO BE ESTABLISHED: CRITERIA FOR NEW MOLECULES WITH NO READ-ACROSS DATA, NO *IN VIVO* DATA