Developing principles for read-across of degradation simulation test endpoints

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ABSTRACT / BACKGROUND

- **Biodegradation simulation tests**, required under EU REACH, aim to provide information on the degradation of substances under environmental conditions.

- These **tests are often complex and expensive** and have important implications for substance evaluation and risk management.

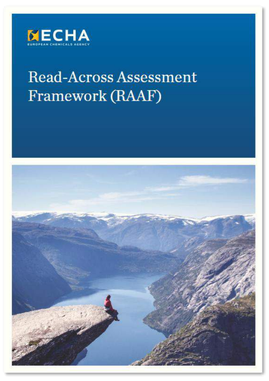
- When test data are missing, ***read-across offers a possible alternative*** - *where data for one or more (source) substance(s) are used to support the data requirements of other (target) substance(s)*.

- Read-across is an established approach for (eco)toxicity endpoints, whilst the **application to degradation endpoints has so far received little attention**.

- This poster explores the **principles of read-across when applied to degradation simulation tests** and discusses the **potential benefits and obstacles to implementation**.

REACH Annex XI details **principles for read-across**:

> *"**Substances** whose … **properties** are likely to **be similar** or **follow a regular pattern** as a result of **structural similarity**, may be considered as **a group, or category**, of substances."*
>
> *"The similarities may be based on any of the following:*
> *(1) a common functional group;*
> *(2) the common precursors and/or the likelihood of common breakdown products via physical and biological processes…;*
> *(3) a constant pattern in the changing of the … properties.*



These principles are further elaborated in the ECHA **Read-Across Assessment Framework (RAAF)**[1], which evaluates read-across according to one of six scenarios each with various assessment elements (AEs). The scenario depends on whether an analogue or category approach is applied, and whether the read-across is based on similar properties or (bio)transformation to common compounds.

A **read-across hypothesis** (a reasoned basis for the prediction) must be provided, along with supporting evidence. Additionally, it is recommended to prepare a **data matrix** presenting all related property data and lines of evidence for the category.

CONSIDERATIONS FOR SIMULATION TESTS

For persistence assessments, simulation tests provide information on:

- **Degradation half-life**
- **Formation of transformation products**

Both are important for the assessment and should be considered for read-across. Two substances may have a similar degradation half-life but different transformation products, or vice versa.

Degradation half-life is typically based on primary transformation, but mineralisation is also possible. It is calculated by fitting degradation data to one of several kinetic models[2]. Further aspects may affect the calculations, such as the treatment of any lag phase, volatilised fraction, and non-extractable residues (NER). Recent changes to NER guidance mean that the NER component of a simulation test is likely to become a distinct and important consideration for read-across. At present, limited knowledge is available as to how intrinsic substance properties impacts NER formation and assessment of persistence.

Relevant **transformation and/or degradation products** (TPs) need to be considered in the persistence assessment. The criteria for when TPs are considered relevant relates to the concentrations formed in the test (N.B. the criteria differ somewhat between REACH and CLP[3]).

Various factors need to be considered in terms of TPs in the context of read-across, including:

- Would the profile of observed TPs be expected to be similar?
- Would the identity of relevant TPs be expected to be the same?
- If different, is assessment of TPs from the source substance useful to inform the assessment of TPs of target substance?

A **read-across hypothesis** for either degradation half-life or transformation products would need to consider structure, phys-chem properties and degradation pathway(s). Phys-chem properties can have a marked influence on partitioning and behaviour in simulation tests, ultimately impacting degradation half-life and pathways observed.

In practice, read-across of simulation test data for regulatory purposes is likely to face considerable challenges and complexity.

Table 1. Potential data matrix with relevant information categories to support read-across of simulation test data

Data category	A	B	C	D
Structural elements				
Phys-chem				
Screening tests				
Simulation test half-life				
Simulation test TPs				
Other expt. (e.g. STP)				
QSARs				
TP predictions				

CONCLUSIONS

- Read-across is an established practice for using data efficiently.
- Read-across of simulation test data:
  - Requires consideration of different elements (i.e. degradation half-life and transformation products).
  - Has potential to reduce testing costs, speed up regulatory evaluation, support assessment of complex substances, and mitigate testing challenges and data variability.
  - Should be possible in principle but is likely to face considerable challenges of complexity and uncertainty that may limit its regulatory application in practice.

Please share your thoughts via this short survey:

References

[1] ECHA, 2017. Read-Across Assessment Framework (RAAF).

[2] ECHA, 2023. Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11: PBT/vPvB assessment. Version 4.0.

[3] ECHA, 2024. Guidance on the Application of the CLP Criteria. Part 4: Environmental hazards and Part 5: Additional Hazards. Version 4.0.

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