

D1.4

SOP on (alternative) data completeness for regulation

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WP 1

INTRODUCTION

- D1.4. outlines aspects to be considered for the criteria and strategy for alternative test data inclusion (omics, modelling, read/across, grouping).
- two major aspects of the use of alternative data for the environment were included:
 1. current state of the art regarding **ALTERNATIVE TEST DATA**, by reviewing literature and scoping the main aspects, including 2 main alternative data: **A - omics, molecular; B - read across, grouping, modelling.**
 2. **APPROACHES AND RECOMMENDATIONS for alternative test data inclusion towards regulation.** A list of criteria for alternative (modelling, read/across, grouping) data and pilot data sets for verification of tools elaborated by WP2 and WP3.

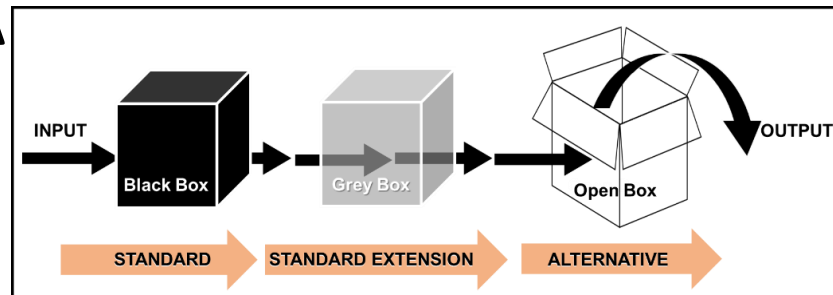


1. ALTERNATIVE TEST DATA

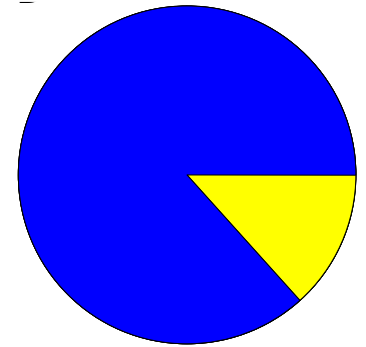
A – omics, molecular

TESTS:

- 1) Standard tests (OECD/ISO),
- 2) Standard tests (OECD/ISO) extensions: time course or prolonged exposures and/or multigenerational, and
- 3) Alternative tests, beyond current OECD/ISO: omics, biomarkers, in vitro, in silico and modelling.

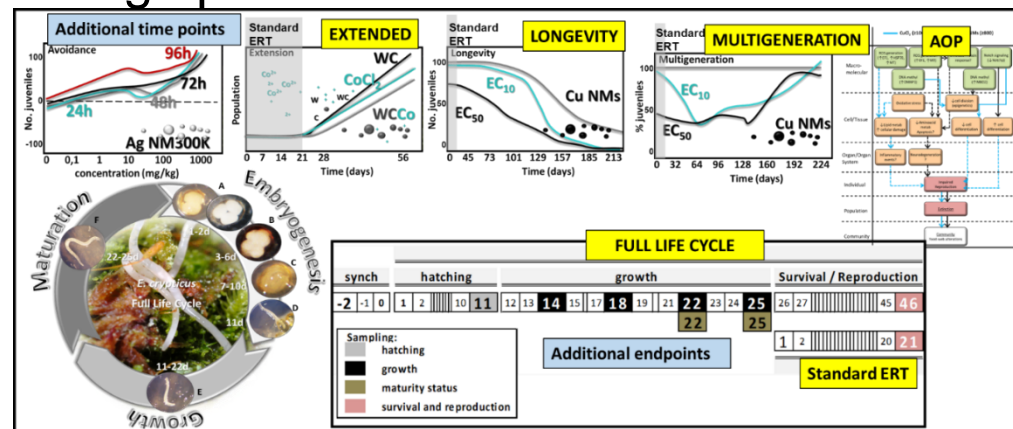
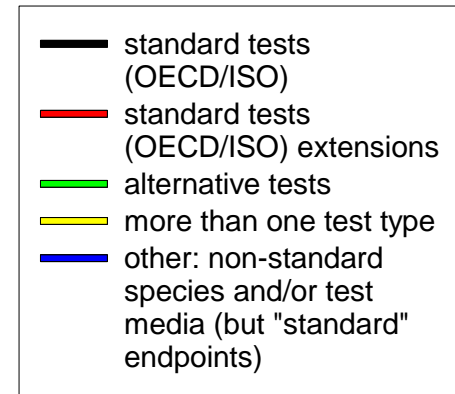


- One of the frameworks' needs [besides data], are fit-for-purpose tools to assess the hazards, and hence the role of standardized tools is a key asset to have consolidated and harmonised between countries.
- there is strong support from regulatory bodies for the development of New Approach Methodologies (NAMs) to establish “Alternative Tests” both in EU, USA, Canada, Australia, Japan, South Korea.



A – omics, molecular

- Large % of data comes from alternative tests;
- Considerable development for a) additional endpoints, b) additional time points, and c) extended exposure period.
- The importance and added-value of alternative methods is particularly recognized for NMs, that are entering the market at a speed never seen before for any class of chemicals, which would benefit from the predictive and read-across potential of NAMs – New Approach Methodologies, also for a safer-by-design production of materials.



Gomes et al, 2021. Nanotoday, 40 101242.
<https://doi.org/10.1016/j.nantod.2021.101242>



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B- read across, grouping, modelling

- European Chemicals Agency (ECHA): grouping and read-across approaches can be applied to reduce the number of tests required for the risk assessment of ENMs (ECHA 2017).
- Grouping regarding ecotoxicity is still in its infancy compared to human toxicity - NANORIGO D1.4 explored this aspect.
- Based on the available information potential groups were defined: 1st materials properties; 2nd: ecotoxicity.
- grouping of materials do not group similarly in terms of ecotoxicity, few exceptions, e.g. ZnO.
- some properties can improve the match, e.g. from QSARs (Quantitative Structure-Activity Relationships), e.g. molecular polarizability, accessible surface area and metal-ion leaching.



2. APPROACHES AND RECOMMENDATIONS

- **DATA:** high quality availability and coverage of diverse NM; regulatory fit-for-purpose; Open data and transparency; solutions for data repositories.
- **TEST DESIGNS:** harmonization for read-across; adopt maturely developed alternative tests;
- **TEST MATERIALS:** periodic table and atomistic modelling; referential type (benchmark), e.g. JRC NMs repository, to generate comparable data; Libraries of NMs, designed for modelling; Specific NMs, designed for functionality;
- **TEST LEVEL:** inclusion of standard, standard extension alternative. Databases should be open to integrate novel data endpoints, and future materials; need for criteria for data quality and completeness of NAMs.
- **DOSE-RESPONSE PARADIGM:** non-monotonic responses of NMs; test dose-response design, beyond “realistic” doses;



2. APPROACHES AND RECOMMENDATIONS

- **READ ACROSS:** less properties than those listed by ECHA (2019) are required for identification of similarity as basis for read-across regarding ecotoxicological endpoints, e.g.:
 - **Algae:** attachment is a relevant property. It can be used as surrogate for the unspecific multiple properties listed by ECHA and directly linked toxicity.
 - **Daphnids:** additional criteria solubility and reactivity for the alignment of groups formed according to EC50 values is material dependent.
 - **Metal and metal oxides:** Expansion to additional groups of ENMs needed.
 - **In test media:** characterization needed.

