

New approach for consideration of non-extractable residues (NER) in persistence assessment suitable in regulatory practice

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INTRODUCTION AND BACKGROUND

Non-extractable residues (NER) are of significance for persistence assessment to identify PBT, vPvB or POP substances. According to ECHA R.11 they have to be considered as non-degraded fraction, if not proven otherwise. NER are formed by various processes depending on substance properties, matrix characteristics and extraction methods. NER can be reversibly bound by adsorption or physical entrapment (type I) **which pose a potential risk to the environment (hidden hazards)**. Otherwise they might be covalently bound to organic matter (type II) or transformed into biomass (biogenic NER, type III) without risk to be remobilised (**safe sink**).

A standardised or commonly accepted method to discriminate NER into the different NER types does not exist up to now making them difficult to assess. Extraction schemes for experimental determination of the NER types in laboratory testing were proposed by BfG/UBA^{1,2} and ECHA (NER discussion paper³). In 2018, the German UBA started a follow-up R&D project.

R&D PROJECT AIMS

Check available approaches and testing strategies for practicability. Develop a harmonised concept to be used in environmental persistence assessment of pesticides, biocides, pharmaceuticals and REACH chemicals.

METHOD

For the ¹⁴C and ¹³C isotope labelled substances Bromoxynil, Isoproturon and Sulfadiazine soil simulation tests (OECD 307) were performed. Different extraction methods to develop a **standard procedure** for determination of **total NER** were applied. Subsequently, samples were extracted by EDTA, silylation and acidic hydrolysis and compared in order to **characterise** the different NER types formed.

INTERIM ACTIVITY NER - WORKSHOP

In February 2021 UBA and its research partners Fraunhofer IME, RWTH Aachen, UFZ Leipzig and the DTU University Lyngby (DK) organised an EU-wide virtual workshop. The project, its results and two proposals for consideration of NER in persistence assessment were presented and discussed with scientists, stakeholders and regulators.

For details visit UBA NER-website: <https://t1p.de/xra80>



RESULTS

A **harmonised new approach** has been developed taking into account comments from the workshop and a subsequent public consultation until September 2021 and is presented here as revised proposal.

The extraction approach starts with a substance specific solvent extraction followed by pressurized liquid extraction (PLE) **or** conducting PLE as only extraction step using a standard solvent mixture (MeOH, acetone, water 50/25/25 at 100°C and 100 bar, 3 cycles) for quantification of **total NER**. Recovery of parent substance has to be proven. Please see the revised flowchart for further extraction steps and query processes.

Figure 1 shows the variability of resulted half-lives (DT50-values) depending on the selected approach and extraction steps.

Approach	Explanation	SFO-DT50 (d)		
		Sulfadiazin NER: 82% CO ₂ : 1.7%	Bromoxynil NER: 63% CO ₂ : 31%	Isoproturon NER: 51% CO ₂ : 25%
a) Solvent (Sol)-extractable parent	Current approach in active substance assessment; NER often considered as sink	5.9	7.3	44.7
b) Sol _{parent} + total NER	According to recommendations in REACH R.11; total NER considered remobilisable	6590.0	279.0	241.0
c) (Sol _{parent} +) PLE _{parent}	Former BfG recommendation	10.1	8.1	53.6
d)* Sol _{parent} + PLE _{parent} + EDTA _{extract} / extractable parent	Revised UBA-Proposal and ECHA discussion paper	48.8/10.2	14.6/7.9	66.6/48.5
Sol _{parent} + PLE _{parent} + Silylation _{extract} / extractable parent	consideration of Type I-NER	39.3/10.4	12.4/8.1	57.9/49.2
e)* Sol _{parent} + PLE _{parent} + XenoNER _{measured}	Revised Proposal and ECHA discussion paper (alternative option);	366.0	132.0	147.0
f) Sol _{parent} + PLE _{parent} + XenoNER _{calculated}	consideration of XenoNER xenoNER = total NER – bioNER -> HCl as proxy for bioNER _{measured} -> bioNER _{calculated} based on MTB-method (Trapp & Libonati Brock)	467.0	161.0	140.0

Figure 1: DT50 values according to the different approaches with respect to NER formation

CONCLUSIONS AND OUTLOOK

- **Revised Proposal**
 - **Pro:** No new trigger needed, already discussed at the workshop
 - **Contra:** Remobilisation rate and degradation rate are set equal → might be too less conservative
- **An alternative approach** is the implementation of a **new trigger** for the reversibly bound NER fraction (NER type I and/or Xeno-NER).
 - **Pro:** Scientifically more justified, as it is not based on an artificial DT50.
 - **Contra:** New trigger is needed, open question: amount of relevant formation rate independent from DT50 parent → might be too conservative
- Both proposals are under discussion by the ECHA NER expert group for **revision of ECHA R.11 (PBT assessment)**
- Standard approach for determination of total NER → **uniform NER definition**
- The proposed NER extraction scheme is applicable for a wide range of substances. EDTA extraction and silylation are suitable for routine laboratory testing.
- Further development regarding methods to identify the biogenic NER required.

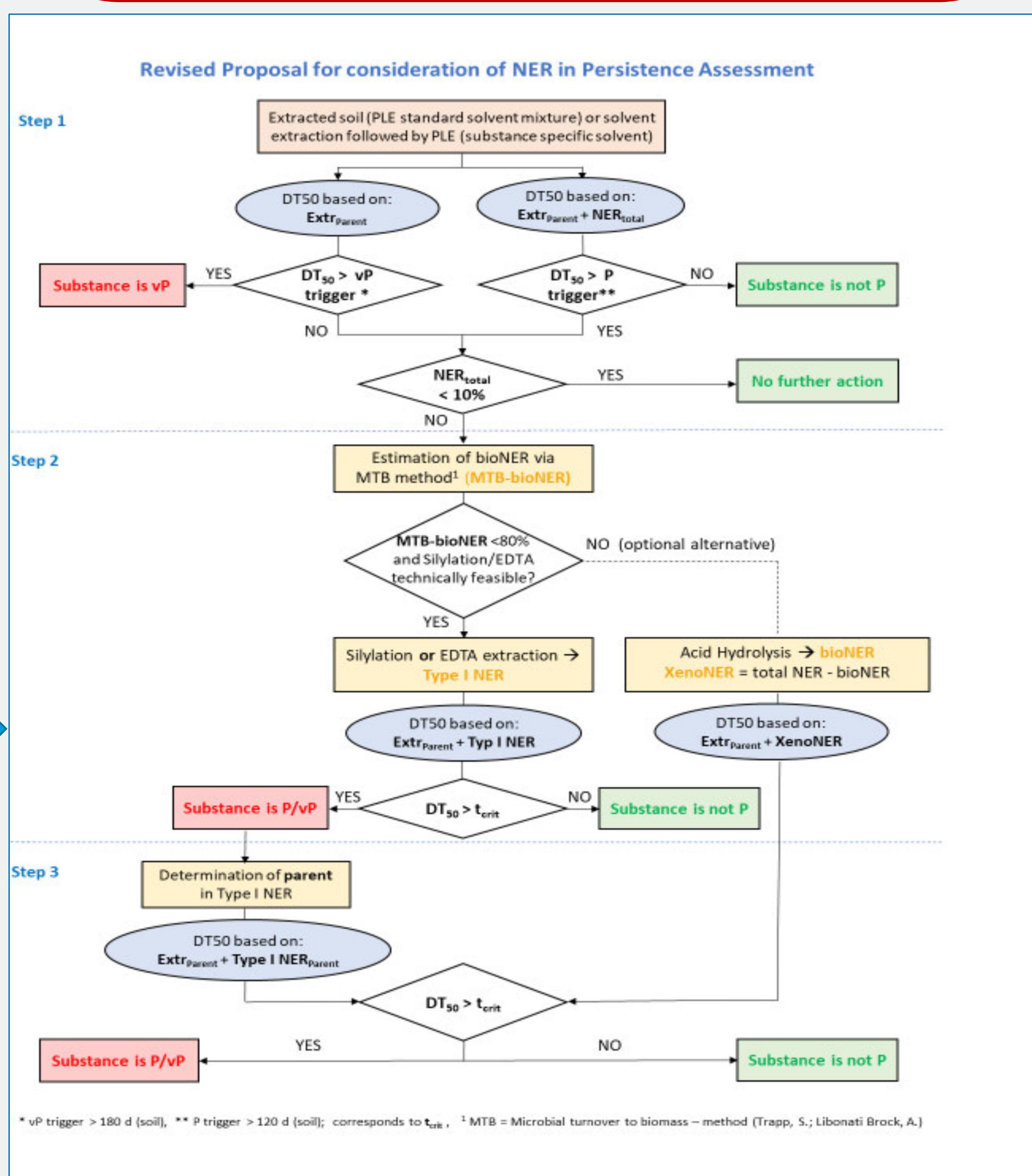


Figure 2: Revised Flowchart for consideration of NER in persistence assessment

REVISED APPROACH – EXPLANATION OF THE FLOW CHART

Step 1: If the substance is very persistent (vP) calculated with DT50-parent only (best case) or is not persistent (not P) with DT50 calculated with parent plus total NER (worst case), no further NER characterisation is necessary for assessment of persistence. Also if total NER are < 10% of total radioactivity (TR) no further action is needed due to technical feasibility.

Step 2: Otherwise a stepwise refinement should be performed. Type I NER is extracted by Silylation or EDTA extraction. Choice of method depends on suitability. If the estimated MTB-BioNER⁴ are > 80% of NER_{total} an optional alternative is extraction with acid hydrolysis for determination of bioNER. Subsequently, the DT50 (parent + type I NER) or the DT50 (total NER – bioNER = XenoNER) have to be calculated.

Step 3: If the substance is P or vP, analysis of parent in type I NER fraction is necessary for further refinement.

¹ Non-extractable residues: experimental examination of suitable extraction methods in view of a long-term risk for the environment, FKZ 3713 63 413 1, UBA-Texte in preparation

² Loeffler D. et al. (2020) Determination of non-extractable residues in soils: Towards a standardised approach; <https://doi.org/10.1016/j.envpol.2019.113826>

³ Kästner M, Trapp S, Schäffer A (2018) Consultancy Services to Support ECHA in Improving the Interpretation of Non-Extractable Residues (NER) in Degradation Assessment. Discussion Paper—Final Report. Edited by the European Chemical Agency ECHA (June 2018). www.echa.europa.eu/publications/technical-scientific-reports

⁴ Trapp et al. (2022) Critical evaluation of the microbial turnover to biomass approach for the estimation of biogenic non-extractable residues (NER) [10.1186/s12302-022-00592-5](https://doi.org/10.1186/s12302-022-00592-5)