

A PROPOSAL FOR A THREE-TIERED APPROACH FOR TARGETED INFORMATION REQUIREMENTS FOR POLYMERS.

ABSTRACT / BACKGROUND

Polymers are part of our daily life and provide a multitude of technical functionalities, are versatile, complex and cover a broad spectrum of chemistries and molecules. By their nature, polymers pose technical/scientific challenges for risk assessment, and conventional risk assessment approaches may not apply to the majority of polymers. Table 1 illustrates a series of basic characteristics.

Since 2018, a dedicated ECETOC Polymers Task Force has been steadfast in its mission to advance the science of polymer risk assessment in a field where limited scientific guidance is available. In 2019, they unveiled the conceptual framework for polymer risk assessment (CF4Polymers), followed by publications on tools/methods applicability and practical case studies (QR links below). Their latest proposal, and the subject of this communication, introduces a visionary three-tiered conceptual approach to test and assess individual and groups of polymers requiring registration (PRRs), for example under the REACH Regulation (Otte JC, Hollnagel HM et al., 2023).

Sectors of Use – a selection	Construction, Aeronautic, Automobile, Electronics, Medical appliances, Cleaning, Cosmetics, Energy generation and storage
Morphological descriptors	Physical state (e.g. solid, liquid) Shape (e.g. spherical, fibre, tubular) Physical form (e.g. amorphous, crystalline);
Composition	Natural and Formed Complex Mixtures (Formed Polymer + residual monomer + Intentionally Added Substances (IAS e.g. stabilisers) + Non-Intentionally Added Substances (NIAS, e.g. impurities)
Nb. Average Molecular Wt	From Low Molecular Weight with < 1000 Da to high molecular weight with > 1'000'000s Da
Solubility	Very high to negligible solubility in water and solvents

THREE-TIERED TESTING AND ASSESSMENT SCHEME FOR POLYMERS REQUIRING REGISTRATION (PRR)

The proposed approach follows a 3-tiered testing and assessment scheme, preceded by an issue formulation step and starting with polymer grouping.

Tier 1 is entirely based on **in silico and in vitro methods** with the exception of non-vertebrate short-term aquatic toxicity testing (algae and invertebrates).

The need for further studies at **Tier 2** is assessed based on the **Tier 1 information, together with information on systemic bioavailability and on use and exposure considerations**.

Further refinement and additional testing needs, assessed at **Tier 3**, is based on **elements of quantitative risk characterisation**.

Tier 1 information may be sufficient for many polymers, and vertebrate testing at Tiers 2 and 3 can be limited to targeted testing.

This approach is a conceptual proposal and does not specifically address the availability of validated methods nor the applicability of existing test guidelines for polymer testing (refer to ECETOC TR 133-2 for key considerations and requirements to adapt existing test guidelines to permit the derivation of meaningful endpoints, as well as identification of research needs).

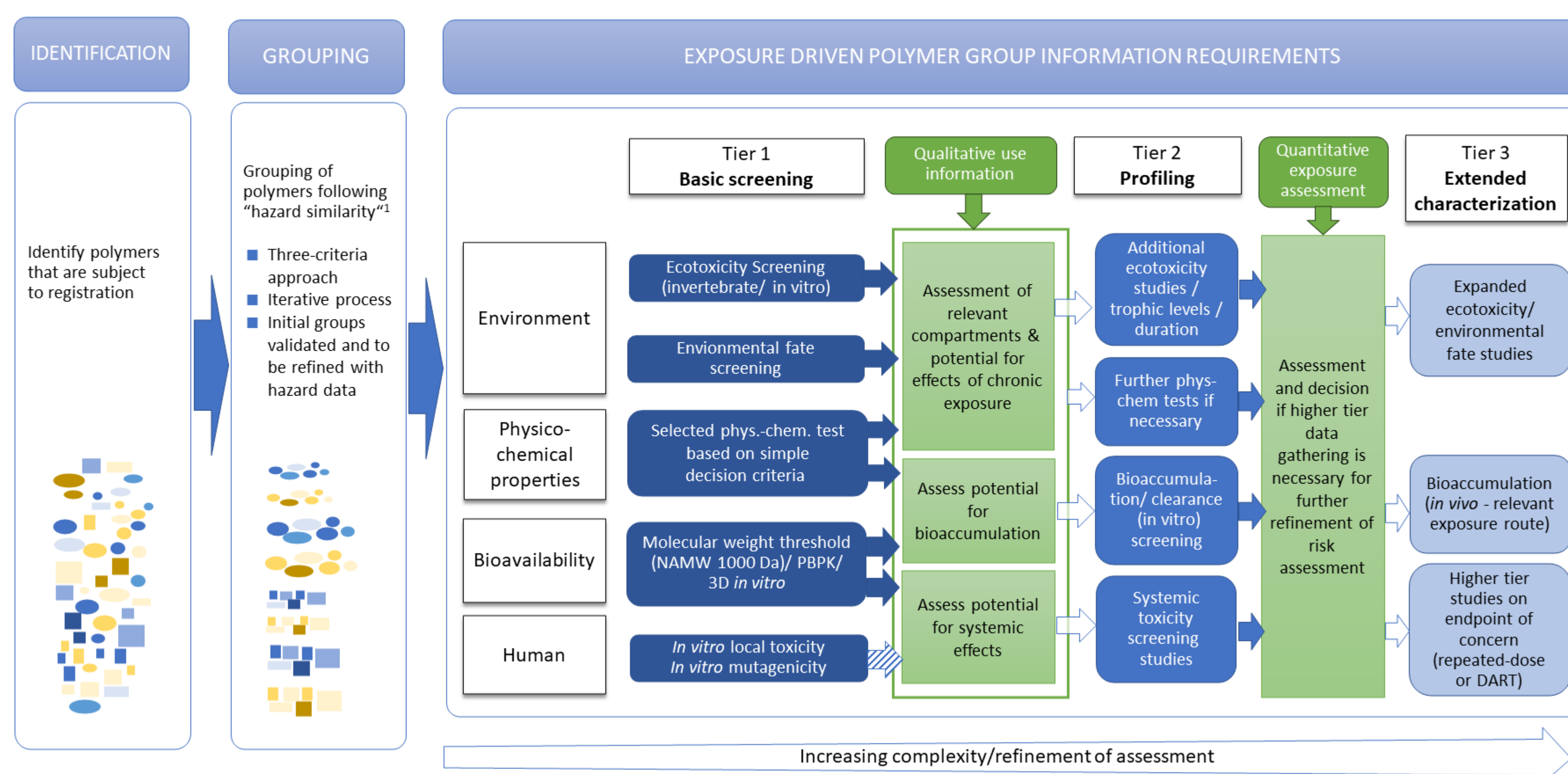


Figure 1: Overview of proposed three-tiered testing and assessment scheme for PRRs

Figure legend:

Blue boxes: property endpoints

Green boxes: decisive boxes based on use and exposure information.

➔ Solid arrows: Information is considered in the following assessment.

➔ Hatched arrow: Further assessment only in case of positive results from in vitro mutagenicity.

➔ Arrows without fill: Assessments might trigger further studies. Testing may be applied only if physico-chemical properties permit. For certain types of polymers sample preparation, e.g., via extraction, may be needed.

Abbreviations: NAMW = number-average molecular weight; PBPK = physiologically based pharmacokinetic modelling; DART = development and reproductive toxicology studies. ¹For an outlined proposal on grouping of polymers, please refer to ECETOC Task Force Report 133-3

The proposed tiered testing scheme offers the advantage of targeted testing:

- Only relevant information is generated in higher tiers as determined by the data at lower tiers.
- All relevant information will be generated which may have been missed by a pre-defined, general trigger, such as production volume.
- Generation of information not relevant to the risk assessment, including vertebrate animal tests, is not required, thus allowing for risk assessments based on no or limited vertebrate animal data.

CONCLUSIONS

- The proposed approach aims at an optimum balance of different aspects: **a tiered approach with no vertebrate animal testing at Tier 1, followed by justified, limited and targeted vertebrate testing in higher tiers considering systemic bioavailability estimates, use and exposure considerations**. This is in line with the phase out of animal testing for chemicals under REACH intended by the EU Commission.
- The proposed scheme provides a basis for **modern and responsible data generation for the next decade** to ensure the selection of polymers for safe production and use in a regulatory domain lacking sufficient technical guidance.
- Reliability and relevance of many guideline methods and NAMs will have to be tested in the coming years to provide confidence on polymer data. In some cases, new methods will have to be developed.
- The ECETOC Polymers Task Force welcomes comments and encourages scientific discussion on the proposal.

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ECETOC Polymers Task Force publications:



ECETOC. 2019. TR 133-1: The ECETOC conceptual framework for polymer risk assessment (CF4Polymers). May 2019.



ECETOC. 2020. TR 133-2: The applicability of analytical tools, test methods and models for polymer risk assessment. Mar 2020.



ECETOC. 2021. TR 133-3: Case Studies Putting the CF4Polymers into Practice. Sep 2021.



Video trailer of publication:



Otte JC, Hollnagel HM, et al. 2023. Three-tiered approach for standard information requirements for polymers requiring registration under REACH. Regul Toxicol Pharmacol.;144:105495.