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A framework for risk assessment of plastic additives – Part 1: fundamental elements

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ABSTRACT

There is a growing worldwide focus on evaluating the risk potential of substances associated with the manufacture and use of plastic, including the intentionally added constituents (additives) that impart specific technical functions as well as their transformation products. To enhance the consistent and effective evaluation of plastic additive uses, the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) is proposing a

Abbreviations: ASTM, American Society for Testing and Materials; CAS, Chemical Abstract Services; CF4Polymers, Conceptual Framework for Polymer Risk Assessment; CLP, classification, labelling and packaging; CosPaTox, Cosmetic Packaging and Toxicology (consortium); DIN, German Institute for Standardisation; DMEL, derived minimal-effect level; DNEL, derived no-effect level; ECETOC, European Centre for Ecotoxicology and Toxicology of Chemicals; ECHA, European Chemicals Agency; EC_x, x% effect concentration; EFSA, European Food Safety Authority; EP, European Parliament; EPA, Environmental Protection Agency; EU, European Union; FAO, Food and Agriculture Organisation of the United Nations; FDA, Food and Drug Administration; GLP, good laboratory practice; ICCA, International Council of Chemical Associations; IPCS, International Programme on Chemical Safety; ISO, International Standardisation Organisation; JECFA, Joint FAO/WHO Expert Committee on Food Additives; JRC, Joint Research Centre; LC_x, lethal concentration for x% of the animals; NIAS, non-intentionally added substances; NO(A)EL/C, no-observed (adverse) effect level/concentration; NTP, National Toxicology Program; OECD, Organisation for Economic Co-operation and Development; PBT, persistent, bioaccumulative, toxic; PMT, persistent, mobile, toxic; PNEC, predicted no-effect concentration; QSAR, quantitative structure–activity relationship; QSPR, quantitative structure property relationship; RCR, risk characterisation ratio; REACH, Registration, Evaluation, Authorisation and Restriction of Chemicals; SI, supplementary information; TDI, tolerable daily intake; TF, Task Force; TSCA, Toxic Substances Control Act; TTC, threshold of toxicological concern; UNEP, United Nations Environment Programme; US, United States; vPvB, very persistent, very bioaccumulative; vPvM, very persistent, very mobile; WHO, World Health Organisation.

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assessment
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Transformation product

framework for risk assessment of plastic additives in complex scenarios. Here, the fundamental elements of the framework are presented, including an overview of available databases, tools and methodologies that enable the safety assessment of individual additives in plastic. The framework is comprised of five modules to identify and efficiently gather pertinent information. Data needs are tailored to the specific plastic additive and/or its major known transformation product(s) and to the scope of the risk assessment. As a risk-based approach, the five modules are pursued in an iterative, 'circular' manner. The risk assessment is terminated as soon as it is possible to either exclude risk potential or to characterise and manage any identified risks. While the framework for plastic additive risk assessment, as presented here, is applicable to individual plastic additives and/or their major known transformation products, it can be supplemented by further considerations for the assessment of aggregate or cumulative exposures and complex material cycles. Building thereupon, the second article by ECETOC shall present such further elements to consider when applying the framework for risk assessment of plastic additives at diverse recycling stages.

1. Introduction

1.1. Background

There is a growing focus worldwide on evaluating the risk potential of substances associated with the manufacture and use of plastic (ECHA, 2019a; OECD, 2021; Maes et al., 2023; US EPA, 2023; Logan et al., 2024; European Commission, undated). Plastic can be defined as "*a material which contains as an essential ingredient one or more organic polymeric substances of large molecular weight, is solid in its finished state, and at some stage in its manufacture or processing into finished articles can be shaped by flow*" (ASTM, 2026; see Appendix I for definitions of key terms). Plastic articles are used in a wide range of products and applications, of which most include the necessary use of additives, as intentionally added substances, to impart a variety of technical functions (OECD, 2019). Further, non-intentionally added substances (NIAS) may be present in plastic. NIAS are impurities or transformation products from additives that may be formed, e.g. during the polymerisation reaction, during technical processing of the polymer product, the intended use or during decomposition of the final plastic article (ECETOC, 2019).

Plastic additives are generally regulated and managed under the purview of chemical legislations as have been established in many jurisdictions including the European Union (EU; European Parliament [EP]) (EP and Council, 2006), Canada (Canada, 1999), Japan (Japanese Government, 2017) and the USA (US Government, 2016). In accordance with Section 0.3 of Annex I to *Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals* (REACH; EP and Council, 2006), the chemical safety assessment shall address substance manufacture and all intended uses, and it "*shall consider all stages of the life-cycle of the substance*". Thus, for many additives, a safety assessment that considers all stages of their (original) life cycle is available.

Also, regulations related to sensitive uses of plastics and their associated additives have been implemented in different jurisdictions (see also Conti et al., 2021). For example, in the EU, the use of additives in food contact materials is regulated under *Regulation (EC) No 1935/2004 on materials and articles intended to come into contact with food* (EP and Council, 2004), *Commission Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food* as well as its recent amendment *Commission Regulation (EU) No 2025/351* (European Commission, 2011, 2025) and *Regulation (EU) 2025/40 on packaging and packaging waste* (EP and Council, 2025). The European standard series DIN EN 1186 set out test methods for determining the overall migration of substances from plastic materials and articles into food simulants (DIN, 2002). Medical devices are regulated under *Regulation (EU) 2017/745 on medical devices* (EP and Council, 2017a) and *Regulation (EU) 2017/746 on in vitro diagnostic medical devices* (EP and Council, 2017b). Conformity of medical devices with the provisions implemented in these Regulations is demonstrated based on standards from the International Standardisation Organisation (ISO), which have been adopted as European standards. The general principles for the risk assessment of medical devices, called "*biological evaluation*" in these standards, are presented in the ISO 10993 series (ISO, 2025). The safety of products intended for use in play by children is regulated under *Directive 2009/48/EC on the safety of toys* (EP and Council, 2009), complemented with the migration testing standards series *EN71-3:2019 + A2:2024 Safety of toys – Specification for migration of certain elements* (BS EN, 2024). Hence, risk assessment principles for intended plastic additive uses are established and are generally applicable for the evaluation of individual additives.

In line with the internationally accepted risk assessment paradigm by the World Health Organisation – International Programme on Chemical Safety (WHO IPCS), the risk assessment of plastic additives, as chemical substances, covers exposure assessment, hazard assessment and risk characterisation, and it should be preceded by problem formulation and substance identification (WHO IPCS, 2004, 2010). Usually, risk is assessed per substance (e.g. a single additive in a plastic during manufacture or article life) considering its unique physicochemical properties as well as exposure, fate and hazard data.

By comparison, the risk assessment of plastic additives in circular uses and at end-of-life introduces additional complexities since chemical alteration of plastic articles can take place over their intended life cycle and since plastics of the same type containing different additives (and NIAS), may be mixed for recycling and can be impacted by different recycling technologies. Therefore, new types of material streams must be described and accounted for to evaluate potential risks associated with plastic additive use within a circular economy (Fig. 1). Risk assessment of plastic additives within a circular economy may have to use more predictions and assumptions to address the additional complexities that may be relevant at the given life cycle stage. Most current regulations do not cover assessments for 'uses' after the end of the original intended use (e.g. recycling) but only for the steps before, see e.g. REACH Regulation (EP and Council, 2006). There is, thus, a need for a science-based approach that is broadly applicable and that specifically addresses the challenges and complexities of performing risk assessment of plastic additives and their transformation products during plastic recycling, reuse and disposal.

1.2. Scope of this article and of the ECETOC Plastic Additives Task Force

To enhance the consistent and effective evaluation of plastic additive uses in complex scenarios, the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) convened the Plastic Additives Task Force (TF). The TF work addresses risk assessment of plastic additives, as intentionally added substances, with a focus on different life stages of their uses and the subsequent recycling and reuse. As such, the TF work may also include consideration of transformation products of additives, as a type of NIAS.

It is the scope of the TF to propose a framework for risk assessment of plastic additives in complex scenarios. In pursuing this goal, this article is the first of a planned sequence of two publications. It is the scope of this article to present and discuss the fundamental elements of the framework for risk assessment of plastic additives based upon a review of the state-of-the-science risk assessment for additives in plastic and the respective databases, tools and methodologies that are being applied to

ensure the safety of individual additives in plastic. Thereby, this article is intended for audiences interested in acquiring a general overview of chemical risk assessment principles and available tools, and how they apply to plastic additives. Building thereupon, more technical considerations on complex scenarios, with a focus on recycling streams, will be offered in a second article (see outlook in Section 5).

The work of the ECETOC Plastic Additives TF builds upon the outcome of the earlier ECETOC Polymers TF who presented the Conceptual Framework for Polymer Risk Assessment (CF4Polymers; ECETOC, 2019, 2020, 2021; Otte et al., 2023). The CF4Polymers was designed to assess the associated risks of polymers, while also considering additives and/or NIAS, that, however, were not in focus. Further, while the CF4Polymers includes consideration of different life cycle stages for polymers, as major components of plastic articles, it does not specifically address the issue of plastics recycling. These aspects are, thus, the focus of the current work.

The ECETOC Plastic Additives TF focusses on additives, i.e. on those substances that are intentionally added to the plastic during production to impart specific technical functions. The TF does not specifically address oligomers, polymer processing aids, catalyst residues or NIAS beyond transformation products. Nonetheless, all these substances will also need to be considered during risk assessment, and the elements of the proposed risk assessment framework are, in principle, also applicable to these. Similarly, the proposed framework is applicable to additives (and other substances) in non-plastic polymers.

Also, the work of the TF focusses on known plastic uses over their life cycle, at end-of-life (e.g. disposal) and during recycling. As such, it considers the risk assessment of plastic additives from 'managed' waste but not from plastic present in the environment due to inappropriate disposal.

Additives used in various types of plastic and commercial articles are generally well-characterised substances, which are selected on account of a specific functionality. This includes substances whose technical function may result in their transformation or consumption during the manufacture or processing of the plastic article, e.g. process stabilising chemicals (Sperling, 2006). Transformation products may include reaction products formed from the initial additive during the life cycle of the plastic article (such as by technical processes during the production of articles). Also, transformation products may be formed via biological/environmental degradation during article service life and during chemical and mechanical recycling processes. For additives that have a functionality intended to remain in the article and support the performance of the plastic article throughout its entire life cycle, considerations of transformation products, which may form either during manufacture and processing (short-term) or over longer time scales (e.g. service life and recycling), may also be required to evaluate risk across the entire life cycle (Stevens, 1993; Sperling, 2006; Hahladakis et al., 2018). This first article of the ECETOC Plastic Additives TF includes general consideration of the major known transformation products from additives with intentional immediate reactions (e.g. antioxidants) or from additives that are known to degrade into specific transformation products at the end of life. Building thereupon, the second article shall include a comprehensive consideration of transformation products within the risk assessment of plastic additives at different stages of a circular economy.

2. Toolbox for the risk assessment of plastic additives

The toolbox for the risk assessment of plastic additives may include databases and applications providing access to data on plastic additives (Section 2.1), *in silico* models and tools for exposure and hazard assessment of plastic additives (Section 2.2), and *in vitro* and *in vivo* test methods for hazard assessment (Section 2.3). It is important to note that the below overview is far from exhaustive but represents the type of databases that are publicly available. Also, recommendations for when to use specific databases, applications, models and/or test methods are deliberately not provided as their usefulness for the given risk assessment scope should be determined on a case-by-case basis.

2.1. Databases and applications providing access to data on plastic additives

With the increasing prevalence of online resources in the form of web-based applications and their underlying databases, recent efforts have expanded to support the retrieval of information on the physicochemical, exposure- and hazard-related properties of substances associated with plastics and polymers, especially regarding additives, extractables and leachables. Below, examples for such online resources are provided, as they may support the risk assessment of plastic additives. These databases range in size from just a few hundred to more than 16,000 chemicals, which may overlap between databases (for details on database inclusion criteria, see Supplementary Information SI-1).

The International Council of Chemical Associations (ICCA) Plastic Additives Database (ICCA, 2026), currently undergoing further development and expansion, consolidates comprehensive safety and regulatory information on the most relevant plastic additives including the use and function of additives currently or recently (past 10 years) in commerce. This publicly available database has sourced data from a myriad of resources, including the United Nations Environment Programme database (UNEP, 2026), industry survey(s) and an external vendor that specialises in curation of plastic additive use information. The information provided in the database includes, e.g. chemical identity, properties including predicted fate and transport, available hazard classifications as well as information on the regions and countries where

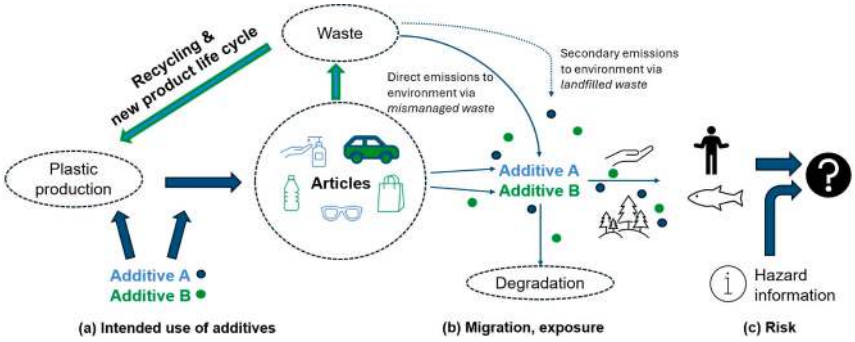

Fig. 1. Considerations for a framework for risk assessment of plastic additives in complex scenarios. (a) Intended use of additives: How is article used and discarded? Which additives and how much are in which plastic? How much additive remains in recycled materials and what happens to them? *Research needs*: What is in the material stream?. (b) Migration, exposure: How much additive is released from plastic? How does additive degrade? Who is exposed? How much are they exposed to? *Research needs*: Which degradants?. (c) Risk: Which combinations of additive, plastic and use would pose a concern?. (Dotted arrow reflects likely lower emission levels for landfilled waste as compared to mismanaged waste.).

the substance is registered, where available.

The largest relevant database in the domain of plastic additives stems from the PlastChem Project funded by the Norwegian Research Council (PlastChem, 2026). The PlastChem database is delivered as a simple downloadable Excel spreadsheet. It includes information on the physicochemical properties, hazards, functionalities, uses, production volumes and regulatory status of more than 16,000 substances that are potentially used or present in plastics. In the accompanying report (Wagner et al., 2024), "*polymers of concern*" are systematically identified and prioritised using a hazard-based approach that focusses on bioaccumulation, mobility, persistence and toxicity including carcinogenicity.

The LitChemPlast database, developed by scientists from the Institute of Environmental Engineering of the ETH Zurich, Switzerland, is also delivered as an Excel spreadsheet. It represents over 3500 chemicals, stemming from all plastic life cycle stages, that have been detected in plastic in more than 47,000 samples from approximately 370 studies using either targeted or non-targeted mass spectrometry (Wiesinger et al., 2024). The LitChemPlast database may be used "*for exposure assessment or substance flow analysis*" (Wiesinger et al., 2024).

The ChemFORWARD Plastic Additives dataset is being developed by a science-based non-profit organisation and contains about 400 chemicals harvested from the European Chemicals Agency (ECHA) plastic additives initiative (ECHA, 2019a) and enriched with data from multiple sources (ChemFORWARD, 2025). The ChemFORWARD Plastic Additives dataset has associated hazard ratings and hazard assessments.

The FCCmigex database, provided by the Food Packaging Forum (Geueke et al., 2022; Food Packaging Forum, 2025), includes more than 4000 chemicals and delivers details regarding migrates and extracts of food contact materials.

The Extractables and Leachables Safety Information Exchange (ELSIE) Knowledge Base is developed by an industry consortium of 22 biotechnological, pharmaceutical and medical device companies and focuses on the safety of substances that are especially associated with packaging and delivery systems as well as medical devices. While the safety data in the database are not publicly accessible, the list of chemicals (511 at the time of writing in June 2026) is available (ELSIE, 2025).

In addition to such chemical databases that were assembled to address specific risk assessment needs with the addition of calculated data or expert annotations associated with these collections, more generic online resources may also be useful to harvest additional data, to perform real time calculations (e.g. quantitative structure–activity relationship [QSAR] predictions based on structural inputs) and to profile large collections of chemicals in terms of physicochemical properties, human health and environmental toxicity and bioactivity. Public databases and web applications host data for hundreds of thousands to tens of millions of chemicals. Examples include PubChem (PubChem, 2026a), the United States Environmental Protection Agency (US EPA) CompTox Chemicals Dashboard (US EPA, 2025) and Cheminformatics Modules (US EPA, 2026a), the ECHA Chemicals Database (ECHA, 2026a), the European Food Safety Authority (EFSA) OpenFoodTox Database (Dorne et al., 2021) and the Joint Food and Agriculture Organisation of the United Nations (FAO)/WHO Expert Committee on Food Additives (JECFA) Database (WHO, 2025).

2.2. *In silico models and tools for exposure and hazard assessment of plastic additives*

As outlined in Section 2.1, an increasing number of databases and datasets is becoming available, whether as downloadable files of chemical identities (e.g. LitChemPlast; Wiesinger et al., 2024) or as websites harvesting and harmonising data from multiple sources (e.g. ChemFORWARD, 2025). While these databases and datasets may be used as sources of data to support hazard assessment of plastic additives, they are focused on rather limited and constrained datasets, and the reliability of the underlying information may be unclear. Further, as potentially new chemicals are added into the corresponding lists, it may be an issue of timeliness of updates before the new information becomes available, and in some cases, this can be a barrier to progress for an assessment. In addition, the databases listed in Section 2.1 do not provide access to real time modelling of relevant physicochemical properties, fate and transport information or to toxicity predictions. An ideal combination to address these limitations would include a database of both curated existing experimental and reliable predicted data, with full provenance, as well as the ability to use relevant predictive models for chemicals *not* in the database(s). Predictive models may include QSAR / quantitative structure property relationship (QSPR) models, simple rules-based or decision tree models (Thomas et al., 2019). As the below examples show, a number of tools are available that integrate database lookup with real time modelling.

Since many plastic additives are well-defined, explicit molecular structures, QSAR modelling can be used to predict a large range of molecular properties either as singleton-based predictions or in batch mode. While there are multiple commercial packages that can be used for general small molecule predictions (e.g. ACD/Labs, 2025; Simulations Plus, 2026; COSMOtherm from BIOVIA, 2026), many packages are also publicly available as downloadable installable tools (e.g. the Organisation for Economic Co-operation and Development [OECD] Toolbox; OECD, 2025a), the US EPA's Toxicity Estimation Software Tool (TEST; US EPA, 2026b), the National Toxicology Program (NTP) Open (Quantitative) Structure-Activity/Property Relationship App (OPERA; Mansouri et al., 2016, 2018; NTP, 2026a). Increasingly, online web-based prediction platforms are available including the Online Chemical Database with Modeling Environment (OCHEM, undated; Sushko et al., 2011) and the US EPA's Cheminformatics Modules (US EPA, 2026a). These modelling platforms can provide details such as access to underlying training sets and relevant model performance statistics, i.e. applicability domain details and 5-fold cross-validation.

To demonstrate what data and predictive models are already available via public tools and to show how the US EPA tools, as an example, can be used to harvest data and generate predictions of hazard and exposure properties, the Supplementary Information SI-2 provides example reports for three specific additives, i.e.

1. Vitamin E (α-tocopherol; Chemical Abstract Services [CAS] No. 59-02-9)
2. Butylated hydroxytoluene (CAS No. 128-37-0)
3. Tetraphenyl dipropyleneglycol diphosphite (CAS No. 80584-85-6)

The example reports include publicly available (predicted and experimental) data on physicochemical properties, fate and transport, hazard, exposure and associations with transformation products.

Notably, examples for guidance and tools to support the exposure assessment of plastic additives are provided in Section 3.2.1.2 (Module 2 – initial exposure assessment). In addition, opportunities to adapt migration modelling developed for specific use scenarios (e.g. substance migration from packaging for pharmaceuticals; Jenke et al., 2017; Cartledge et al., 2020; Mercea et al., 2024a, 2024b) to other assessment needs may be considered on a case-by-case basis.

2.3. *In vitro and in vivo test methods for hazard assessment*

The hazard assessment of a plastic additive, just like any other chemical, serves to establish whether it has the potential to elicit toxicological or ecotoxicological effects, and, if so, to determine its (eco-) toxic potency and, if possible, mechanism(s) of action. If the available hazard-related information (also from *in silico* modelling; Section 2.2) is inconclusive, new experimental data may need to be generated. To facilitate the mutual acceptance of data (OECD, 2025b), (eco-)toxicological information is preferably generated using standardised and internationally agreed upon test methods, performed in compliance with

the formally adopted OECD test guidelines (OECD, 2026) and in adherence to the principles of good laboratory practice (GLP; OECD, 1998). Despite the preference for data from test guideline-conforming test methods, also, e.g. from the US EPA (US EPA, 2026c), data from non-standardised studies may also be used with proper scientific justification (including applicability domain) and relevant quality assessment (see below at the end of this paragraph).

The assessment of many – especially complex, systemic – (eco-) toxicological endpoints may involve the need for vertebrate animal testing. To address animal welfare concerns, the 3Rs principle to replace, reduce and refine animal testing (Russell and Burch, 1959) is also a legal mandate in many jurisdictions and has been implemented, e.g. in the EU *Directive 2010/63/EU on the protection of animals used for scientific purposes* (EP and Council, 2010) and in the US *Toxic Substances Control Act* (TSCA; US Government, 2016; see also US EPA, 2026d). For many decades, efforts have aimed at developing and validating alternatives to animal testing (see, e.g. Desprez et al., 2018; Tarazona et al., 2025) and at facilitating their regulatory acceptance (Patterson et al., 2021; Ball et al., 2022; Zuang et al., 2024; Cronin et al., 2025). Thus, *in vitro* test methods and combinations of methods such as defined approaches have become available for regulatory use for a number of (eco) toxicological endpoints (see e.g., OECD, 2017, 2020, 2024; Tarazona et al., 2025). Tiered testing strategies (also known as integrated approaches for testing and assessment) may include lower tier non-testing approaches (such as *in silico* modelling; Scheufen Tieghi et al., 2024), *in vitro* assessments and/or assessments using non-vertebrate animals or early life stages of non-mammalian vertebrates (Padilla et al., 2012; Teixidó et al., 2020), so that vertebrate animal studies are only considered as a last resort. This tiered approach is also reflected in the framework for risk assessment of plastic additives presented in this article when the need for additional information for hazard characterisation is only established after an initial assessment of potential risk based on all available information.

Further, while *in vivo* studies may provide general indications for mechanisms of toxicity, more detailed information on a substance's mode-of-action may be available from *in vitro* assessments and *in silico* predictions, as these may inform on the substance's activity on the cellular and molecular level (Paini et al., 2022; Brescia et al., 2023; Carnesecchi et al., 2023; Zuang et al., 2024). *In vitro* bioactivity testing, as exemplified by the US EPA's ToxCast program (Judson et al., 2010; Thomas et al., 2013; Richard et al., 2016; US EPA, 2026e) and Tox21 program, a collaborative project between the US EPA, the National Institutes of Health, the NTP and Food and Drug Administration (FDA) (US EPA, undated; Thomas et al., 2018) were established with the intention to transform chemical safety assessment through high-throughput screening methods by increasing the efficiency and effectiveness of chemical toxicity testing. High-throughput screening utilises both a battery of biological assays to screen hundreds to thousands of chemicals and advanced computational methods for analysis. This approach reduces reliance on traditional animal testing and speeds up the assessment. Vast amounts of data on the biological activity of chemicals have been generated within the ToxCast/Tox21 programs. These data are made publicly available for analysis by the scientific community (e.g. US EPA, 2026e) and have been used to develop predictive models (e.g. Rusyn et al., 2012; Ribay et al., 2016). New high-throughput screening technologies continue to be developed, and in recent years the ToxCast/Tox21 programs have embraced transcriptomics (Harrill et al., 2021; Bundy et al., 2024) and phenotypic profiling (Willis et al., 2020). These techniques offer advantages in terms of scale, depth and breadth of analysis and insights into gene expression and cellular phenotypes. The scope of available high-throughput screening studies enables prioritisation of chemicals for further testing and can help to optimise the allocation of resources for more detailed studies.

Finally, all hazard information (from study reports or the peer review literature) that is retrieved or generated for regulatory assessments, should first be evaluated for its reliability, relevance (including biological plausibility and significance, adaptive response and human relevance) and adequacy for the risk assessment (Klimisch et al., 1997; Isigonis et al., 2015; Beronius et al., 2018; Johnson et al., 2022). When assessing the relevance of *in vitro* data, concentration levels at which *in vitro* effects were observed should be related to relevant *in vivo* plasma concentrations, e.g. by quantitative *in vitro* to *in vivo* extrapolations (Meek and Lipscomb, 2015; Landsiedel et al., 2024). If *in vitro* effects are only observed at concentration levels exceeding *in vivo* plasma concentrations at the *in vivo* maximum tolerable dose, these should be assessed as irrelevant (Li et al., 2017; Louisse et al., 2017). Also, *in vitro* systems often lack sufficient metabolic activity, so that potential hazards of relevant metabolites are not identified leading to false negative results (see e.g. Nesslany, 2017).

To enhance transparency on the evaluation of the inherent quality of (eco-)toxicological data, the EU Joint Research Centre has developed and published the Toxicological data Reliability Assessment Tool (ToxRTool; JRC, undated; Schneider et al., 2009).

3. Fundamental elements of the framework for risk assessment of plastic additives

The framework for risk assessment of plastic additives is comprised of five modules that are described in further detail below: (1) problem formulation; (2) retrieval and evaluation of available information, including lower tier non-testing approaches: risk characterisation possible? If not: (3) higher tier generation and assessment of new exposure information; and/or (4) higher tier generation and assessment of new hazard information; (5) final risk characterisation (Fig. 2). The order of Modules 3 and 4 can be inverted depending on data availability and assessment needs.

The structure of the framework for risk assessment of plastic additives aligns with the internationally accepted chemical risk assessment paradigm presented by the WHO IPCS (WHO IPCS, 2004, 2010) and the US EPA (US EPA, 2014) as well as with other previously developed risk assessment frameworks, such as the Health and Environmental Sciences Institute Risk21 (Moretto et al., 2017) and the ECETOC CF4Polymers (ECETOC, 2019). Unlike hazard-based approaches, risk-based assessments enable the characterisation and quantification of both the potential for adverse effects (hazard) as well as the probability of eliciting those effects (exposure). This hazard and exposure information can be used for a quantitative risk assessment, i.e. to calculate risk quotients, which can then be utilised to support the management and communication of risks that might be associated with the particular use of the evaluated substance.

Regarding plastic additives, the added value of a risk-based approach is that it specifically considers and quantifies migration of the additive from the plastic matrix. Migration is driven by Fick's law of diffusion (Fick, 1855) where the diffusion coefficient depends on parameters such as molecular mass. The higher the molecular mass, the lower the tendency for an additive to migrate out of the plastic article (JRC, 2015). Also, the properties of the matrix may affect the migration potential of the additive. An additive that has reacted with the plastic matrix and becomes covalently bound, can in principle not migrate out of the plastic article, and human and environmental exposure does not occur. Exceptions may exist where the plastic article partially degrades e.g. during its manufacturing or intended use so that the additive concerned may be released. A risk-based approach is applicable for plastic additive assessment as migration modelling and testing can be performed to estimate the amount of the additive migrating into, e.g. the food or medicine during its intended use. For example, for plastic materials and articles intended to come into contact with food, the migration test conditions are specified in Annex V *Compliance testing* of the Food Contact Material Regulation (European Commission, 2011), and human exposure potential can be estimated from this approach. Migration and exposure considerations are particularly valuable for the risk assessment of additives posing a hazard concern. Where an additive with a known

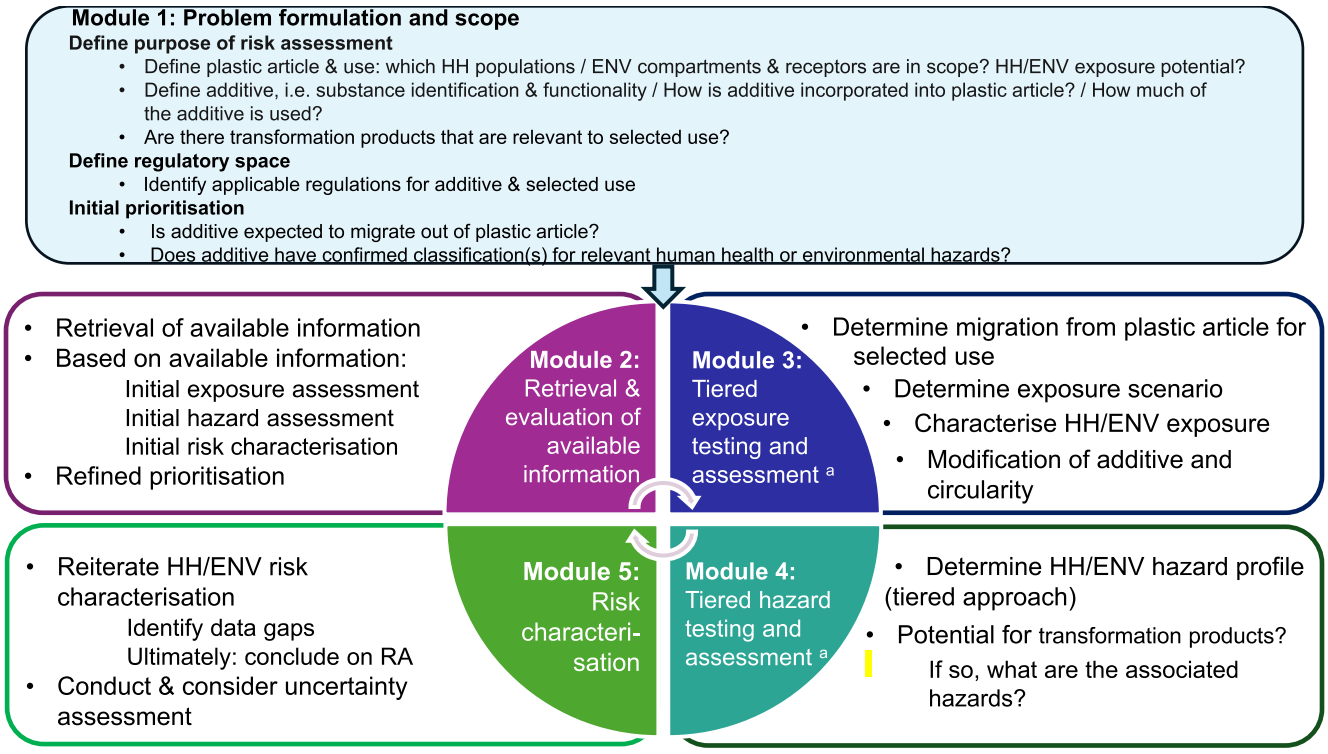

Fig. 2. Overview of the proposed framework for risk assessment of plastic additives. The framework is comprised of five modules for the risk assessment of plastic additives (and/or their transformation products). The outcome of the risk assessment may be refined by iteration of Module 2, 3 and/or 4 if the risk quotient is determined to be > 1 upon first pass through Module 5. [a] The order of Modules 3 and 4 can be inverted depending on data availability and assessment needs. (HH: human health; ENV: environmental; RA: risk assessment).

hazard can be shown to have negligible potential to migrate from the polymer matrix under specified conditions of use, there is strong evidence for limited exposure potential and subsequent risk (for general principles of additive migration, see Section 3.6.1 in ECETOC, 2019).

3.1. *Module 1: Problem formulation and initial prioritisation*

3.1.1. *Module 1.1: Problem formulation and scope of the assessment*

The risk assessment of plastic additives should always begin with problem formulation as a fundamental component. Problem formulation requires a clear articulation of the objectives and scope of the assessment. This serves to guide the subsequent identification and collection of relevant and reliable data and to ensure that the risk assessment is conducted in an efficient and transparent manner and is suitable to meet the defined purpose. A clear problem formulation supports the communication of results and an independent evaluation of the assessment by third parties (US EPA, 1992, 1998; WHO IPCS, 2009a; Embry et al., 2014).

For example, it may be the scope of the risk assessment to conduct a preliminary screen to prioritise a large number of additives for further evaluation and/or to identify additional data needs. Alternatively, the scope may be directed towards more detailed assessments, such as evaluating risks associated with a single additive and use scenario (e.g. use of an antioxidant additive in a consumer packaging product or use of a colourant in a garden tool), especially when requested for regulatory purposes.

The problem formulation for additives includes the identification of the additive, including how it is incorporated within the plastic matrix and associated plastic article(s), as well as its intended use(s) and relevant life cycle stage(s). Also, structurally similar substances may be identified as this may support grouping and read-across (Section 3.2.1.3). While existing hazard and exposure information is generally retrieved in Module 2.1 as described in this framework (Section 3.2.1.1), general information on confirmed hazard classifications (Section 3.2.1.5) may already be available from e.g. safety data sheets or databases during problem formulation.

Problem formulation often helps restrict the scope of the risk assessment by identifying those articles or uses, which are in scope. Similarly, the environmental receptors, which are in scope, are identified, e.g. environmental organisms only or also humans, a specific population subgroup, such as workers, professional users and/or consumers.

Additionally, it is determined whether relevant transformation products of the additive may be formed, at what quantity, and whether these may be in-scope for the risk assessment. The present article includes general consideration of the 'major known transformation products' of additives. Further details on the identification and evaluation of transformation products within the framework for risk assessment of plastic additives shall be presented and discussed in the planned second article.

3.1.2. *Module 1.2: Options for initial prioritisation*

When the numbers of additives and/or of their major known transformation products that shall be submitted to the risk assessment and/or of the intended uses of the additive(s) of interest are too large to assess them all at once, it is recommended to prioritise the 'additive + uses' by the urgency of the risk assessment. Based on the information that is available after the (Module 1.1) problem formulation, the (Module 1.2) includes an initial prioritisation by the intended use(s) of the additive(s) under investigation. For example, a higher urgency for a quantitative risk assessment may be mandated if sensitive applications are foreseen (e.g. medical devices, food contact material), in due consideration of the provisions of the relevant sector-specific legislation. In case hazard classification information and/or additive concentrations are known at this early stage, they can be included in the initial prioritisation, if useful (further discussed in Section 3.2.1.5).

A quantitative risk assessment of the plastic additive (i.e. progression to Module 2) may not be needed if its release from the plastic matrix is likely negligible as described in Section 3.2 of the ECHA *Practical guide for industry on describing uses of additives in plastic material for articles and estimating related exposure* (ECHA, 2020). As indicated in this practical guide, negligible release of an additive "*usually applies when the substance is contained in the plastic matrix in a concentration*" below 0.1–10% depending on its hazard classification. Also, the "*quantitative exposure estimation might be replaced by qualitative argumentation supporting 'negligible release exposure'*" if the substance has a very high molecular weight (>700 g/mol) and high *n*-octanol–water partition coefficient (log K_{ow} > 9), very low solubility in water (<0.01 mg/L) or low vapour pressure (10^{-4} Pa) or if it is reacted into the polymer chain (ECHA, 2020). Importantly, these thresholds only represent "*indicative benchmarks*" that should not be used "*in isolation from other contextual information*" (ECHA, 2020).

3.2. Modules 2–5: Iterative, 'circular' approach to the risk assessment

If the (Module 1.1) problem formulation and (Module 1.2) options for initial prioritisation indicate that a quantitative risk assessment of the plastic additive(s) and/or major known transformation products is mandated, Modules 2–5 are pursued in an iterative manner. This 'circular' approach serves to ensure that the risk assessment is conducted efficiently so that it is terminated as soon as it is possible to either exclude risk potential or to characterise and manage any identified risks.

The starting point for the 'circular' approach to the risk assessment of plastic additive(s) and/or major known transformation products is always Module 2, i.e. the retrieval and evaluation of the available information that is relevant for the risk assessment scope. The exposure assessment and the hazard assessment are structured into tiers to proceed from (Module 2) the lower tier initial exposure and hazard assessment, which makes use of the available information alone (also by enhancement via non-testing approaches), to (Modules 3 and/or 4) the higher tier generation of new, experimental exposure and/or hazard information, only when this is necessary to refine the risk assessment. Notably, the order of the (initial / higher tier) exposure assessment and hazard assessment can be inverted depending on data availability and assessment needs.

In Fig. 2, the 'circular' approach of the framework for risk assessment of plastic additives is illustrated by the circular arrows connecting Modules 2–5. Further, the tiers of the exposure and hazard assessment are interconnected: a conclusion related to exposure potential may drive the information needs for the hazard assessment and *vice versa*. The interconnectedness between the tiers of the exposure and hazard assessment represents an important component of the framework for the risk assessment of plastic additives. In Fig. 3, this is graphically represented by a 3 × 3 matrix of possible scenarios. Identifying which tier of

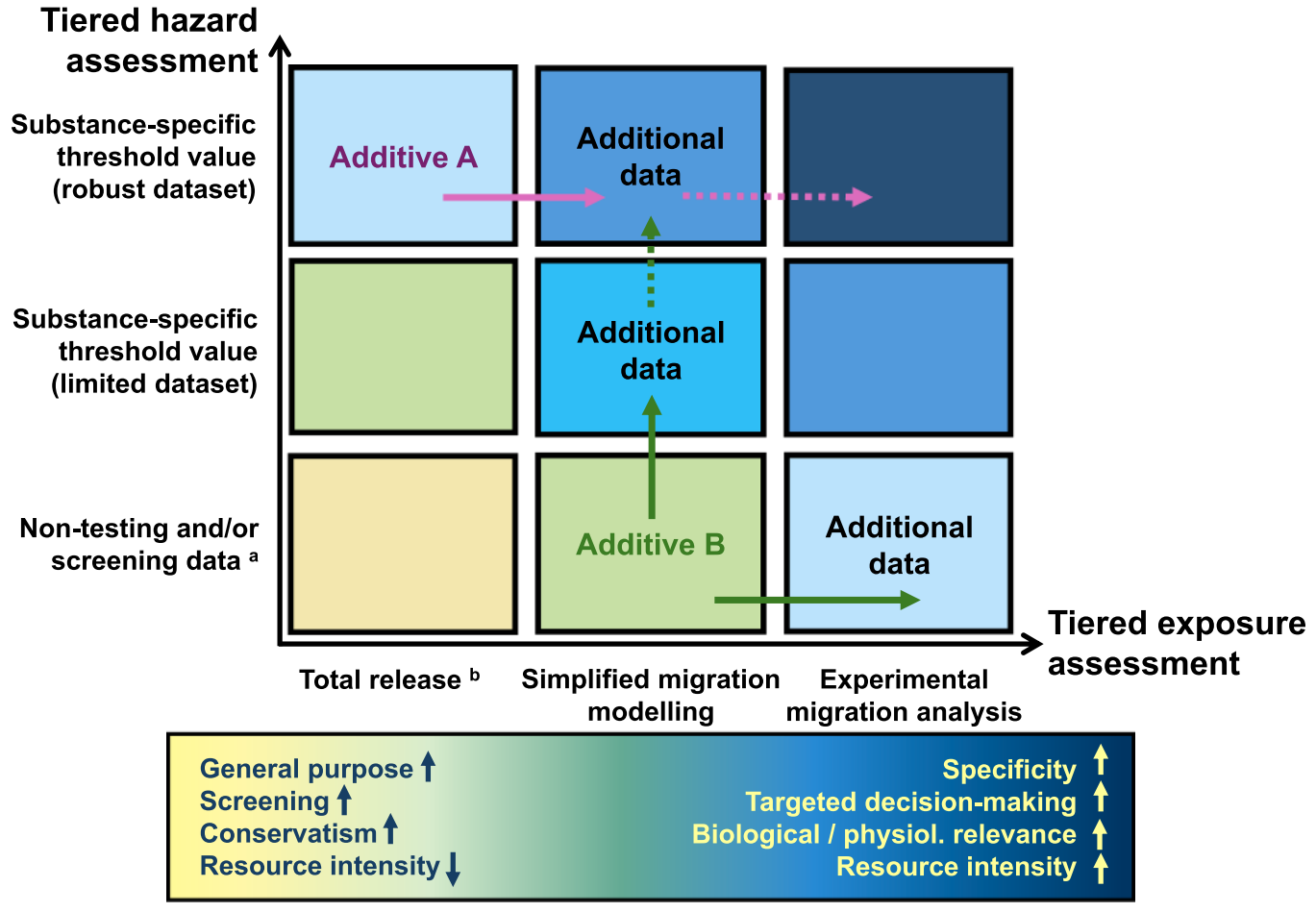

Fig. 3. Tiered hazard and exposure assessment following a 'heat-map approach'. Within the framework for risk assessment of plastic additives, the exposure assessment (Module 2.2 and Module 3) and the hazard assessment (Module 2.3 and Module 4) are structured into tiers (exemplified here by three tiers each). The interconnectedness between the hazard and exposure assessment represents an important component of the framework. This is graphically depicted through a 'heat map' with a 3 x 3 matrix of possible scenarios. The darkening of the colour-shading from left to right and bottom to top in the matrix relates to the increasing complexity between the tiers for exposure assessment and hazard assessment, respectively. This increasing complexity is based upon changes in key characteristics between tiers (e.g. specificity, conservatism, resource intensiveness) as depicted with the corresponding shading in the box below. See introduction to Section 3.2 for application of the matrix. [a] Use of non-testing and/or screening data: read-across, QSAR or other modelling approaches. [b] Total release: assumption of 100% release.

the exposure assessment and which tier of the hazard assessment to enter and to progress is dependent on the scope of the risk assessment (Module 1.1), the availability of existing exposure and hazard data (Module 2.1) and the outcome of the interim risk characterisation conducted at the given stage. The assessment is concluded when the collected data and interpretation of the results are determined to be of sufficient relevance, reliability, and adequacy to support the risk characterisation and subsequent decisions.

3.2.1. *Module 2: Retrieval and evaluation of available information*

Building from the specific elements of problem formulation defined in Module 1, it is the objective of Module 2.1 to retrieve all available information that may be relevant for the risk assessment, based on its scope. This information is then further evaluated during (Modules 2.2 and 2.3) the initial exposure and hazard assessment to determine whether (Module 2.4) it is adequate to exclude risk or to characterise and manage any identified risks or whether the risk assessment needs to be refined. If large numbers of additives and/or of their major known transformation product are submitted to the evaluation and/or many intended uses need to be considered, the (Module 2.5) refined prioritisation serves to focus the risk assessment on those 'additive + use' combinations posing the greatest likelihood for a concern for risk to humans and/or the environment. In this paper presenting the theoretical elements of the framework for risk assessment of plastic additives, the approach to refined prioritisation is described in Module 2.5 (Section 3.2.1.5). In practice, the prioritisation exercise can be conducted either at the end of Module 1 or during the early steps of Module 2, depending on the risk assessment scope and data availability.

3.2.1.1. Module 2.1: Retrieval of available information. Given the regulatory landscape for plastic additives (Section 1), physicochemical, hazard- and exposure-related data for the additive, its major known transformation products and which types of plastic articles it is being used for may be available at the onset of the risk assessment. Module 2 serves to ensure that such information is retrieved and evaluated for its relevance and reliability (Section 2.3) before considering the need to generate new experimental exposure and hazard data in Modules 3 and 4. The relevant information also covers similar substances. This implies that either the chemical structure of each substance under investigation is known or (in the case of e.g., multi-constituent substances) that the substance has been tested following a whole mixture approach (Lai et al., 2022; Salvito et al., 2022).

Relevant information may be available from databases (Section 2.1), from *in silico* modelling, from the peer reviewed public literature and/or from unpublished study reports. All physicochemical, exposure- and hazard-related information retrieved should be submitted to a weight-of-evidence assessment (EFSA Scientific Committee, 2017; Li et al., 2022; Arnot et al., 2023; Merrington et al., 2024).

Notably, it is up to the risk assessor to decide on the level of detail that is needed for the initial exposure and hazard assessments in Module 2.2 and 2.3 and on opportunities to prioritise large numbers of 'additive + use' combinations for the subsequent risk assessment, if relevant (Module 2.5). For example, depending on the risk assessment scope, a full literature search and hazard characterisation for all additives in scope may be relevant for the initial hazard assessment. Alternatively, the retrieval of the relevant information may be restricted to screening-level hazard information, including, e.g. genotoxicity QSAR predictions or threshold of toxicological concern (TTC) potencies evaluated using a weight-of-evidence approach (further discussed in Section 3.2.1.3).

3.2.1.2. Module 2.2: Initial exposure assessment based on available information. Depending on the scope of the risk assessment defined in the problem formulation (Section 3.1), the exposure assessment of plastic additive(s) and their major known transformation products may consider two fundamental aspects:

1. *Potential exposure to workers and the environment during production and processing or recycling of the plastic article that contains the additive*. Addressing this aspect may require information on the tonnage of the plastic additive intended to be used for that purpose as well as on those physicochemical properties of the additive and the plastic article that are relevant, e.g. To robustly assess migration of the additive out of the polymer matrix into any receiving compartment. Potentially relevant properties may include, e.g. Solubility in different media (e.g. To cover hydrophilic and lipophilic properties) and partition coefficients (e.g. Log K_{ow}). Furthermore, any available information on use scenario(s) and the presence of exposure minimisation controls, including occupational controls, personal protective equipment as well as on-site treatment and release minimisation technologies is useful to refine the assessment already at an initial stage
2. *Potential exposure to consumers and the environment during use, recycling and disposal of the plastic article that contains the additive.* In addition to the information requirements listed under bullet 1, addressing this aspect may further require information on the physical and chemical interactions of the additive with the plastic matrix, to inform on leaching/migration potential and the influence of relevant environmental effects (e.g. weathering) across the life cycle of the plastic article. Also, considerations of the exposed / sensitive human population and/or environmental compartment may be relevant

Importantly, specific data are only required (1) if they contribute to the level of detail that is necessary for the risk assessment scope (e.g. screening level assessment vs more elaborated assessment for regulatory purposes; Section 3.1); and (2) if they relate to the relevant exposure scenario (e.g. assessment of exposure of consumers to an additive included in toys requires different information than assessment of environmental exposure from mechanical recycling of a polymer containing an additive).

In line with the existing exposure paradigm (WHO IPCS, 2004), the exposure assessment may include (1) the determination of generic exposure scenarios of the plastic article and the additive; and (2) the refined, substance-specific exposure characterisation for humans (occupational, consumer, and man via the environment) and the environment. As available and relevant, the (Module 2.2) initial, lower tier exposure assessment and/or (Module 3) higher tier exposure assessment may rely on existing guidance to determine exposure scenarios, general exposure models and/or specific migration models (Box 1). Basic principles as well as more detailed knowledge of chemical exposure assessment are laid down in the *ECHA guidance documents on occupational exposure assessment* (ECHA, 2016a), *consumer exposure assessment* (ECHA, 2016b) and *environmental exposure assessment* (ECHA, 2016c), respectively.

The (Module 2.2) initial exposure assessment preferably begins with the application of general exposure models depending on the scenario under scrutiny. General exposure models rely on fundamental physicochemical and fate-related properties of the substance of interest, such as log K_{ow}, water solubility and vapour pressure. These data are used in combination to identify relevant exposure pathways and to estimate release potential and human or environmental exposures. Since substance-specific and polymer-specific migration data are often unavailable at this stage of the assessment, the general exposure modelling includes assumption of the worst-case scenario, i.e. 100% migration of the additive from the plastic matrix (i.e. total release) within short time. Some variation to the worst-case scenario may be applied if reasonable assumptions on the time course of release kinetics can be made (e.g. if it can be realistically assumed that migration of the additive is distributed over a certain timeframe).

If an interim risk characterisation that is based upon general exposure modelling assuming the worst-case scenario indicates that the margin of exposure between the health-based guidance value and the

Box 1
Guidance and tools to support the exposure assessment of plastic additives.

The usefulness of the listed guidance and tools for the given risk assessment scope and 'additive + use' scenario should be determined on a case-by-case basis considering, e.g. the applicability domains of the respective tools.

Examples for use maps and conditions to characterise emission and exposure.

– Use maps from the ECHA use maps library, and, notably, the use maps and associated use descriptors (e.g. environmental release categories and worker exposure determinants) developed by the European Plastics Converters Association (EuPC) to address safety assessment of plastic additives (ECHA, undated no. 1)

– OECD emissions scenario documents (ESDs; see, e.g. OECD, undated; OECD, 2009; OECD, 2019)

– Specific worker, consumer, and environmental release categories (e.g. published by the European Solvents Industry Group; ESIG, undated)

– US EPA ExpoBox, a Toolbox for Exposure Assessors (US EPA, 2026f)

Examples for general models to assess exposure potential.

– EU System for Evaluation of Substances (EUSES; ECHA, undated no. 2)

– Chesar (Chemical Safety Assessment and Reporting Tool; ECHA, 2024a)

– US EPA ExpoCast Exposure Forecasting (Wambaugh and Rager, 2022)

– US EPA Consumer Exposure Model (US EPA, 2026g)

– Plastics Exposure Scenario Tool (PESTool) (based on ECETOC TRA and EUSES) designed to estimate the human health and environmental exposures resulting from the use of plastic additives (mono-constituent substances) throughout the plastics supply chain (PESTool, undated)

– ECETOC Targeted Risk Assessment Tool (ECETOC, undated)

– ConsExpoWeb (RIVM, 2024)

– Eas-E Suite (ARC 2020)

– Environmental migration modelling of additives from plastic material(s) (CEFIC LRI, undated)

– US EPA E-FAST-Exposure and Fate Assessment Screening Tool Version 2014 (US EPA, 2026h) and many other exposure assessment tools (US EPA, 2026i)

Examples for specific models to predict additive migration.

– US EPA AMEM-ADL Polymer Migration Estimation Model (US EPA, 2026j)

– Advanced Kinetics and Technology Solutions – specific migration limits (SML) software (AKTS, undated)

– FABES Migratest® EXP (FABES, undated; JRC, 2015)

– FACET: Flavourings, Additives, and food Contact materials Exposure Tool (JRC, 2026)

– MERLIN-expo/VERMEER toolbox (Ciffroy et al., 2022)

Examples of guidance on migration test methods for substances in plastics.

– Guidance on Migration Test Methods for the evaluation of substances in printing inks and varnishes for food contact materials (EuPIA, 2023)

– Guidelines for risk assessment of non-listed substances and non-intentionally added substances under the requirements of Art 3 of the Framework Regulation (EC) 1935/2004 (FCA, 2023)

– Migration testing of adhesives intended for food contact materials (FEICA, 2016)

– Guidance for industry: preparation of premarket submissions for food contact substances (chemistry recommendations) (US FDA, 2007)

– Applicability of generally recognised diffusion models for the estimation of specific migration in support of EU Directive 2002/72/EC (JRC, 2010)

Example for tool to evaluate environmental exposure data for specific complex substances.

– PETRORISK for petroleum hydrocarbons (Redman et al., 2014)

estimated human exposure is too small (Section 3.2.1.4), the exposure assessment may be refined (Module 3).

For this purpose, simplified migration modelling may also be applicable for the initial exposure assessment, as it includes assumptions of partitioning in relevant media (ECETOC, 1994) and/or default values for estimated losses (OECD, 2009); see also JRC (2015). Simplified migration models generally also rely on a substance's physicochemical properties (e.g. molecular weight, log K_{ow}) while further considering general properties of the plastic article or polymer (thickness, polymer type). As such, the simplified migration modelling may be reasonably applied in an automated fashion, supporting batch evaluation of large numbers of additives and polymer matrices.

Information pertaining to the potential for an additive to migrate from the plastic is an essential component of its exposure assessment (ECHA, 2020). While some tools for specific applications (e.g. ConsExpoWeb, FABES; Section 2.2) address migration, this aspect is not currently incorporated broadly within existing generic exposure scenarios or general models to assess exposure potential (e.g. EUSES, Chesar, the ECETOC Targeted Risk Assessment Tool; Box 1). Various models, with varying degrees of complexity, are available to estimate

migration potential. While some of these have been designed to support specific end uses (e.g. food contact applications), they can often be adapted for other specific end uses, or broader or more general exposure assessments. Finally, before generating new migration data (Module 3), existing data, generated for alternative purposes (i.e. food contact migration data) may be applied, with expert judgement.

3.2.1.3. Module 2.3: Initial hazard assessment based on available information. In Module 2.3, the available hazard information is evaluated to determine whether it is sufficient to support the (Module 2.4) initial risk characterisation for the additive and/or major known transformation products. For example, if the additive under investigation has been registered under the REACH Regulation (EP and Council, 2006), health-based guidance values (e.g. derived no-effect levels [DNELs]) and/or effects-based guidance values (e.g. predicted no-effect concentrations [PNECs]; Box 2) may have been established, which may be used for the risk characterisation.

Data associated with points of departure and guidance values can be obtained from a variety of sources, including but not limited to:

- The ECHA Chemicals Database (ECHA, 2026a),
- The EFSA OpenFoodTox database (Dorne et al., 2021) or the FAO/WHO JECFA database (WHO, 2025) for authoritative food-related health-based guidance values,
- The US EPA ToxVal database (US EPA, 2021), which is integrated into the US EPA CompTox Chemicals Dashboard (US EPA, 2025).

If relevant and reliable guidance values (or sufficient toxicological data) are unavailable for the additive and/or major known transformation products, the initial hazard assessment may also be enhanced by further evaluating the available information using non-testing approaches. Potentially useful non-testing approaches include:

- *In silico* modelling, such as validated (Q)SARs (Section 2.2), giving due consideration to their applicability domains and the robustness of the underlying data, to predict hazard concerns and general modes-of-action (e.g. genotoxicity) of the substance of interest. The conclusiveness of (Q)SAR results should always be carefully considered and may require confirmation, e.g. by grouping and read-across (see below) or testing approaches (Section 3.2.3).
- The threshold of toxicological concern (TTC) approach can be used to assign *substances with known structure* into one of several classes of (human health) toxic potency; generally, the TTC approach is available for the endpoints of repeated-dose toxicity, genotoxicity / carcinogenicity and reproductive toxicity, unless the additive / transformation product has a structural component that is not included in any general or specific Cramer class (Cramer et al., 1978; Kroes et al., 2004; Munro et al., 2008; Koster et al., 2011; Boone and Di Toro, 2019a, 2019b; EFSA Scientific Committee, 2019).
- For *unidentified or not fully identified substances*, the TTC approach can only be used if analytics and/or expert judgement enable the conclusion that the substance does not belong to any of the TTC-excluded classes of chemicals (e.g. heavy metals or dioxins; Koster et al., 2011). The substance can then be categorised in different classes of toxic potency depending on the amount of information available, such as absence of organophosphates or N-methyl carbamates demonstrated with e.g. gas chromatography coupled with specific detectors and/or absence of mutagenicity in an *in vitro* Ames test (Rennen et al., 2011; Koster et al., 2015; Schilter et al., 2019). Key advantage of this approach is the ability to classify chemicals by their toxic potency without knowing their (full) chemical structure.
- Grouping and read-across as formal approaches to predict the hazard properties and subsequent points of departure of the additive or major known transformation product (i.e. the 'target substance') if their deeper structural analysis reveals similar substances (i.e. 'source substances') for which substance-specific hazard data are available (OECD, 2014; ECHA, 2017). While grouping and read-across may be elaborate as available data from similar substances have to be retrieved and evaluated for relevance and reliability, and the appropriateness of the read-across has to be assessed, computational tools such as the OECD QSAR Toolbox (OECD, 2025a) can assist in the identification and evaluation of similar substances. Potential uncertainty associated with read-across should be taken into consideration for derivation and/or use of points of departure and health-based guidance values.

Non-testing approaches may be especially useful for a rapid, conservative hazard assessment (e.g. when assessing a large number of additives), and they can generally also be (re-)applied in the (Module 4) higher tier hazard assessment to increase the efficiency of the assessment.

It is important that any hazard properties of concern be evaluated based upon all available information, applying a weight-of-evidence approach (EFSA Scientific Committee, 2017). If relevant and reliable substance-specific hazard data and appropriate points of departure (and health-based guidance values) for the additive and/or its major known transformation product(s) have been identified in Module 2.3, the hazard assessment should be based on these, without the need to generate new experimental hazard data in Module 4.

3.2.1.4. Module 2.4: Initial risk characterisation. The (Module 2.4) initial risk characterisation serves to determine whether the information that is available at this point of the assessment is already adequate to exclude risk or to manage any identified risks that may arise due to a particular use of the plastic additive of interest or its major known transformation product(s). Two numerical values should generally be available for a quantitative risk assessment:

1. The health-based guidance value (e.g. DNEL, TDI) or effects-based guidance value (e.g. PNEC) indicating a safe dose level / concentration level for the respective use and its route of exposure (Box 2 in Section 3.2.1.3); and
2. The exposure level that is relevant for the specific use and its route of exposure. For example, if an oral toxicity study yields the lowest health-based guidance value or if this endpoint is of specific concern due to the given use of the plastic article that includes the additive (e.g. toys), then the anticipated exposure level should be estimated for the oral route of exposure.

A safe use can be anticipated if the estimated exposure level is below the health-based guidance value. In practice, this comparison is often displayed as a quotient whose naming and configuration may differ depending on the given jurisdiction and/or sector-specific legislation. For example, for substances registered under the REACH Regulation (EP and Council, 2006), the risk characterisation ratio (RCR) is the ratio of the estimated exposure and the DNEL for a threshold effect (ECHA, 2016d). In accordance with Point 6.4 in Annex 1 to the REACH Regulation, risks can be considered to be adequately controlled if the "*if exposure levels do not exceed the appropriate DNEL,* i.e. *if the RCR* < 1" (ECHA, 2016d). Other programmes may include the estimation of margins of exposure or margins of safety, etc. (Duffus, 2001; US EPA, 2015; ECHA, 2016d; EFSA, 2023; see Appendix I for definitions).

The risk assessment is concluded after the (Module 2.4) initial risk characterisation when the collected data and interpretation of the results are determined to be of sufficient relevance, reliability and adequacy to support a conclusion on the possible risk and subsequent decisions. For example, the initial risk characterisation may yield the conclusion that there is no risk due to a particular use of the plastic additive, also since the margin of safety is sufficiently high indicating that any identified hazards do not pose a risk to consumers or the

Box 2
Derivation of health-based and effects-based guidance values indicating safe use levels.

Human health toxicological endpoints: For substances registered under the REACH Regulation (EP and Council, 2006), DNELs may be established for threshold endpoints (e.g. specific-target organ toxicity). DNELs are generally based on the findings from the most sensitive toxicological endpoint in question, e.g. the no-observed adverse effect level (NOAEL), which then serves as point of departure for the derivation of the DNEL (ECHA, 2012a). Depending on the uses of a chemical, multiple DNELs may exist for different routes of exposure (oral / dermal / inhalation), duration of exposure (acute / long-term) and populations (workers / consumers). For non-threshold endpoints (e.g. mutagenicity), derived minimal-effect levels (DMELs) may be established (ECHA, 2012a). Similarly, tolerable daily intake (TDI) levels may be established for plastic additives that may be present in food or beverages due to their migration from the packaging. TDIs are also based on points of departure and reflect the amount of the additive in the food or beverage, which can be "*can be consumed over a lifetime without presenting an appreciable risk to health*" (EFSA, undated; EFSA Scientific Committee, 2021).

Ecotoxicological endpoints: Effects-based guidance values may include PNECs, which are typically based on study outcomes reflecting the "*concentrations at which x % (*e.g. *50%) mortality or inhibition of a function (*e.g. *growth) was observed and* [that] *are expressed as the lethal concentration (LC_x) or the effect concentration (EC_x),* e.g. *LC_{50} or EC_{50}*" (ECHA, 2008). Points of departure for chronic ecotoxicological effects are typically no-observed effect concentrations (NOECs).

Since the points of departure (e.g. NOAEL, LC_{50}, EC_{50}) are generally established from animal studies, **assessment factors** (also known as uncertainty factors or safety factors) are applied for the derivation of health-based or effects-based guidance values to account for, e.g. intra-species and interspecies variation, exposure duration extrapolation, the quality of the database, as applicable (ECHA, 2012a; EFSA Scientific Committee, 2012).

environment, or that identified risks can be adequately managed, e.g. in the occupational and professional setting, by risk mitigation measures.

If, however, the information that is available for the (Module 2.4) initial risk characterisation is not adequate for the particular use of the plastic additive, e.g. because it indicates a low margin of safety or an unacceptable risk, the outcome of the initial risk characterisation serves to identify opportunities to refine the risk characterisation in a tiered risk assessment by generating more accurate, substance-specific experimental data on exposure and/or hazards of concern (Modules 3 and/or 4).

Especially at this initial stage of the risk characterisation (i.e. Module 2.4), its outcome should be assessed carefully, considering the margins of exposure and inherent uncertainties, which strongly depend on the quality and robustness of the exposure- and hazard-related input data (for details on the uncertainty analysis, see ECHA, 2012b; WHO IPCS, 2018; EFSA Scientific Committee, 2018). If substance-specific experimental exposure and/or hazard data are unavailable, the confidence level of the initial risk characterisation is likely low, and its further refinement may be warranted. The refinement of the risk characterisation should consider the overall quality and robustness of the existing input data, to identify additional exposure and/or hazard data that will likely reduce uncertainty and add robustness to the assessment once available. In this regard, the effort needed to generate the new data should also be considered just as their potential to significantly influence the risk characterisation and improve its robustness.

This process and options to refine the risk characterisation are displayed in Fig. 3 taking the hypothetical examples of "Additive A" for use in food contact and "Additive B" for use in medical devices. Should the data available for "Additive A" from the (Module 2.2) initial exposure assessment not allow concluding on its safe use for the given intended use because the anticipated exposure level exceeds the health-based / effects-based guidance value indicating safe use (e.g. the DNEL or PNEC), progression to Module 3 may be required to refine the worst-case exposure assumption by higher tier migration studies (Fig. 3). This will yield more precise, substance-specific estimations of migration potential and relevant exposure concentrations thereby significantly supporting adjustments to the risk quotient.

By comparison, when a risk quotient that is based on the initially available hazard information (e.g. from *in silico* modelling and/or read-across) indicates a potential risk, progression to the (Module 4) higher tier hazard testing and assessment may be useful to generate more robust input data. For example, from data available for "Additive B", the (Module 2.3) initial hazard assessment and subsequent resulting risk quotient may indicate a need to generate substance-specific threshold values through additional testing as it is intended for use in medical devices. This higher tier testing should focus on the hazard of concern and the relevant route of exposure (Fig. 3). The new substance-specific hazard data may permit lowering the assessment factors applied for the derivation of a DNEL or PNEC (Box 2 in Section 3.2.1.3) and thus also adjusting the risk quotient.

For specific use cases, it may also be advisable to consider accepted risk management measures to reduce a specific exposure. This approach is often pursued for occupational exposures (e.g. personal protective equipment or enhanced air exhaust) but is also applicable to reduce environmental emissions and, to a limited extent, consumer exposure to additives in plastic articles. The *ECHA guidance document on risk management measures and operational conditions* (ECHA, 2012c) provides useful advice to support the assessor in this task. Also, basic principles and more detailed information on chemical risk assessment are provided in the *ECHA guidance document on risk characterisation* (ECHA, 2016d).

3.2.1.5. Module 2.5: Refined prioritisation. When the number of additives and/or of their major known transformation products requiring initial and/or higher tier exposure and/or hazard assessment, and/or of the intended uses considered, is too large to allow assessing them all at once, a refined prioritisation making use of the already available exposure and hazard information may be useful to determine the urgency for the subsequent risk assessment.

Below, the scientific background to prioritisation is provided followed by a proposal for a transparent, structured prioritisation scheme that combines exposure and hazard criteria with a scoring scheme.

Notably, prioritisation implies that the urgency for risk assessment is determined based on qualitative categories for exposure and hazard concerns. By comparison, the tiered approach to risk assessment that is included in Module 2.4 and Module 5 utilises quantitative risk assessment outcomes to decide whether higher tier exposure and/or hazard information is necessary to refine the risk assessment and manage any identified risks (Section 3.2.1.4 and Section 3.2.4).

Types of information available for prioritisation

The refined prioritisation serves to determine the priority and necessary level of detail for exposure, hazard and risk assessment. It is often more straightforward for additives with confirmed hazards, such as with harmonised classification under *Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures* (CLP

Regulation; EP and Council, 2008), provided that the respective hazards are in scope of the assessment. Therefore, consideration of confirmed hazard classifications may also be used for the (Module 1.2) initial prioritisation (Section 3.1.2).

Higher priority for risk assessment may be assigned to additives and/or their major known transformation products if they are known to exert effects of high severity:

- They have confirmed hazard classifications for carcinogenicity, mutagenicity, toxicity to reproduction or specific target organ toxicity (EP and Council, 2008; United Nations, 2023), or
- They are confirmed persistent, bioaccumulative, toxic / persistent, mobile, toxic (PBT / PMT; US EPA, 1999; Canada, 1999; EP and Council, 2006) or very persistent, very bioaccumulative (vPvB) / very persistent, very mobile (vPvM; EP and Council, 2006, 2008; European Commission, 2023).

Confirmed in this context implies established by an authoritative body, such as the ECHA Risk Assessment Committee (ECHA, undated no. 3) or the NTP of the US Department of Health and Human Services (NTP, 2026b). Other sources may serve as flags for future evaluations. Depending on the scope of the risk assessment or the use and/or end-of-life fate of the plastic material, other hazard classifications or properties of concern may be pertinent to consider (e.g. endocrine disruption or category 1A skin sensitisation).

While hazard classifications only provide general information on the respective effect, but no information on the actual toxicological potency, substances with confirmed classifications typically have a sound dataset for derivation of health- or effect-based guidance values facilitating hazard characterisation. The planned second article of the ECETOC Plastic Additives TF will explore strategies to deal with the increased chemical complexity of plastics in circular product cycles. In such cases, substances of similar concerns, e.g. due to structural similarities to the parent compound and its breakdown products, could be prioritised as a group for further risk assessment. Notably, however, hazard-based prioritisation does not equate to a robust risk-based assessment. Hence, hazard-based prioritisation indicates very clearly where exposure assessment (Section 3.2.1.2 and 3.2.2) becomes crucial for risk-based decision making.

The refined prioritisation should preferably consider migration potential and the amount of each additive and/or major known transformation product present in the plastic article for the given use in relation to possible exposure and hazard concerns, which may have arisen, e.g. due to *in silico* modelling indicating structural alerts and/or application of the TTC approach (Section 3.2.1.3).

If structurally similar substances have been identified (Module 1.1; Section 3.1.1), grouping and read-across (OECD, 2014; ECHA, 2017) may help refining the initial prioritisation. If applicable, groups of substances may be ordered by anticipated toxic potential, whereby the scope of the assessment may be narrowed. For example, a certain subgroup may be regarded as safe due to its low toxicological profile whereas another subgroup may be identified as critical, e.g. since it displays effects with high potency and/or can migrate easily. The additives and/or major known transformation products from the latter subgroup may be assigned high priority to proceed to the higher tier exposure and hazard assessment.

Proposal for a prioritisation scheme

To ensure traceability of all decisions taken, it is essential that the prioritisation is undertaken by a structured and transparent approach. Therefore, a prioritisation scheme is proposed here that is based on pre-defined criteria (relating to both exposure and hazard) combined with a pre-defined scoring scheme.

In the current paper, the approach to refined prioritisation is described as Module 2.5, i.e. after the (Module 2.4) initial risk characterisation. In practice, prioritisation is also applicable at an intermediate stage without full retrieval and evaluation of all hazard and exposure information, and, particularly, risk characterisation is not part of the pre-defined criteria (see next paragraph). Hence, the prioritisation exercise can also be conducted at the end of Module 1 or during the early steps of Module 2, as appropriate.

Table 1 presents exposure and hazard criteria that may be relevant for prioritising assessment needs from the human health perspective, and Table 2 presents exposure and hazard criteria that may be relevant for prioritising assessment needs from the environmental perspective (both sets of criteria adapted from Shin et al., 2014). For both human health and environmental assessments, criteria informing on exposure include the intended use of the plastic article, the concentration of the additive in the plastic matrix and the potential of the additive to migrate from the matrix. Criteria informing on hazard include hazard potential (e.g. determined by existing hazard classifications; see above in this section) and hazard potency (e.g. determined by established potency thresholds indicating safe exposure levels).

To aid in the prioritisation of large numbers of 'additive + uses', the exposure and hazard criteria may be combined with a scoring method to assign a numerical value indicating the level of concern with respect to each criterion, e.g. high priority = 4 to very low priority = 1 (see also Shin et al., 2014). If data are unavailable for any given criterion, it is neither possible to conclude that there is a concern nor that there is no concern. Therefore, criteria for which data are unavailable are assigned moderate priority (= 3) in the prioritisation scheme. If a prioritisation criterion presented in Table 1 or 2 is out of scope of the assessment, it can be set aside entirely.

To demonstrate how the Table 1 and Table 2 prioritisation matrices informing on human health and environmental concern level, respectively, might be applied in combination with the scoring method, Appendix II provides examples of stepping through the outlined criteria for different use scenarios of (1) α-tocopherol, the bioactive form of Vitamin E, (2) butylated hydroxytoluene, and (3) tetraphenyl dipropyleneglycol diphosphite (i.e. the three additives referred to in Section 2.2). The resulting total priority scores for human health assessment and/or environmental may then be used to support the determination of the urgency of the higher tier risk assessment.

This prioritisation scheme is intended as an integral part of the framework for risk assessment of plastic additives. Importantly, however, the prioritisation scheme is not prescriptive, just as no other element of the framework for risk assessment of plastic additives is prescriptive. As an alternative to the scoring method presented above, software tools, such as ToxPi (Reif et al., 2010; Marvel et al., 2018), may be useful in providing scoring/metrics for the underlying criteria and in integrating these to facilitate prioritisation. It is up to the risk assessor to decide whether the prioritisation of large numbers of additives for risk assessment is relevant (which is also dependent on the given problem formulation) and, if so, whether the criteria and the scoring scheme presented here are deemed useful. Based on the problem formulation, the risk assessor may choose to use different combinations or weightings of the criteria to customise the prioritisation, as needed.

3.2.2. *Module 3: Higher tier exposure testing and assessment*

The (Module 3) higher tier exposure testing and assessment may be relevant if the exposure modelling conducted in Module 2.2 (Section 3.2.1.2) indicates that the exposure assessment of the additive in the plastic article with a particular intended use requires further refinement. Similarly, depending on the scope of the risk assessment and the outcome of the (initial or refined) hazard assessment, new exposure data may need to be generated to refine the initial risk assessment (Fig. 3). (Depending on data availability and assessment needs, the risk assessor may decide to conduct the Module 4 higher tier hazard testing and assessment before Module 3.).

The higher tier exposure testing may involve the utilisation of specialised extraction and/or migration models (e.g. JRC, 2015; Cefic LRI, undated) and/or the performance of experimental migration studies for the additive in representative polymer matrices at relevant, realistic

Table 1
Prioritisation matrix informing on independent human health criteria.

Human health priority	Independent criteria informing on exposure			Independent criteria informing on hazard	
	Plastic use	Concentration [c]	Migration potential (plastic type, additive properties) [d]	Hazard potential	Hazard potency (expert judgement to determine critical effect)
High priority	Medical devices	> 10% (> 100,000 ppm)	Significant migration potential during use	CMR, ED	e.g. mammalian NOAEL/C ≤ 10 mkd
Moderate priority	Food contact, toys (for children > 3 years)	0.1-10% (1,000-100,000 ppm)	Unknown migration potential	Sensitisation	e.g. mammalian NOAEL/C > 10 to ≤ 100 mkd
Low priority	Other consumer applications, professional uses	0.01% to < 0.1% (100 to < 1,000 ppm)	Low / slow migration	No classification [a]	e.g. mammalian NOAEL/C > 100 to ≤ 1,000 mkd
Very low priority	Industrial uses / rare contact	< 0.01% (< 100 ppm)	Negligible migration	Industrial uses / rare contact	< 0.01% (< 100 ppm)

Abbreviations: bw: body weight; CMR: carcinogenicity, mutagenicity, reproductive toxicity; ED: endocrine disruptor; mkd: mg/kg body weight/day; MW: molecular weight; NOAEL/C: no-observed adverse effect level / concentration.
Depending on the scope of the assessment, either full risk assessment can be done for all 'additive + use' combinations, or one or more of the above prioritisation criteria can be applied to exclude those additives/uses being of lower priority for the context. Note that a given 'additive + use' can be of low concern in one aspect and of high concern in another. Other criteria than mentioned here, e.g. to determine hazard potential, may be relevant for the given prioritisation exercise, further considering that prioritisation criteria are often driven by policy context.
[a] Conclusion on hazard concern not possible in (complete) absence of hazard data.
[b] Approximation for individual additive constituents.
[c] Indicative thresholds that may apply unless specific limits are in place.
[d] The "*quantitative exposure estimation might be replaced by qualitative argumentation supporting 'negligible release exposure*'" if the substance has a very high molecular weight (>700 g/mol) and high octanol–water partition coefficient (log K_{ow} > 9), very low solubility in water (0.01 mg/L) or low vapour pressure (10–4 Pa) or if it is reacted into the polymer chain (ECHA, 2020).

environmental conditions. In this regard, the solvent and temperature conditions that are commonly applied for migration studies (JRC, 2015) may be sufficiently conservative to reflect general environmental migration scenarios under ambient conditions (Guazzotti et al., 2024).

3.2.3. Module 4: Higher tier hazard testing and assessment

The (Module 4) higher tier hazard testing and assessment may be relevant if the (Module 2.4) initial risk assessment does not support the conclusion that any risks that may arise due to the presence of the additive in the plastic article with a particular intended use can be adequately managed. The exact substance-specific hazard data that may need to be generated depend on (1) the problem formulation, (2) the outcome of the (initial or refined) exposure assessment, and/or (3) the robustness of the hazard data retrieved in Module 2.

As a first step, Module 4 includes substance-specific testing while avoiding the use of vertebrate animals (including "*independently feeding larval forms*" or "*foetal forms of mammals as from the last third of their normal development*"; EP and Council, 2010). Hence, this step of the hazard assessment may include, as relevant, assays making use of *in vitro* test systems, non-vertebrate animals (e.g. *Daphnia* for aquatic toxicity assessments) or early life stages of vertebrate animals (e.g. zebrafish embryos up to the eleutheroembryo stage). Many of these assays can be performed for large numbers of substances, thereby allowing for optimisation of resources. For example, if a certain plastic additive and/or its major transformation product(s) need to be investigated for a certain toxicological endpoint, *in vitro* screening bioassays may help establish whether assumed toxicological properties are potentially present (Mayrhofer et al., 2023; Schwarz et al., 2023) subject to, e.g. considerations for human relevance, biological plausibility and applicability domain.

The *in vitro* screening may be supported with advanced *in silico* modelling (1) for more in-depth structural analysis of the additive and/or major known transformation products to either confirm or refute a structural alert; and/or (2) for refined searches for similar substances. In case the toxicological relevance of a structural alert can be refuted, it may be helpful to return to the generic hazard assessment approach prior to consideration of *in vivo* assessments.

In case the *in vitro* screening indicates or substantiates a concern, a refined and robust substance-specific hazard assessment may be considered. This involves the performance of *in vivo* short-term and/or long-term (eco-)toxicity studies. As such, this step of the hazard assessment is likely to be resource intensive, requiring a high level of expertise to generate and evaluate the experimental data on the additive and/or its major known transformation product(s). Therefore, the generation of *in vivo* data should generally be restricted to three primary scenarios, first giving due consideration to the applicable sector-specific legislation and to the indispensability of such animal testing:

1. There is reliable evidence of significant exposure to the additive and/or known transformation product indicating a risk potential; or
2. The lower tier hazard information and/or higher tier *in vitro* information that is available for the additive and/or known transformation product indicates a human health and/or environmental

Table 2
Prioritisation matrix informing on independent environmental concern level.

Environment priority	Independent criteria informing on exposure			Independent criteria informing on hazard	
	Plastic use [a]	Concentration [b]	Migration potential (plastic type, additive properties) [c]	Hazard potential	Hazard potency (reflected by chronic NOEC/EC_{10})
High	Environmental application with likelihood of long-lasting exposure (e.g. agricultural use)	> 10% (> 100,000 ppm)	Significant migration potential during intended use	Confirmed PBT / vPvB	≤ 0.1 mg/L (NRD) ≤ 0.01 mg/L (RD)
Moderate	Wide-dispersive consumer use (e.g. single use plastic)	0.1-10% (1,000-100,000 ppm)	Unknown migration potential	Chronic aquatic Cat. 1-3 Suspected PBT / vPvB	> 0.1 to ≤ 1 mg/L (NRD) > 0.01 to ≤ 0.1 mg/L (RD)
Low	Applications with defined recycling/waste stage (e.g. automotive applications) and low anticipated environmental exposure	0.01% to < 0.1% (100 to < 1,000 ppm)	Low / slow migration during intended use	No classification [d]	> 0.1 to ≤ 1 mg/L (NRD)
Very low	Long-term environmental exposure unlikely (e.g. use in construction)	< 0.01% (< 100 ppm)	Negligible migration during intended use	MW > 1,000 Da indicating limited systemic bioavailability [e]	> 1 mg/L (NRD, RD)

Abbreviations: EC_{10}: 10% effect concentration; MW: molecular weight; NOEC: no-observed effect concentration; NRD: non-rapidly degradable ingredient (Table 4.1.2 in United Nations, 2023); PBT: persistent, bioaccumulative, toxic; RD: rapidly degradable ingredient (Table 4.1.2 in United Nations, 2023); vPvB: very persistent, very bioaccumulative.
Depending on the scope of the assessment, either full risk assessment can be done for all 'additive + use' combinations, or one or more of the above prioritisation criteria can be applied to exclude those additives/uses being of lower priority for the context. Note that a given 'additive + use' can be of low concern in one aspect and of high concern in another. Other criteria than mentioned here, e.g. to determine hazard potential, may be relevant for the given prioritisation exercise, further considering that prioritisation criteria are often driven by policy context.
[a] This category considers only the intended use e.g. in articles and managed waste. Mismanaged waste is not covered as it cannot be properly treated within the risk assessment approach proposed in this manuscript.
[b] Indicative thresholds that may apply unless specific limits are in place.
[c] The "*quantitative exposure estimation might be replaced by qualitative argumentation supporting 'negligible release exposure*'" if the substance has a very high molecular weight (>700 g/mol) and high octanol–water partition coefficient (log K_{ow} > 9), very low solubility in water (0.01 mg/L) or low vapour pressure (10–4 Pa) or if it is reacted into the polymer chain (ECHA, 2020).
[d] Conclusion on hazard concern not possible in (complete) absence of hazard data.
[e] Approximation for individual additive constituents.

concern that cannot be managed by appropriate risk mitigation measures; or
3. The additive and/or major known transformation product exhibits a hazard concern that cannot be managed by appropriate risk mitigation measures, and the additive has widespread use in sensitive applications.

Taken together, if it is deemed necessary to refine the risk characterisation of the additive and/or major known transformation product(s) by the generation of new, substance-specific hazard data, such testing should preferably begin with non-vertebrate animal testing. *In vivo* testing should only be considered if relevant to provide additional lines of evidence, to confirm *in vitro* mechanistic findings and/or to enhance the understanding of population effects. Finally, all available and newly generated hazard information should be evaluated following a weight-of-evidence approach (EFSA Scientific Committee, 2017) to conclude on the hazard potential and hazard potency of the additive and/or its major known transformation product(s). This tiered approach is consistent with efforts to replace, reduce and refine the use of vertebrate animals in toxicity testing (Russell and Burch, 1959; EP and Council, 2010; Choudhuri et al., 2018) and it is also aligned with the emerging interest in new approach methodologies, which are increasingly gaining regulatory acceptance (Stucki et al., 2022).

3.2.4. Module 5: Risk characterisation

Generally, the (Module 5) risk characterisation is conducted in the same manner as the (Module 2.4) initial risk characterisation while considering the additional substance-specific exposure and/or hazard testing data that were newly generated in Modules 3 and/or 4. Giving due consideration to identified uncertainties and margins of safety (Section 3.2.1.4), the outcome of the final risk characterisation may yield the conclusion that any identified risks can be adequately managed. For example, as regards occupational exposures, appropriate risk mitigation measures may be implemented. If the final risk characterisation does not allow concluding that the identified risks can be adequately managed, it may be necessary to select a different additive with an alternative chemistry for the given plastic article and its intended use.

4. Current approaches for risk assessment of plastic additives

There is no specific and generally accepted approach for risk assessment of plastic additives. The aim of this section is to show how the proposed framework here aligns with sector-specific approaches that have already been undertaken for many years.

For plastic additives in food contact applications, a risk assessment is conducted, e.g. by EFSA (EP and Council, 2004; European Commission, 2011), the US FDA (US CFR, 2026) and, at the global level, the FAO/WHO JECFA (WHO, undated). Similarly, a risk assessment of plastic additives in medical devices is conducted, in the EU, by notified bodies, which are designated and accredited by the Member States, and with involvement from the European Medicines Agency. This serves to ensure

absence of toxicity, material safety and biocompatibility of medical devices in line with the provisions from the Medical Devices Regulations (EP and Council, 2017a, 2017b) and the subsequent ISO 10993 standard series (ISO, 2025); see Section 1. Less specific uses may already be covered via assessments available under sector-unspecific legislation, e.g. the REACH Regulation (EP and Council, 2006).

In these instances, the focus of the risk assessment is on the plastic additive itself to evaluate its suitability for an intended application making use of substance-specific toxicological information (Box 2 in Section 3.2.1.3). For the assessment of food contact materials, NIAS also need to be considered. Recently, this has been reinforced by amendments to the Food Contact Materials Regulation (European Commission, 2011) especially with the introduction of the new Article 3a on purity criteria for substances used in the manufacturing of plastic materials and articles (European Commission, 2025).

An approach for how to conduct the risk assessment of substances that may migrate from plastic articles, which explicitly includes transformation products and other NIAS, has been presented by the Cosmetic Packaging and Toxicology (CosPaTox) consortium. The *Voluntary industry guideline – safety assessment of recycled plastics in packaging materials for cosmetic products and home care products* (CosPaTox, 2024) has been developed to assist industry in ensuring the safe use of post-consumer recycled plastic materials in cosmetic and household product packaging. The CosPaTox guideline includes a holistic approach to identify and evaluate transformation products and other NIAS, which may be present in post-consumer recycled plastic materials. This holistic approach is based on established human health risk assessment principles (e.g. US EPA, 1992, 1998, 2014), and it includes, as core elements, an analytical testing strategy and a safety evaluation scheme that consists of a rigorous and structured process to evaluate risk and conclude on the consumer safety of the packaging. It demonstrates the utility and feasibility for assessing post-consumer recycled plastic materials given their complexity. In April 2025, the CosPaTox consortium successfully completed the German Institute for Standardisation (DIN) SPEC 91521 certification whereby the CosPaTox guideline (CosPaTox, 2024) has become a formal DIN technical specification (DIN, 2025).

The CosPaTox approach presents a complementary approach to the framework for risk assessment of plastic additives described in the present article that is specific to packaging materials for cosmetic products and home care products. While CosPaTox was originally developed for mechanically recycled post-consumer resin (PCR), the principles and methodologies are highlighted here because they are adaptable to other plastic types and recycling contexts. These approaches can be used alongside one another to strengthen risk assessment outcomes. In particular, the explicit inclusion of transformation products and NIAS through analytical determination will be as we look toward addressing the complex scenarios of circular product cycles.Both approaches are conservative, which is a basic tenet of safety evaluations. The framework for risk assessment of plastic additives described here expands beyond a specific type of polymer or type of application.

5. Conclusion and outlook

In this article, the fundamental elements of a framework for risk assessment of plastic additives and their major known transformation products have been presented and discussed. The framework is aligned both with the internationally accepted chemical risk assessment paradigm and with legal requirements for plastic additive risk assessment (taking the applicable EU legislation as example, with brief reference to other jurisdictions).

The framework for risk assessment of plastic additives is comprised of five modules providing a transparent and structured approach to identify and efficiently gather pertinent information. Data needs are tailored to the specific plastic additive and/or its major known transformation product(s) and to the scope of the risk assessment. As a risk-based approach, the five modules are pursued in an iterative, 'circular' manner; this serves to ensure that the risk assessment can be run with little resource investment in some cases and is terminated as soon as it is possible to either exclude risk potential or to characterise and manage any identified risks. Further adaptations to the internationally accepted chemical risk assessment paradigm to address the specificities of plastic additives include the element of prioritisation in case large numbers of additives shall be submitted to the risk assessment and special consideration of physicochemical properties, as these may determine migration potential as a key driver for exposure potential.

The framework for plastic additive risk assessment, as it has been presented here, is applicable to individual plastic additives and/or their major known transformation products. Building thereupon, the second article under preparation by the ECETOC Plastic Additives TF shall present further elements to consider when applying the framework for risk assessment of plastic additives and their transformation products in complex scenarios of circular product cycles. The manufacture of plastics may involve post-use alterations of the underlying polymers. Also, recycling streams often include mixed plastics and, therefore, mixed additive inventories. All such issues need to be considered during risk assessment of plastic additives in complex scenarios. For example, when the test item is recycled feedstock, it may not be appropriate to limit the risk assessment to single plastic additives and their major known transformation products. Instead, non-targeted analysis tools (see e.g. Koster et al., 2025) may be relevant to identify the spectrum of extracts / leachates, which would then include additives, transformation products as well as further NIAS present in the recycled feedstock.

Consideration of these further elements of the risk assessment of plastic additives in complex scenarios shall enable risk assessors to conclude which combinations of use/life cycle stage/additive may (1) necessitate limitation or substitution due to an unacceptable risk; (2) be deprioritised due to low risk; or (3) have uncertainties and/or knowledge gaps that prevent robust conclusions and how this may be addressed. Depending on how many use/life cycle stage/additive combinations are in scope, the risk assessment can be straightforward or very complex, with different degrees of uncertainty, which need to be described transparently.

Taken together, the work of the ECETOC Plastic Additives TF aims to support the efficient and reliable assessment of both environmental and human health risks of plastic additives in a manner that allows to select those uses of additives, for which any risk that may arise across the life cycle, including recycling, reuse and disposal, can be appropriately managed.

CRediT authorship contribution statement

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Heli Miriam Hollnagel: Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Conceptualization.

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Author contributions

CD, DEA, CWD, BH, TAK, SK, ER, SSS, TS, KT, AJW are members of the ECETOC Plastic Additives TF. SNK (as of March 2025) and HMH are Stewards from the ECETOC Scientific Committee. UGS, a scientific writer, was hired by ECETOC to assist in the preparation of the manuscript. All authors contributed to the conceptualisation, preparation and finalisation of the manuscript.

Disclaimer

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Appendix I. Glossary of Terms Referenced

Additivation: Addition of a chemical substance to a matrix or mixture (TF working definition).

Additive: "a *substance which is intentionally added to plastics to achieve a physical or chemical effect during processing of the plastic or in the final material or article; it is intended to be present in the final material or article"* (European Commission, 2011; Article 3(7)).

Chemical recycling (synonyms: feedstock recycling, advanced recycling): Process that "*converts e. g. polymeric waste by changing its chemical structure to produce products* (e.g. *waxes) or substances* (e.g., *oil and gas) that are used as raw materials for the manufacturing of plastics or other products. Products exclude those used as fuels or means to generate energy. There are different chemical recycling technologies such as pyrolysis, solvolysis, gasification, hydro-cracking and depolymerisation"* (https://plasticseurope.org/glossary/chemical-recycling/).

Circular economy: "*A circular economy keeps materials, products, and services in circulation for as long possible. …uses a systems-focused approach and involves industrial processes and economic activities that are restorative or regenerative by design, enables resources used in such processes and activities to maintain their highest value for as long as possible, and aims for the elimination of waste through the superior design of materials, products, and systems (including business models)… A circular economy reduces material use, redesigns materials, products, and services to be less resource intensive, and recaptures "waste" as a resource to manufacture new materials and products*" (https://www.epa.gov/circulareconomy/what-circular-economy). In the context of the ECETOC TF work, this term is used specifically as it relates to plastic additives.

Feedstock: "*Raw material or material that is the principal input for an industrial production process"* (https://plasticseurope.org/glossary/feedstock/).

Health-based guidance value: "*A numerical value derived by dividing a point of departure (a no observed-adverse-effect level, benchmark dose or benchmark dose lower confidence limit) by a composite uncertainty factor to determine a level that can be ingested over a defined time period* (e.g. *lifetime or 24 h) without appreciable health risk*" (WHO IPCS, 2009b).

Life cycle (of a product): The entire lifespan of a product, i.e. all stages from raw material extraction through materials processing, manufacturing, distribution, use, repair and maintenance, and eventual disposal or recycling (adapted from ICCA, 2021).

Margin of exposure: "*Ratio of the no-observed-adverse-effect level or benchmark dose lower confidence limit for the critical effect to the theoretical, predicted or estimated exposure dose or concentration*" (WHO IPCS, 2009b).

Margin of safety: "*The margin between the health-based guidance value (reference dose) and the actual or estimated exposure dose or concentration. For some experts, the margin of safety has the same meaning as the margin of exposure*" (WHO IPCS, 2009b).

Mixture: "*A mix or solution of two or more substances. Under the EU chemicals legislation, mixtures are not considered substances*" (https://echa.europa.eu/support/substance-identification/what-is-not-a-substance).

Non-intentionally added substance (NIAS; in context of food contact materials): *"An impurity in the substances used or a reaction intermediate formed during the production process or a decomposition or reaction product"* (European Commission, 2011; Article 3(9)).

Plastic:

- ASTM (2026): "*A material which contains as an essential ingredient one or more organic polymeric substances of large molecular weight, is solid in its finished state, and at some stage in its manufacture or processing into finished articles can be shaped by flow.*"
- EP and Council (2019): "*A material consisting of a polymer as defined in point 5 of Article 3 of Regulation (EC) No 1907/2006, to which additives or other substances may have been added, and which can function as a main structural component of final products, with the exception of natural polymers that have not been chemically modified.*"

Polymer:

- IUPAC: "*Substances composed of macromolecules, very large molecules with molecular weights ranging from a few thousand to as high as millions of*

grams/mole" (https://iupac.org/polymer-edu/what-are-polymers)

• REACH (Article 3(5)): *"A substance consisting of molecules characterised by the sequence of one or more types of monomer units. Such molecules must be distributed over a range of molecular weights wherein differences in the molecular weight are primarily attributable to differences in the number of monomer units. A polymer comprises the following:*

o *a simple weight majority of molecules containing at least three monomer units which are covalently bound to at least one other monomer unit or another reactant;*

o *less than a simple weight majority of molecules of the same molecular weight.*

• *In the context of this definition a 'monomer unit' means the reacted form of a monomer substance in a polymer"* (EP and Council, 2006).

Polymer matrix: The continuous phase in multi-constituent or multi-phase (composite) systems (adapted from Wang et al., 2011).

Recyclate: The product of a recycling process. Adapted to plastic recycling, the term "recyclate" is therefore synonymous to recycled, reprocessed plastics (adapted from: https://www.hk-mueller.de/de/rezyklate/).

Risk characterisation ratio (RCR): "*For threshold effects for which a DNEL* [derived no-effect level] *can be set, the RCR is the ratio of the estimated exposure and the DNEL*" (ECHA, 2016d).

Transformation products: Reaction products formed from the initial additive during the life cycle of the plastic article, including, but not limited to, technical processes during production of articles, biological/environmental degradation processes during article service life, as well as chemical and technical processes during recycling (TF working definition).

Waste stream: *"Flows of specific waste, from its source through to recovery, recycling or disposal"* (EP, 2015).

Appendix II. Six 'additive + use' examples showing how plastic additives may be prioritised for the further risk assessment

Introduction

This appendix serves as a proof-of-concept to demonstrate how the prioritisation matrices to establish human health and environmental concern levels (Table 1 and Table 2, respectively, in the main article) can be used when the numbers of additives and/or of the intended uses that shall be submitted to the risk assessment are too large to assess them all at once. Altogether six examples of stepping through the hazard and exposure criteria outlined in the prioritisation matrices are provided for three additives, which were each assigned two common use scenarios:

Example 1a. use of α-tocopherol (CAS No. 59–02-9), i.e. the bioactive form of Vitamin E, at 100–300 ppm in polypropylene (PP) for automotive applications, such as bumpers.

Example 1b. use of α-tocopherol at 100–300 ppm in PP for food contact applications, such as single-use kitchenware.

Example 2a. use of butylated hydroxytoluene (BHT; chemical name: 2,6-di-tert-butyl-p-cresol, CAS No. 128-37-0) at 1000 ppm in polyethylene (PE) for agricultural films.

Example 2b. use of BHT at 500 ppm in polyvinyl chloride (PVC) for medical tubing.

Example 3a. use of tetraphenyl dipropyleneglycol diphosphite (TphDD; chemical name: oxybis(1-methylethylene) tetraphenyl diphosphite, CAS No. 80584-85-6) at 1500 ppm in PE for drinking water pipes.

Example 3b. use of TphDD at 500 ppm in PE for a toy for children above three years of age.

α-Tocopherol, BHT and TphDD are also considered in the Supplementary Information SI-2, which is linked to Section 2.2 of the main article.

The prioritisation matrices include these criteria informing on human (consumer only) and environmental exposure (Table 1 and Table 2 in main article):

- ***The type of the intended use of the plastic article***.
- ***The concentration of the additive in the plastic*** (for the given use).
- ***The migration potential of the additive from the plastic matrix***. For the purpose of the six examples, an additive is assessed as having negligible migration potential if it exhibits very high molecular weight (>700 g/mol), a high *n*-octanol–water partition coefficient (log K_{ow} > 9), very low solubility in water (<0.01 mg/L) or low vapour pressure (10^{-4} Pa) (ECHA, 2020; see Section 3.1.2 for further discussion).

The prioritisation matrices include these criteria informing on hazard (Tables 1 and 2 in main article):

Hazard potential based on existing hazard classifications. For the purpose of the six 'additive + use' examples, it is established whether the respective additive has

- a harmonised classification and labelling (CLH) in accordance with Title V of *Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures* (EP and Council, 2008), or
- a notified classifications in accordance with Article 7(4)d of *Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals* (REACH; EP and Council, 2006), or
- a classification in accordance with the *United Nations Globally Harmonised System of Classification and Labelling of Chemicals* (GHS; United Nations, 2023), or
- whether information on potential additional hazard concerns is available, which might eventually lead to the corresponding CLH.

Hazard potency based on established potency thresholds indicating safe exposure levels. For the purpose of the six 'additive + use' examples, focus is on no-observed adverse effect levels (NOAELs) from mammalian oral repeated-dose and chronic toxicity studies and on no-observed effect concentrations (NOECs) from long-term aquatic toxicity studies provided in the REACH registration dossiers for the three additives and which are, therefore, available in the European Chemicals Agency (ECHA) Chemicals Database (ECHA, 2026a). If relevant information was unavailable in this database, the hazard information retrieved from the US Environmental Protection Agency databases was also considered (Section 2.1 in main article

and Table SI-2.2).

The ECHA Chemicals Database was selected as primary source to retrieve hazard information for α-tocopherol, BHT and TphDD to ensure ease of traceability. While this data source is not sufficient to support a comprehensive risk assessment of plastic additives, this is not the goal of the present case examples, which serve to illustrate how 'additive + use' combinations may be prioritised for risk assessment.

The six examples also serve to demonstrate how a scoring method may aid in the prioritisation of large numbers of 'additive + use' combinations for the further risk assessment. Application of the proposed here (adapted from Shin et al., 2014) yields a numerical value indicating the priority level for further risk assessment: high priority corresponds to 4, moderate priority to 3, low priority to 2 and very low priority to 1. Absence of data is generally assigned moderate priority for further risk assessment (numerical score: 3), giving due consideration to the specific assessment objectives. The rationale is that the absence/lack of data should not be translated into "high" level of concern/priority but should rather be considered a flag for further data generation needs. The total assessment priority score is calculated by multiplying the sum of the numerical values assigned independently to each hazard criterion with the sum of the numerical values assigned independently to each exposure criterion. Total human health and environmental assessment priority scores are estimated separately.

$$TotalPriorityScore = \sum_{i=1}^{2} HazardPriority_i \sum_{j=1}^{3} ExposurePriority_j$$

It is important to note that the **six** examples presented here only serve to generally illustrate how the prioritisation scheme might be applied. In practice, the prioritisation scheme has been proposed for scenarios where dozens to hundreds of additives shall be prioritised for risk assessment, further considering that opportunities for such prioritisation are also dependent on the given risk assessment scope (Section 3.1.1 in main article). **In the six examples, it is the goal of the prioritisation to pre-select those additives for which a full risk assessment is most urgent. Therefore, high priority is assigned to those 'additive + use' scenarios, which yield high total assessment priority scores. By comparison, if it is the goal of the prioritisation to identify those additives that most likely do not pose a risk concern for a given use scenario, the pre-selection may focus on those additives yielding a low total assessment priority score.**

In practice, there may also be opportunities to refine total assessment priority scores for data-poor additives by utilising *in silico* tools (Section 2.2 in main article) to predict relevant hazard-related and/or physicochemical properties. While *in silico* predictions of hazard-related properties may help refine the underlying hazard scores, *in silico* predictions of physicochemical properties may be useful to refine the underlying exposure scores, e.g. by yielding information on the migration potential of the additive. Such considerations are not included in the six 'additive + use' scenarios, which serve generic, illustrative purposes.

Utilisation of the prioritisation matrix (Table 1 in main article) to establish human health assessment priority scores for the six 'additive + use' examples

Establishment of human exposure scores

Example 1a/1b. (:) **α-Tocopherol** is widely used as a (phenolic) antioxidant in plastic due to its effectiveness in different types of polymers under various conditions (Al-Malaika, 2000). The use scenario of car bumpers (Example 1a), where there is minimal contact to consumers, corresponds to a very low priority level, whereas the use scenario of single-use kitchenware (Example 1b) corresponds to a moderate priority level due to the higher potential for consumer exposure. The selected concentration of 100–300 ppm α-tocopherol in PP (Example 1a/1b) corresponds to a low priority level (for concentration range, see Table 1 in main article). Given the physicochemical properties of α-tocopherol (see below), its migration potential is established as being low/slow leading to a low priority level for this property.

α-Tocopherol: molecular weight: 430.7 g/mol; log k_{ow}: 12.2 at 25 °C; water solubility: 1.3 μg/L at 20 °C; vapour pressure: 1.87×10^{-8} hPa at 25 °C (ECHA, 2019b; Haz-Map, 2026).

Human exposure score for α-tocopherol in Example 1a (Table A-II.1): For the use of α-tocopherol at 100–300 ppm in PP for car bumpers, the sum of the very low priority level regarding intended plastic use (numerical value: 1) and the low priority levels regarding additive concentration (numerical value: 2) and migration potential (numerical value: 2) yields a human exposure score of 5 (= 1 + 2 + 2).

Human exposure score for α-tocopherol in Example 1b (Table A-II.1): For the use of α-tocopherol in single-use kitchenware, the sum of the moderate priority level regarding intended plastic use (numerical value: 3) and low priority levels regarding additive concentration (numerical value: 2) and migration potential (numerical value: 2) yields a human exposure score of 7 (= 3 + 2 + 2).

Example 2a/2b. (:) **BHT** is also a widely used phenolic antioxidant, and it is used in a broad variety of applications from food contact materials to petroleum products (Yehye et al., 2015). As regards intended use of the plastic, the use for agricultural films (Example 2a) corresponds to a very low priority level for direct consumer exposure, whereas the use for medical tubing (Example 2b) corresponds to a high priority level. The selected concentrations of 1000 ppm BHT in PE (Example 2a) and 500 ppm BHT in PVC (Example 2b) are assigned moderate and low priority levels, respectively (for concentration ranges, see Table 1 in main article). Given the physicochemical properties of BHT (see below), its migration potential from PE or PVC is established as high leading to a high priority level (Example 2a/2b).

BHT: molecular weight: 220.4 g/mol; log k_{ow}: 5.1 at 20 °C; water solubility: 0.76 mg/L at 20 °C; vapour pressure: 0.011 hPa at 20 °C (ECHA, 2024b).

Human exposure score for BHT in Example 2a (Table A-II.1): For the use of BHT at 1000 ppm in PE for agricultural films, the sum of the very low priority level related to intended use of the plastic (numerical value: 1), the moderate priority level related to its concentration in the polymer (numerical value: 3) and the high priority level regarding migration potential (numerical value: 4) yields a human exposure score of 8 (= 1 + 3 + 4).

Human exposure score for BHT in Example 2b (Table A-II.1): For the use of BHT at 500 ppm in PVC for medical tubing, the sum of the high priority level related to intended use of the plastic (numerical value: 4), the low priority level related to its concentration in the polymer (numerical value: 2) and the high priority level regarding migration potential (numerical value: 4) yields a human exposure score of 10 (= 4 + 2 + 4).

Example 3a/3b. (:) **TphDD** is reported to be used as a stabiliser in certain polymers (PubChem, 2026b). As regards intended uses of the plastic, both use in drinking water pipes (Example 3a) and use in toys for children above three years of age (Example 3b) are assigned moderate priority levels. The concentrations of 1500 and 500 ppm TphDD in PE correspond to moderate and low priority levels, respectively (see Table 1 in main article for

concentration ranges). Since information on log K_{ow}, water solubility and vapour pressure of TphDD is not available in the ECHA or PubChem databases (ECHA, undated no. 4; PubChem, 2026b), it was not possible to establish the migration potential of TphDD, yielding a moderate priority level for this property.

Human exposures scores for TphDD in Example 3a (Table A-II.1): For the use of TphDD at 1500 in PE for drinking water pipes, the sum of the moderate priority levels related to intended use (numerical value: 3), concentration of TphDD in the polymer (numerical value: 3) and migration potential (numerical value: 3) add up to a human exposure score of 9 (= 3 + 3 + 3).

Human exposures scores for TphDD in Example 3b (Table A-II.1): For the use of TphDD at 500 ppm in PE for toys for children above 3 years of age, the sum of the moderate priority level related to intended use (numerical value: 3), the low priority level related to the concentration of TphDD in the polymer (numerical value: 2) and the moderate priority level regarding migration potential (numerical value: 3) add up to a human exposure score of 8 (= 3 + 2 + 3).

Establishment of human health hazard scores

Example 1a/1b. (:) **α-Tocopherol** does not have any human health hazard-related classifications (ECHA, undated no. 5). In the REACH registration dossier, the key rat oral repeated-dose toxicity study was conducted on Vitamin E (d-α-tocopheryl acetate), yielding a 90-day NOAEL of 500 mg/kg body weight/day (mkd) in rats, from which read-across (ECHA, 2017) was applied to address this endpoint for α-tocopherol (Section 7.5.1, Study 003, in ECHA, 2019b).

Human health hazard score for α-tocopherol (Table A-II.1): α-Tocopherol is assigned a low priority level for both hazard potential (i.e. no classification) and hazard potency (i.e. mammalian NOAEL > 100 mkd to ≤1000 mkd; see Table 1 in the main article). Hence, both criteria are assigned numerical values of 2, yielding a human health hazard score of 4 (= 2 + 2) for α-tocopherol.

Example 2a/2b. (:) **BHT** currently does not have any classifications for human health hazards (ECHA, undated no. 6); however, it is under evaluation for endocrine disruption under the REACH Article 44(2) Community Rolling Action Plan (ANSES, 2016; SCCS, 2021; ECHA, undated no. 7) with the status "information requested" (ECHA, 2026b). From the oral repeated-dose and chronic toxicity studies available in the REACH dossier, the key NOAEL for chronic systemic effects in rats was determined to be 25 mkd (Summary to Section 7.5.1 in ECHA, 2024b).

Human health hazard score for BHT (Table A-II.1): For the present prioritisation exercise, BHT is assigned a high priority level with respect to hazard potential since it is under evaluation for endocrine disruption and a moderate priority level with respect to hazard potency (i.e. mammalian NOAEL >10 to ≤100 mkd; see Table 1 in main article). Accordingly, hazard potential and potency are assigned numerical values of 4 and 3, respectively, yielding a human health hazard score of 7 (= 4 + 3) for BHT.

Example 3a/3b. (:) **TphDD** does not have any active REACH registration dossiers (ECHA, undated no. 4); therefore, the ECHA Chemicals Database does not include any relevant data to establish the hazard potential or potency for TphDD. Similarly, the US EPA databases and applications do not include any mammalian repeated-dose or chronic systemic toxicity data for TphDD (Table SI-2.2). In the US National Library of Medicine PubChem database, it is indicated that TphDD has GHS classifications for skin irritation and serious eye irritation (PubChem, 2026b).

Human health hazard score for TphDD (Table A-II.1): Due to the unavailability of data for TphDD, hazard potential and hazard potency are each assigned numerical values of 3 (see introduction to Appendix II), yielding a human health hazard score of 6 (= 3 + 3) for TphDD.

Establishment of human health assessment priority scores

As an outcome of the proof-of-concept of the prioritisation matrix presented in Table 1 of the main article, α-tocopherol is assigned the lowest priority for further human health risk assessment, with the human health assessment priority score being slightly lower for the intended use in car bumpers than for the intended use in single-use kitchenware (20 vs 28; Table A-II.1). TphDD is assigned medium priority for human health risk assessment due to the current information gaps. Given the different concentrations of TphDD in PE (500 ppm vs 1500 pm), the total priority score for use in children's toys is slightly lower than that for use in drinking water pipes (48 vs 54). BHT for use in agricultural films is assigned as similar total priority score (56). Finally, BHT for use in medical tubing is assigned the highest priority for further human health risk assessment (total priority score: 70).

Utilisation of the prioritisation matrix (Table 2 in main article) to establish environmental assessment priority scores for the six 'additive + use' examples

Establishment of environmental exposure scores

The thresholds to establish priority levels related to (1) the concentration of the additive in the polymer and (2) its migration potential are identical in the human health- and environment-related prioritisation matrices. Therefore, this section focusses on the establishment of environmental priority levels related to the intended use of the plastic, while taking over the priority levels for additive concentration and migration potential established for the human health assessment priority scores (Table A-II.1).

Example 1a/1b – α-Tocopherol. (:) In line with the prioritisation matrix presented in Table 2 of the main article, the (Example 1a) intended use in car bumpers is an application with a well-defined recycling/waste stage and low anticipated environmental exposure, corresponding to a low priority level (numerical value: 2). The (Example 1b) intended use in single-use kitchenware corresponds to a moderate priority level (numerical value: 3) given it is a wide-dispersive consumer use and, thus, potential for environmental exposure.

Environmental exposure score for α-tocopherol in Example 1a (Table A-II.2): For the use of α-tocopherol at 100–300 ppm in PP for automotive applications, such as bumpers, the sum of the low priority levels related to plastic use (numerical value: 2), the concentration of the additive in PP (numerical value: 2) and its migration potential (numerical value: 2) yields an environmental exposure score of 6 (= 2 + 2 + 2).

Environmental exposure score for α-tocopherol in Example 1b (Table A-II.2): For the use of α-tocopherol at 100–300 ppm in PP for single-use kitchenware, the sum of the moderate priority level regarding plastic use (numerical value: 3) and low priority levels regarding additive concentration (numerical value: 2) and migration potential (numerical value: 2) yields an environmental exposure score of 7 (= 3 + 2 + 2).

Example 2a/2b – BHT. (:) The intended use of the plastic for agricultural films corresponds to a high priority level (numerical value: 4), whereas

medical tubing corresponds to a low priority level due to the limited environmental exposure potential (numerical value: 2).

Environmental exposure score for BHT in Example 2a (Table A-II.2): For the use of BHT at 1000 ppm in PE for agricultural film, the sum of the high priority level assigned to plastic use (numerical value: 4), the moderate priority level related to additive concentration (numerical value: 3) and the high priority level related to its migration potential (numerical value: 4) yields an environmental exposure score of 11 (= 4 + 3 + 4).

Environmental exposure score for BHT in Example 2b (Table A-II.2): For the use of BHT at 500 ppm in PVC for medical tubing, the sum of the low priority levels assigned to plastic use (numerical value: 2) and additive concentration (numerical value: 2) and the high priority level related to its migration potential (numerical value: 4) yields an environmental exposure score of 8 (= 2 + 2 + 4).

Example 3a/3b: TphDD:. Plastic use in water pipes corresponds to a high priority level (numerical value: 4), whereas the use scenario of use in children's toys is assigned a low priority level from the environmental exposure perspective (numerical value: 2).

Environmental exposure score for TphDD in Example 3a (Table A-II.2): For the use of TphDD at 1500 ppm in PE for water pipes, the sum of the high priority level related to plastic use (numerical value: 4), the moderate priority levels related to additive concentration (numerical value: 3) and migration potential, due to data gaps (numerical value: 3) yield an environmental exposure score of 10 (= 4 + 3 + 3).

Environmental exposure score for TphDD in Example 3b (Table A-II.2): For the use of TphDD at 500 ppm in PE for a children's toy, the sum of the low priority levels related to plastic use (numerical value: 2) and additive concentration (numerical value: 2) and the moderate priority level due to data gaps with respect to migration potential (numerical value: 3) yield an environmental exposure score of 7 (= 2 + 2 + 3).

Establishment of environmental hazard scores

Example 1a/2b:. **α-Tocopherol** does not have any classification for environmental hazards (ECHA, undated no. 5). α-Tocopherol is considered inherently biodegradable in water (Section 5.2.1 in ECHA, 2019b); therefore, it is unlikely to accumulate in aquatic organisms. α-Tocopherol is not considered to exhibit potential for long-term toxicity to aquatic organisms: "As the substance is highly insoluble, it will not be significantly bioavailable and no significant exposure of aquatic organisms is expected. Furthermore, the substance is commonly used as food and feed additive (as Vitamin E supplement and antioxidant) and is therefore considered to have no long-term toxicity effects in aquatic organisms" (Section 6.1.4 in ECHA, 2019b).

Environmental hazard score for α-tocopherol (Table A-II.2): α-Tocopherol is assigned low priority with respect to environmental hazard potential (numerical score: 2) and very low priority with respect to environmental hazard potency (numerical score: 1) yielding an environmental hazard score of 3 (= 2 + 1).

Example 2a/2b:. **BHT** has an industry self-classification for chronic aquatic toxicity Category 1 (Section 2.1 in ECHA, 2024b), which indicates that the substance is "very toxic to aquatic life with long lasting effects". BHT is not considered either readily or inherently biodegradable in water (Section 5.2.1 in ECHA, 2024b); however, since its bioconcentration factor is below 2000, BHT is "not regarded as B [bioaccumulative] according to REACH Annex VIII" (Section 5.3 in ECHA, 2024b). Long-term aquatic toxicity studies yielded very high no-observed effect concentrations (NOECs) indicating high hazard potency of BHT: NOEC in Medaka fish (42-day exposure): 0.053 mg/L BHT (Section 6.1.2 in ECHA, 2024b); NOEC in Daphnia magna (21-day exposure): 0.023 mg/L BHT (Section 6.1.4 in ECHA, 2024b).

Environmental hazard score for BHT (Table A-II.2): BHT is assigned a moderate level of concern for hazard potential (numerical value: 3) and a high level of concern for hazard potency (numerical value: 4; see Table 2 in main article for threshold levels) yielding an environmental hazard score of 7 (= 3 + 4) for BHT.

Example 3a/3b – TphDD:. Just as there are no human health hazard data for TphDD, there are also no data on the environmental hazard potential or potency of this additive.

Environmental hazard score for TphDD (Table A-II.2): Due to the unavailability of data for TphDD, environmental hazard potential and hazard potency are each assigned moderate priority (numerical values of 3; see introduction to Appendix II), yielding an environmental hazard score of 6 (= 3 + 3) for TphDD.

Establishment of environmental assessment priority scores

As an outcome of the proof-of-concept of the environmental assessment prioritisation matrix presented in Table 2 of the main article, α-tocopherol is assigned the lowest priority for further environmental risk assessment, with the total environmental assessment priority score being slightly lower for the intended use in car bumpers than in that for single-use kitchenware (18 vs 21; Table A-II.2). TphDD for use in toys (Example 3a) is assigned medium priority for environmental risk assessment due to the current information gaps (total priority score: 42). By comparison, given the potential environmental impact of the intended use in water pipes and the relatively high TphDD concentration of 1500 ppm in PE (and the data gaps with respect to hazard potential, hazard potency and migration potential), the Example 3a "TphDD + water pipe" scenario yields a higher total environmental assessment priority score (60), which is even slightly higher than the total environmental assessment priority score for BHT for use in medical tubing (total priority score: 56). By comparison, BHT for use in agricultural films is assigned highest priority for further environmental risk assessment (total priority score: 77) since the underlying priority levels with respect to hazard potency, intended use and migration potential are high. Notably, this total score is even slightly higher than the highest human health assessment priority score of 70 assigned to the 'BHT + medical tubing' scenario (Table A-II.1).

Table A-II.1
Human health assessment priority scores for the six additive + use examples.

"Additive + use" example	Independent Criteria informing on exposure			Independent Criteria informing on hazard		Human health priority score
	Plastic use	Additive concentration	Migration potential	Hazard potential	Hazard potency	
1a) Use of α-tocopherol at 100-300 ppm in PP for automotive applications, such as bumpers	Very low priority (1)	Low priority (2)	Low priority (2)	Low priority (2)	Low priority (2)	(2+2) x (1+2+2) = **20**
1b) Use of α-tocopherol at 100-300 ppm in PP for single-use kitchenware	Moderate priority (3)					(2+2) x (3+2+2) = **28**
2a) Use of BHT at 1,000 ppm in PE for agricultural film	Very low priority (1)	Moderate priority (3)	High priority (4)	High priority (4)	Moderate priority (3)	(4+3) x (1+3+4) = **56**
2b) Use of BHT at 500 ppm in PVC for medical tubing	High priority (4)	Low priority (2)				(4+3) x (4+2+4) = **70**
3a) Use of TphDD at 1,500 ppm in PE for water pipes	Moderate priority (3)	Moderate priority (3)	Moderate priority due to data gaps (3)	Moderate priority due to data gaps (3)	Moderate priority due to data gaps (3)	(3+3) x (3+3+3) = **54**
3b) Use of TphDD at 500 ppm in PE for toy for children > 3 years of age	Moderate priority (3)	Low priority (2)				(3+3) x (3+2+3) = **48**

Abbreviations: BHT: butylated hydroxytoluene; PE: polyethylene; PP: polypropylene; PVC: polyvinylchloride; TphDD: tetraphenyl dipropyleneglycol diphosphite.
Note: These examples consider the scenario that the prioritisation serves to pre-select those additives for which a full risk assessment is most urgent. Therefore, high priority is assigned to those "additive + use" scenarios, which yield high total assessment priority scores. By comparison, if it is the goal of the prioritisation to identify those additives that most likely do not pose a risk concern for a given use scenario, the pre-selection may focus on those additives yielding a low total assessment priority score.

Table A-II.2
Environmental assessment priority scores for six "additive + use" examples.

(*continued on next page*)

Table A-II.2 (*continued*)

"Additive + use" example	Independent Criteria informing on exposure			Independent Criteria informing on hazard		Environment priority score
	Plastic use	Concen-tration	Migration potential	Hazard potential	Hazard potency	
1a) Use of α-tocopherol at 100-300 ppm in PP for automotive applications, such as bumpers	Low priority (2)	Low priority (2)	Low priority (2)	Low priority (2)	Very low priority (1)	(2+1) x (2+2+2) = **18**
1b) Use of α-tocopherol at 100-300 ppm in PP for single-use kitchenware	Moderate priority (3)					(2+1) x (3+2+2) = **21**
2a) Use of BHT at 1,000 ppm in PE for agricultural film	High priority (4)	Moderate priority (3)	High priority (4)	Moderate priority (3)	High priority (4)	(3+4) x (4+3+4) = **77**
2b) Use of BHT at 500 ppm in PVC for medical tubing	Low priority (2)	Low priority (2)				(3+4) x (2+2+4) = **56**
3a) Use of TphDD at 1,500 ppm in PE for water pipes	High priority (4)	Moderate priority (3)	Moderate priority due to data gaps (3)	Moderate priority due to data gaps (3)	Moderate priority due to data gaps (3)	(3+3) x (4+3+3) = **60**
3b) Use of TphDD at 500 ppm in PE for toy for children > 3 years of age	Low priority (2)	Low priority (2)				(3+3) x (2+2+3) = **42**

Abbreviations: BHT: butylated hydroxytoluene; PE: polyethylene; PP: polypropylene; PVC: polyvinylchloride; TphDD: tetraphenyl dipropyleneglycol diphosphite.
Note: These examples consider the scenario that the prioritisation serves to pre-select those additives for which a full risk assessment is most urgent. Therefore, high priority is assigned to those "additive + use" scenarios, which yield high total assessment priority scores. By comparison, if it is the goal of the prioritisation to identify those additives that most likely do not pose a risk concern for a given use scenario, the pre-selection may focus on those additives yielding a low total assessment priority score.
Notes: All websites were accessed June 2026. This bibliography also includes the references from Appendices I and II provided.

Appendix III. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2026.110403.

Data availability

No data was used for the research described in the article.

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