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Critical Review

Toward the Development and Application of an Environmental Risk Assessment Framework for Microplastic

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Abstract: Emissions of plastic waste to the environment and the subsequent degradation into microplastic particles that have the potential to interact with biological organisms represent a concern for global society. Current understanding of the potential impacts on aquatic and terrestrial population stability and ecosystem structure and function associated with emissions of microplastic particles is limited and insufficient to fully assess environmental risks. Multistakeholder discussions can provide an important element in helping to identify and prioritize key knowledge gaps in assessing potential risks. In the present review, we summarize multistakeholder discussions from a 1-d International Council of Chemical Associations–sponsored symposium, which involved 39 scientists from 8 countries with representatives from academia, industry, and government. Participants were asked to consider the following: discuss the scientific merits and limitations of applying a proposed conceptual environmental risk assessment (ERA) framework for microplastic particles and identify and prioritize major research needs in applying ERA tools for microplastic particles. Multistakeholder consensus was obtained with respect to the interpretation of the current state of the science related to effects and exposure to microplastic particles, which implies that it is unlikely that the presence of microplastic in the environment currently represents a risk. However, the quality and quantity of existing data require substantial improvement before conclusions regarding the potential risks and impacts of microplastic particles can be fully assessed. Research that directly addresses the development and application of methods that strengthen the quality of data should thus be given the highest priority. Activities aimed at supporting the development of and access to standardized reference material were identified as a key research need. *Environ Toxicol Chem* 2019;38:2087–2100. © 2019 The Authors. *Environmental Toxicology and Chemistry* published by Wiley Periodicals, Inc. on behalf of SETAC.

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INTRODUCTION

Operationally, risk can be viewed as the possibility of a harm arising from a specific set of conditions, such as magnitude, duration, and frequency of exposure to an agent (Hester and Harrison 2006). Characterizing, assessing, and quantifying risk occur throughout many disciplines, with several relying on it heavily such as engineering and chemical manufacturing. In 1983, the National Research Council published a report defining risk assessment practice in the US federal government

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(commonly referred to as the Red Book) that defined risk characterization broadly and provided the basis for current approaches for chemical risk assessment. In practice, risk characterization encompasses both exposure and dose–response assessments and serves as the intermediary between risk assessment and risk management. The Red Book also specifies that risk characterization should summarize key uncertainties in each risk-assessment step and may include statistical and biological uncertainty as well as uncertainty pertaining to the assessment type and exposed populations (National Research Council 1983).

Typically, deterministic approaches are used to estimate environmental risks by calculating the ratio between exposure and a toxicity criterion, although more complex assessments often make use of probabilistic methods. The typical deterministic approach is based on the assumption that, for a noncancer risk, there is a level of exposure below which there is a negligible probability of an adverse effect being observed (Williams and Paustenbach 2002). A common method for assessing environmental risk, for instance, involves estimating a risk quotient (RQ), a ratio between the predicted-environmental concentration (PEC) and the predicted-no-effect concentration (PNEC; European Chemicals Bureau 2003). Lower-tier chemical risk-assessment estimates typically employ very conservative assumptions, such that an $RQ < 1$ indicates a low-risk probability and an $RQ > 1$ indicates a priority for undertaking a higher-tier, more detailed, data-driven risk evaluation and/or possible risk management.

Like chemical risk assessment, characterizing the potential environmental risks associated with microplastic particles also requires similar components used in deriving risk–exposure estimates relative to the potential to elicit a negative effect, for example. There has been increasing concern about the environmental presence of microplastic particles, commonly defined as plastic particles <5 mm in size, particularly with respect to the potential to cause harm to biota (Cole et al. 2011). The challenge in characterizing the risk for microplastic particles, however, is that these materials lay outside the applicability domain for current standardized test and assessment systems, and assay optimization is often needed to ensure the reliability and applicability of the test results (Connors et al. 2017; ECETOC 2019). Nevertheless, numerous studies conducted on microplastic particles over the last decade report observed adverse effects (OAEs) associated with exposure to microplastic particles (Connors et al. 2017; Burns and Boxall 2018; ECETOC 2019; Science Advice for Policy by European Academies 2019). Concerns associated with the detection of microplastic particles in numerous aquatic systems and wildlife species as well as in various food and beverage commodities have led to increased media coverage on microplastic particle exposures and a growing awareness within the public domain and regulatory agencies of the issue (Science Advice for Policy by European Academies 2019).

Quantifying dose–response relationships is key in characterizing chemical risk (National Research Council 1983). For microplastic particles, however, interpreting concentration dose–response relationships is not straightforward and can be quite challenging because OAEs associated with microplastic particles appear to be influenced by physical interactions between organisms and elevated particle quantities. Examples of OAEs include various indirect effects, such as growth inhibition and reproduction, where the microplastic particles impede an organism's ability to access nutrients (Cole et al. 2015; Welden and Cowie 2016; Paul-Pont et al. 2018), or an effect caused by a physical obstruction of the particle on the surface of the organism or within the gastrointestinal tract (Watts et al. 2016; Choi et al. 2018). Thus, a key question to consider is the applicability of deriving an RQ value for microplastic particles using a PEC/PNEC relationship that is representative of an extrinsic effect and influenced by system-dependent parameters, such as the relative magnitude of the exposure in relation to food availability, as opposed to an intrinsic toxicity, where an effect occurs within the cells of an organism as a sequela of chemical interactions at a molecular level.

As summarized in 2 recent scientific expert reports (ECETOC 2019; Science Advice for Policy by European Academies 2019), interpreting OAEs and utilizing data that have been generated thus far within a regulatory decision-making process for microplastic particles is complicated by various factors: Inconsistency in microplastic definitions, resulting in uncertainties within government and industry regarding how to best address regulatory concerns. Lack of standardized test methods applicable to microplastic particles (including methodology, endpoints, test organisms, exposure, and effects metrics). Insufficient mechanistic understanding regarding the relative relationship between intrinsic physicochemical properties and extrinsic properties that influence exposure and effects. Differences in how OAEs are reported and communicated, resulting in different ways of framing the question that correspond to differences in interpreting risks. Consequently, helping to address the various challenges will require collaborations that would benefit from engagement with an interdisciplinary group of experts representing the various stakeholders (ECETOC 2019; Science Advice for Policy by European Academies 2019). As a preliminary activity toward the development and application of a risk-assessment framework for microplastic particles, the International Council of Chemical Associations sponsored a 1-d symposium, which brought together approximately 40 scientific expert stakeholders representing industry, regulators, and academia on 3 November 2018 in Sacramento, California, USA. The following summarizes the background information used to facilitate discussions held during the symposium and captures the key discussion outputs. It is important to emphasize that, given the broad representation from participants at the symposium, there was consensus on the need for a robust risk-assessment framework that would also enable a broader understanding of the potential impacts from environmental microplastic particles.

OBJECTIVES ALIGNED TO MULTISTAKEHOLDER DISCUSSION

The International Council of Chemical Associations–sponsored symposium on the development and application of an

TEXTBOX 1: Summary of key discussion points that would benefit from multistakeholder engagement

- Clarity on common definitions for particle categorization and exposure metrics
- Consensus on reporting requirements aligned to the physicochemical properties of the microplastic particles being tested and availability of analytical methods to characterize the test material, as well as those properties of the test system that might influence particle aggregation, agglomeration, sedimentation, dissolution, etc.
- Inclusion of chemical leaching controls (e.g., monomers, chemical additives) to help differentiate adverse effects associated with chemicals versus those associated with physicochemical properties of the microplastic particles themselves
- Development of protocols for creating and maintaining dispersions, sample preparation, and analytical methods to minimize test artifacts and strengthen reproducibility and interpretability
- Standardized methods to assess environmental transformation processes
- Development and use of standard reference materials for method validation and test control
- Research aligned to identifying and prioritizing environmentally relevant exposure
- Development of evidence-based environmental protection goals to enable a transparent and robust regulatory assessment of the environmental risks of microplastic particles
- Identification of sentinel test species based on species sensitivity distributions that build on mechanistic understanding of physiological and behavioral traits
- Consensus regarding appropriate effect endpoint(s), ideally based on environmentally relevant chronic exposure scenarios

environmental risk assessment (ERA) framework had 2 main objectives: 1) discuss the scientific merits and limitations of applying a proposed conceptual ERA framework for microplastic particles, whereby stakeholders are asked to consider if such an approach would be helpful in ascertaining environmental risks, and 2) identify major knowledge needs to increase confidence in applying ERA tools for microplastic particles and prioritize research activities to best strengthen framework implementation.

Text box 1 summarizes several key areas that would benefit from constructive multistakeholder input in helping to define an ERA framework that could be used within a regulatory context and were used to help guide expert discussions. It is widely anticipated that research in these areas would benefit our ability to address recent concerns while also helping to educate the public about the benefits of reducing plastic waste and strengthen future innovation associated with "safer-by-design" strategies (Science Advice for Policy by European Academies 2019). The current scenario, characterized by minimal quantitative and mechanistic understanding, limits our capability to apply toxicity test data to risk assessments and hinders implementing risk-mitigation strategies (Petersen et al. 2014; Romero-Franco et al. 2017; European Commission 2018b; Science Advice for Policy by European Academies 2019).

Hypothetically, if standardized methods appropriate for assessing OAEs of microplastic particles could be developed, risk-assessment frameworks could support risk screening and prioritization, as well as risk-based tool development. Figure 1 illustrates the key elements associated with risk assessment, as defined in the Red Book (European Commission 2018b) and adopted from Romero-Franco et al. (2017) in their summary of challenges associated with risk-assessment frameworks that have been proposed for nanomaterials.

It is notable that many of the knowledge gaps and challenges identified by Romero-Franco et al. (2017) for nanomaterials are consistent with those identified for microplastic particles and thus represent significant opportunities to learn from nanomaterials research, such as those related to characterization of exposure and ecologically relevant endpoints (Syberg et al. 2015; Hüffer et al. 2017; Rist and Hartmann 2018). Building on the insight provided by Romero-Franco et al. (2017), the ERA framework presented in Figure 1 can be perceived as a tiered approach that includes a screening and prioritization evaluation component.

A PROPOSED ERA FRAMEWORK

Regarding the ERA framework itself, several fundamental components could benefit from discussion and possible alignment: Problem formulation—Is the decision context for assessing environmental risk well defined? For instance, ecological chemical risk assessment is based on assessing risk at the population level. Should the same context be adopted for microplastic particles, or is there another decision context that should be adopted? Do the available test methods sufficiently address the variability and uncertainty in enabling laboratory-to-field extrapolation? Are toxicological modes of action of microplastic particles consistent with an intrinsic toxicity typically used for evaluating dose–response relationships in characterizing environmental risk, or are they indirect system-dependent effects for which extrapolation to the environment may not be relevant? What is the level of detail needed for assessing the potential environmental risk of microplastic? Given the large variability and spatial and temporal heterogeneity in environmental systems, what level of uncertainty is acceptable? How can this be characterized and/or communicated? How might complementary information obtained using hazard-based and/or life-cycle assessment approaches be leveraged in the various decision-making contexts? Do the current methods, for instance, sufficiently evaluate data quality and weigh and integrate evidence

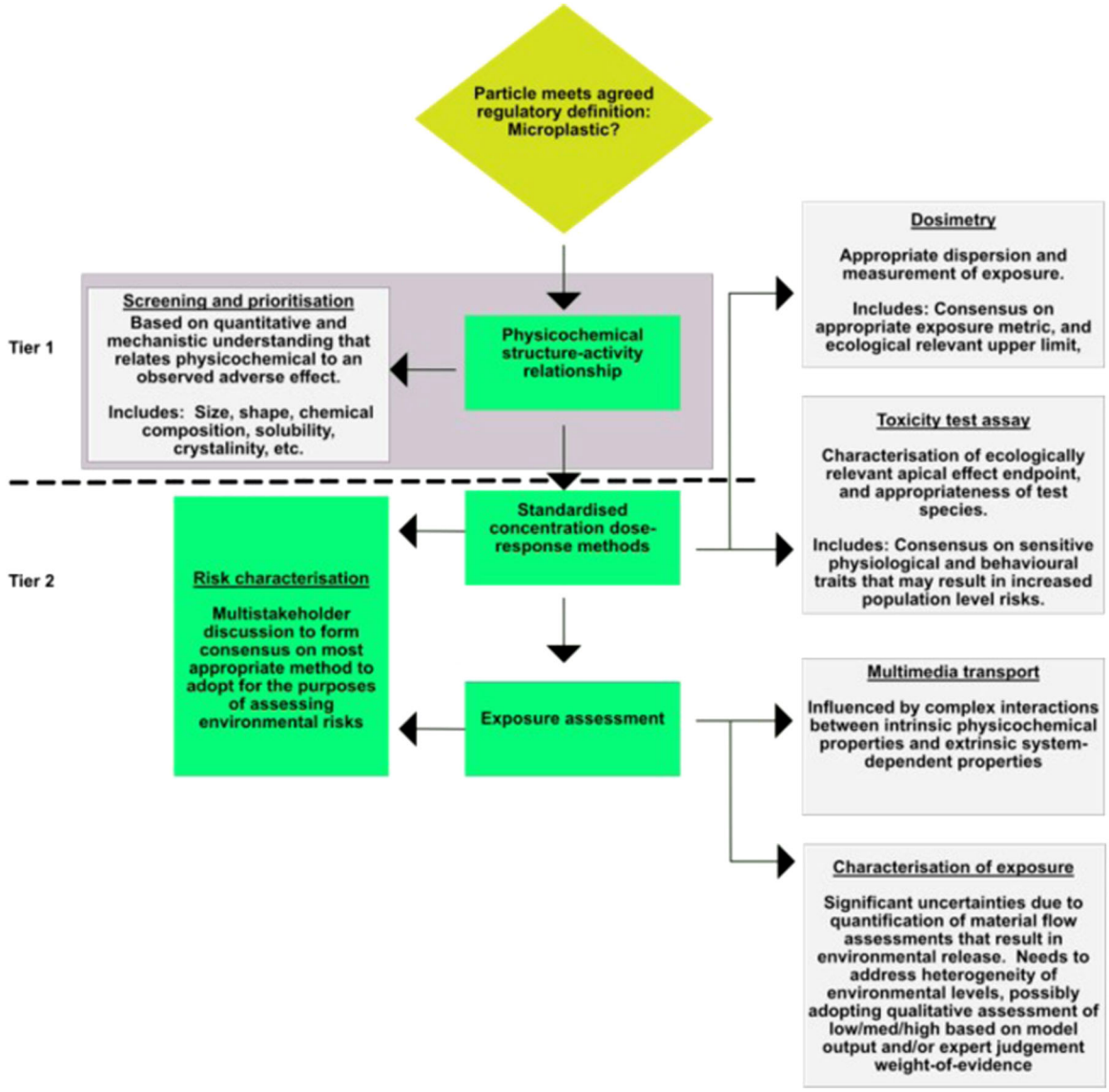

FIGURE 1: Summary of the challenges identified in implementing an environmental risk assessment framework for microplastic particles, adopted from Romero-Franco et al. (2017).

from different sources to ensure that subjectivity in analysis is minimized and transparency and objectivity are maximized? What are the appropriate scientific and policy approaches for addressing public concern regarding legacy issues related to plastic debris so that the potential risks associated with exposure to plastic are not ignored now or in the future?

A key objective for developing a microplastic particle risk-assessment framework pertains to how data from screening tools might advance quantitative and mechanistic understanding. In turn, this knowledge can assist in developing standardized ecotoxicity tests and environmental fate modeling approaches for use within higher ERA tiers. To that end, Figure 2 illustrates a proposed risk-assessment framework for microplastic particles.

In developing fundamental understanding related to environmental fate and exposure and effects, laboratory test systems are likely to be important. These systems will allow for dependent variable control as well as assessment of complex interactions and relationships. Consequently, there is a need to carefully consider test system design and data interpretation. The following sections explore the key elements, sorted by effects and environmental fate testing, which the symposium participants discussed.

Adverse effects and dose–response relationships

Assessing potential microplastic particle effects requires assessing many factors—factors that influence the particle exposure within the test system (i.e., the dose) and characterization of an ecologically relevant effect endpoint (i.e., the response). The physicochemical properties of microplastic particles can influence both the exposure and effect endpoints (ECETOC 2019). Factors such as aggregation, agglomeration, and sedimentation can work alone or in combination to

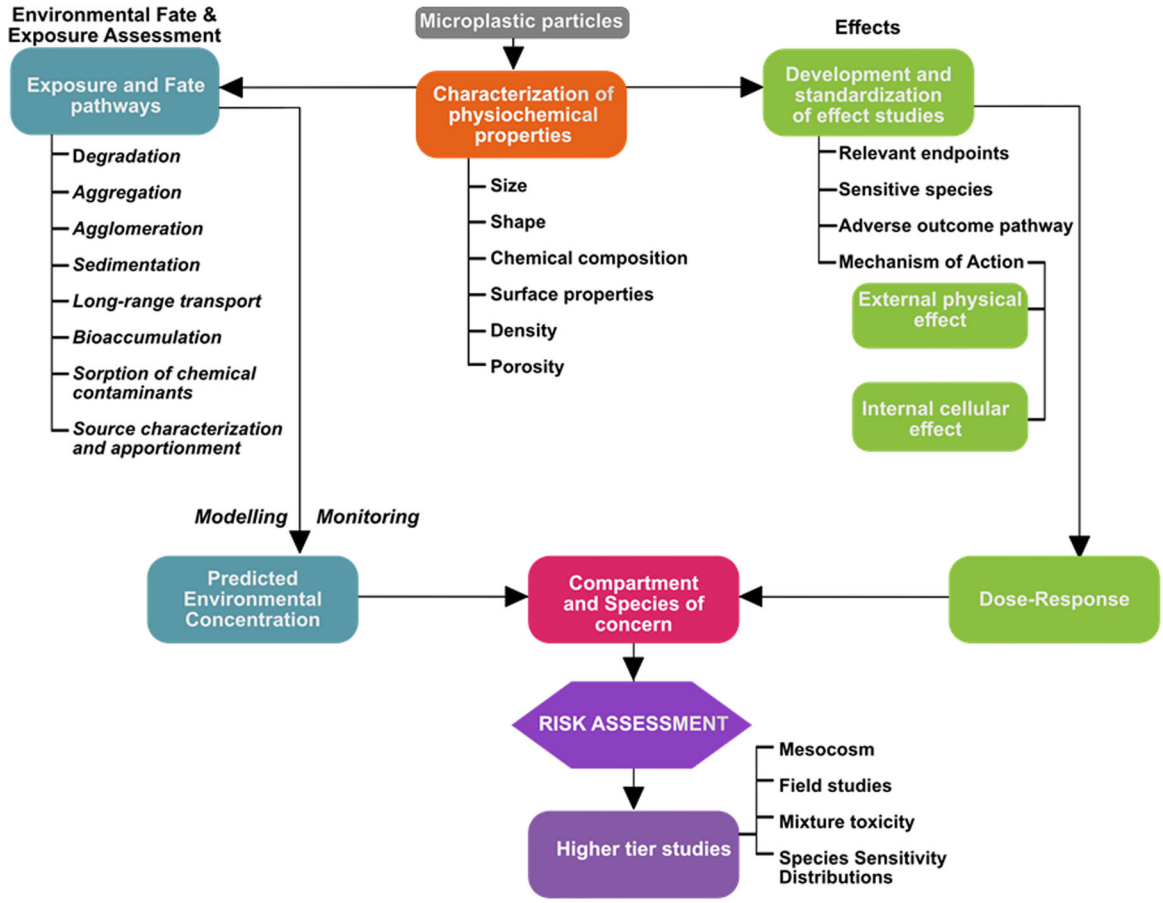

FIGURE 2: Schematic representation of proposed environmental risk assessment framework for microplastic particles, which is based on enabling the characterization of the relationship between the predicted-environmental concentration and the predicted-no-effect concentration.

complicate the ability to control a stable and homogenous particle dispersion. These factors are known to influence the dispersion stability of nanomaterials, with considerable effort being directed toward test protocol development for creating and maintaining stable nanomaterial dispersions (Römer et al. 2011; Kaur et al. 2017; Organisation for Economic Co-operation and Development 2017). It is suggested that similar approaches would improve the quality of dose–response quantification for microplastic particles and strengthen intra- and interlaboratory reproducibility of toxicity test systems (Karami 2017). It should be noted, however, that although efforts to address dispersion stability will enable better control of exposure in laboratory-based aqueous test systems, they may not represent environmental conditions characterized by a heterogenous exposure to microplastic particle agglomerates and aggregates (Long et al. 2015; Kowalski et al. 2016; Michels et al. 2018). Therefore, it may be necessary to consider how the data generated from an aqueous test system fit into the risk-assessment process, particularly with respect to laboratory-to-field extrapolation using environmentally relevant concentrations and exposure scenarios.

In considering the exposure scenario for chemical substances, there has been an emphasis on creating and maintaining stable homogenous concentrations within the test system. Is this approach applicable to microplastic particles? Creating and maintaining a uniform dispersion within an ecotoxicological test system serves several important purposes. First, the creation and maintenance of a stable dispersion enable reproducibility of the test system between laboratories. The capability to compare results from various laboratories thus provides the potential for higher-quality data that can be used within a regulatory context. A key component of enhancing the reproducibility of the exposure scenario is that adverse effects would lend themselves to reproducibility, in that the exposure is not subject to variability, whereby the organism may encounter high and low "exposure pockets" within the test system, which may vary between tests and laboratories. Second, it could be argued that a uniform distribution represents a worst-case exposure scenario for the organism because there are no regions within the test system to avoid exposure. Lastly, by enabling a stronger evaluation of the relationship between exposure dose and adverse effect, greater mechanistic understanding should follow.

However, reliance on the application of a homogenously dispersed system for microplastic particles may not be equivalent to results obtained from higher-tier mesocosm or environmental data, where particles are unlikely to be uniformly dispersed. Furthermore, under environmentally relevant conditions, the physicochemical properties of the microplastic particles themselves may be significantly different from those

tested in the laboratory, having succumbed to a variety of weathering and aging and surface biofilm processes leading to a heterogeneous mixture of particle shapes and sizes (Jahnke et al. 2017; Lambert et al. 2017; Gigault et al. 2018; Paul-Pont et al. 2018; ECETOC 2019).

Understanding the interaction between organisms and microplastic particles will benefit from greater mechanistic understanding through the application of well-controlled test systems (Paul-Pont et al. 2018). A species' propensity to ingest microplastic particles, for example, is aligned with physiological and behavioral traits (Scherer et al. 2017; Triebskorn et al. 2019). These traits may include filter mesh sizing in filter-feeding organisms and particle interactions based on active or passive feeding strategies (Berman and Heinle 1980; Geller and Muller 1981; Gophen and Geller 1984; Hart 1991; Jerling and Wooldridge 1995; Tanaka et al. 2006; Filella et al. 2008; Motta et al. 2010; Riisgård and Larsen 2010; Vinther et al. 2014; Scherer et al. 2017; Hermsen et al. 2018). Moreover, species sensitivity distributions that account for biological traits may help to define appropriate species and endpoints to include within toxicity test systems (Koelmans et al. 2017a). In particular, these systems need to better understand the factors that influence biological uptake, especially in relation to the size and shape of the microplastic particles (Paul-Pont et al. 2018; ECETOC 2019; Triebskorn et al. 2019). We also stress the current, limited understanding regarding microplastic particle fate within an organism (ECETOC 2019; Triebskorn et al. 2019). For instance, what are the properties of microplastic particles that might influence their potential to translocate from the gastrointestinal tract into tissues of the organism; what factors influence the residence time of microplastic particles within the gastrointestinal tract; how do differences with respect to where the particles reside within an organism (i.e., the gastrointestinal tract, internal tissues, external surface) influence an OAE?

To date, published studies concerning adverse effects from microplastic particles have reported many endpoints (Connors et al. 2017; Rochman et al. 2017; Arias-Andres et al. 2018; Espinosa et al. 2018; Foley et al. 2018; Pitt et al. 2018; Prokić et al. 2019). These effects can be classified broadly into 2 categories: 1) elevated particle concentrations that may reduce the ability of an organism to access nutrients, and therefore affect energy budgets and growth (Green et al. 2017; Choi et al. 2018), and 2) particles that result in a physical obstruction within or on the surface of the organism, which can result in a variety of effects, including stress and impacts on growth and reproduction, as well as mortality (Gray and Weinstein 2017; Zhang et al. 2017; Jin et al. 2018; Lu et al. 2018; ECETOC 2019; Science Advice for Policy by European Academies 2019). In some instances, effects based on the monitoring of biomarkers, such as reactive oxygen species formation or inflammation, are reported (von Moos et al. 2012; Jeong et al. 2016; Espinosa et al. 2018; Prokić et al. 2019) and may be associated with either of the 2 categories described. For this reason, it would be beneficial to strengthen our overall understanding of mode of action associated with microplastic particles and to verify such effects in more complex micro- or mesocosm studies. These data could also better define ecologically relevant endpoints for dose–response relationships to use within risk-assessment frameworks (Jahnke et al. 2017; Koelmans et al. 2017a). Lessons from the development of ecotoxicity test methods for nanomaterials could also prove helpful in facilitating progress in defining an ecologically relevant endpoint for microplastic particles (Handy et al. 2012).

Recognizing the complexities that surround the developing of an ERA framework for microplastic particles, several fundamental elements require attention. Problem formulation is a critical component, whereby the development of standard test systems should focus on environmental compartments, organisms, and exposure scenarios that are ecologically relevant (Lenz et al. 2016; Koelmans et al. 2017a; Burns and Boxall 2018). For instance, although there have been several studies assessing effects in various aquatic species, there is currently less understanding of effects for freshwater-, sediment-, and terrestrial-dwelling organisms (Burns and Boxall 2018). But awareness of the environmental fate and exposure potential of microplastic particles for organisms in freshwater systems and sediment is increasing (Corcoran 2015; Blettler et al. 2018; Burns and Boxall 2018; Triebskorn et al. 2019). Consequently, methods aimed at addressing effects for freshwater pelagic and benthic organisms are likely to prove useful in providing a more holistic understanding associated with past and current releases of microplastic particles. Further, exposure to microplastic particles for organisms outside localized hot spots is more likely to be better assessed through the adoption of tests that focus on chronic endpoints, such as growth and reproduction for both freshwater and marine-water organisms, utilizing ecologically relevant concentrations of microplastic particles.

Given the considerations addressed, the development of a relatively complex testing matrix is likely (Figure 3) and will encourage the development of efficient methods. Limited resources will compel researchers to develop efficient methods to screen and prioritize the most ecologically relevant scenarios and cross-species extrapolation methods to progress understanding of microplastic particle effects.

This challenge has also been acknowledged in a recent publication by Koelmans et al. (2017a), who propose a tiered approach based on a systematic assessment of adverse outcome pathways (AOPs) applying ecologically relevant exposures. This approach suggests that input through consultation with an expert panel at a low evaluation tier would help prioritize combinations, as illustrated in Figure 3, advancing our understanding of environmental risks of microplastic particles (Koelmans et al. 2017a). These ecologically relevant AOPs would thus apply to specific species and exposure scenarios by combining knowledge of physiological and behavioral traits, as well as environmental monitoring data, regarding the presence of microplastic particles relative to the species in question. Nontraditional test species and exposure scenarios that might emerge through expert knowledge, and consequently the development of test systems, should follow best practices, as detailed by Connors et al. (2017). Specifically, methods must include robust method development documentation, including the adoption of the appropriate quality assurance and quality control measures needed to ensure a high

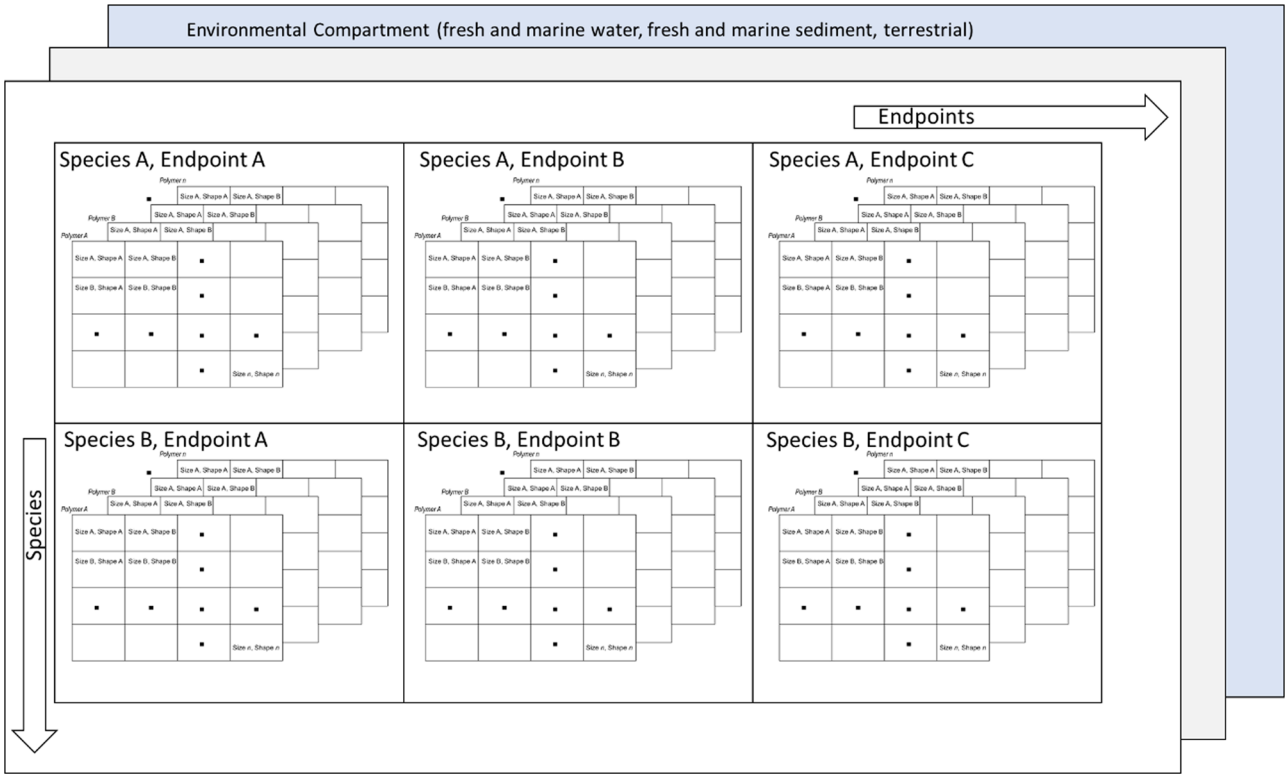

FIGURE 3: Schematic representation of ecotoxicity testing matrix, which attempts to account for different types of polymers, shapes and sizes, species, endpoints, and environmental compartments.

level of quality associated with the data acquired (Connors et al. 2017; Triebskorn et al. 2019). Consistent with recommendations that have emerged from various publications (Holden et al. 2016; Koelmans et al. 2017a; Paul-Pont et al. 2018; ECETOC 2019; Science Advice for Policy by European Academies 2019), efforts to support regular multistakeholder discussions represent a critical component to progress understanding of potential risks and environmental impacts, particularly when addressing chemicals and/or materials for exposure scenarios that are not addressed within existing standardized effects test systems, such as for microplastic particles.

Inconsistencies in the dose metric used for dose–response relationships regarding microplastic particles may also benefit from multistakeholder engagement (Phuong et al. 2016; Connors et al. 2017; Burns and Boxall 2018). Several different units of exposure or dosing have been reported in microplastic particle studies, including concentrations based on mass/volume, mass/mass, particle/volume, and particle/mass. These inconsistencies create challenges when comparing studies and subsequently limit dose–response assessments for risk-assessment purposes. Furthermore, ecologically relevant maximum concentration threshold values continue to be undervalued by the scientific community (Burton 2017; Koelmans et al. 2017a). When testing soluble organic chemicals, the maximum threshold concentration is defined as the chemical's solubility limit. Testing above the solubility limit can result in forming liquid droplets or solid precipitate; both may lead to physical effects that interfere with toxicity. It is unclear, however, how to define a maximum threshold concentration of dispersed particles in an aqueous test system (ECETOC 2019). Is there a particle concentration, for example, for which effects observed are simply attributable to the stress that the presence of particles themselves causes on the test organism? These may not be an intrinsic property of the microplastic particle being tested but rather represent an effect that is intrinsic to the organism, that is an effect caused by any type of particle, but that may not be applicable at lower dose concentrations. Test systems should therefore ensure the use of appropriate particle controls (such as size and shape with respect to test material) to clarify if OAEs are indeed caused by microplastic particles (Connors et al. 2017; Burns and Boxall 2018; Ogonowski et al. 2018; ECETOC 2019). It is likely that organisms will have varying thresholds in relation to changes in turbidity (Newcombe and Macdonald 1991; Gordon and Palmer 2015); therefore, deriving thresholds based on species sensitivity for suspended solids could provide useful insight in defining if effects observed are intrinsic to the particle or are representative of an intrinsic response of the organism to particles in general (Ogonowski et al. 2018; ECETOC 2019). Although a few studies have addressed this specific question (Casado et al. 2013; Ogonowski et al. 2016; Watts et al. 2016; Straub et al. 2017), more research in defining appropriate particle controls appears warranted, which may help address concerns related to exposure to microplastic particles and responses that an organism may have to any particle, naturally occurring or synthetically derived (Ogonowski et al. 2018; ECETOC 2019).

Lastly, in addition to including appropriate particle controls, it has been proposed that future research must consider how to

control for effects caused by the chemical additive leaching or the release of chemical mixture contaminants sorbed by the microplastic particles. There has been considerable interest in the role of microplastic particles acting as vectors of transport for hydrophobic organic chemicals (HOCs), and numerous studies have investigated the presence of HOCs in microplastic particles, as well as the process of microplastic particle sorption and biological uptake of chemicals sorbed to microplastic particles (Endo et al. 2005; Teuten et al. 2009; Rochman et al. 2013). Some research efforts directed toward addressing the vector hypothesis for microplastic particles argue that the relative importance of the process remains inconclusive (Beckingham and Ghosh 2017; Besseling et al. 2017a). Recently, however, there have been several extensive reviews summarizing the role of microplastic particles acting as a significant vector which question the quantitative importance of the potential of such an exposure pathway representing a considerable risk (Bakir et al. 2016; Koelmans et al. 2016; Ziccardi et al. 2016; Wang et al. 2018). This research has shown that other exposure routes likely play a more dominant role in delivering HOCs to organisms. Consequently, it is proposed that future efforts focus primarily on developing an improved understanding of effects associated with the particles themselves. This is not to diminish the importance of assessing the potential risks associated with chemicals for which microplastic particles may act as a vector, including chemical additives that might be used in the production of plastic. For these chemicals it is recommended that the ERA for the chemicals themselves should include an exposure scenario that accounts for the leaching of the chemicals, both during the use of the product as well as leaching that may accompany the unintentional release of the plastic to the environment. By separating chemical effects from effects solely attributable to microplastic particles, it may be possible to identify and prioritize research aimed at addressing the properties of chemicals and microplastic particles that have the potential for greatest concern. A risk assessment of exposure to multiple stressors, such as exposure to environmental chemical mixtures and particulates, for instance, microplastic particles and/or nanomaterials, could then follow, adopting a mechanistic understanding obtained using a targeted effects testing strategy.

Environmental fate and exposure assessment

Complex interactions that occur between the intrinsic physicochemical properties of the particles and the variable extrinsic system-dependent environmental properties represent the primary challenge for characterizing the environmental fate and estimating the PEC. Further challenges include characterization of particles generated during the life cycle of a product from manufacture, use, and environmental release and the subsequent transformation of the particles that might occur throughout this process (Batley et al. 2013; Lassen et al. 2015; Besseling et al. 2017b; Hüffer et al. 2017; Nowack 2017; Romero-Franco et al. 2017).

Strengthening our understanding of the environmental fate of microplastic particles and quantifying PECs can be facilitated by developing environmental fate mass-balance models. Simulations aimed at quantifying the sources, pathways, and sinks of microplastic particles can be useful for testing hypotheses, help prioritize knowledge gaps, and provide guidance for monitoring activities (Hardesty et al. 2017). Existing monitoring data quality vary, attributable in part to unstandardized empirical measuring techniques and lack of analytical methods (Silva et al. 2018). Thus, the relative importance of environmental fate mass-balance models is likely to play a significant role in assessing the environmental risks of microplastic particles.

Developing environmental fate mass-balance models for microplastic particles, however, represents a nontrivial component to the risk-assessment framework (Figure 2). Several key processes are potentially important in influencing the environmental release, transport, and fate of microplastic particles: 1) quantification of direct or indirect formation and emissions of microplastic particles; 2) particle–particle interactions, such as aggregation and agglomeration; 3) biofouling; 4) biological uptake and bioaccumulation; 5) sedimentation; 6) fate in estuarine and coastal mixing zones; 7) transport via global oceanic circulation; and 8) understanding of sinks for microplastic particles. Figure 4 represents the environmental fate and transport processes that might influence the exposure of microplastic particles relative to spatial and temporal scales. Although the literature describes microplastic as ubiquitous in the environment, there is substantial heterogeneity associated with exposure (Everaert et al. 2018). As a result, estimates of PEC using an environmental fate mass-balance model will require robust strategies to address spatial and temporal resolution.

The physiochemical properties of microplastic particles (size, shape, density, and chemical composition) can change as a function of time and influence the environmental fate and transport processes shown in Figure 4, complicating the exposure assessment. Yet, nanomaterial fate and transport modeling may provide guideposts for developing approaches for microplastic particle exposure models (Hüffer et al. 2017). In reviewing different nanomaterial modeling approaches, both Dale et al. (2015) and Markus et al. (2017) draw attention to the challenges associated with temporal and spatial resolution. They demonstrate the need to ensure appropriate model development to properly address the question being raised (Dale et al. 2015; Markus et al. 2017). If the question, for example, concerns exposure of benthic organisms to microplastic particles, whereby the size, surface charge, and shape of particles can influence the heteroaggregation/agglomeration and/or sedimentation of the microplastic particles, then it may be necessary to employ computationally intensive techniques and/or particle dynamic modeling tools. Alternatively, if the question concerns environmental fate and microplastic particle transport is required for screening and prioritization purposes, then a unit-world multimedia fate model may be better suited.

Models developed for nanomaterials, such as the multimedia models of nanoFate (Garner et al. 2017) and SimpleBox4Nano (Meesters et al. 2014) have been useful for strengthening overall understanding of how temporal

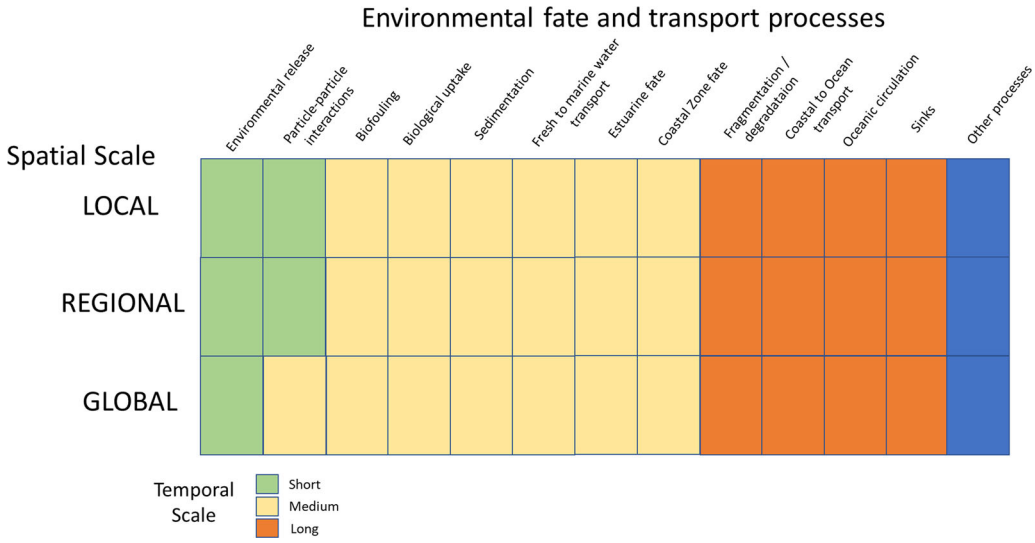

FIGURE 4: Schematic representation of key environmental fate and transport processes of microplastic particles (*x*-axis) relative to different spatial scales. Colors illustrate a gradation with respect to temporal scale, with some environmental fate and transport processes requiring short-, medium-, and long-term assessment. The different fate and transport processes may thus require a variety of modeling approaches depending on the temporal and/or spatial resolution required.

processes might influence environmental fate. Spatial factors that might influence environmental fate and transport of nanomaterials have also been investigated, using the spatially explicit hydrological model NanoDUFLOW (Quik et al. 2015), and recently adapted to microplastic particles (Besseling et al. 2017b).

In the context of risk assessment, whereby multimedia mass-balance models represent important tools for regulatory chemical risk assessment in estimating PECs for chemicals (Wania and Mackay 1999), the question of how to apply mass-balance models for particles, such as for nanomaterials and microplastic particles, has been raised (Jacobs et al. 2016; Nowack 2017; Steinhäuser and Sayre 2017). Given the acceptance of the multimedia mass-balance approach in registering chemicals, Nowack (2017) argues that the use of SimpleBox4Nano represents an appropriate lower-tier regulatory tool for helping to identify the environmental sinks and exposure concentrations of nanomaterials. Higher-tier approaches may involve the application of temporally and spatially resolved models (Nowack 2017). Accordingly, similar tiered approaches for assessing exposure to microplastic particles can also be developed and applied. Like nanomaterials, however, these models must address transport and fate knowledge gaps. Furthermore, uncertainty characterization is needed to help support the decision-making process, for the purposes of either screening and prioritization or ERA (Jacobs et al. 2016; Koelmans et al. 2017a).

Few models exist that characterize the environmental fate and transport of microplastic particles (Hardesty et al. 2017). These include spatially explicit models and models utilizing particle dynamic calculations (Besseling et al. 2017b). Models have also been employed to assess oceanic distribution, which have been useful to better understanding the relative impact of specific sources, such as the impact of shipping activities, and identifying potential hot spots (Kako et al. 2011; Lebreton et al. 2012). Other models have also been developed to assess biological uptake and the influence of microplastic particles as vectors of transport for HOCs (Zarfl and Matthies 2010; Gouin et al. 2011; Koelmans et al. 2016, 2017b; Lee et al. 2019). In general, the existing models have proved useful in helping guide research and address specific issues. Nonetheless, the development and application of environmental fate and transport models for the purposes of ERA remains an important scientific need.

KEY CHALLENGES AND RESEARCH PRIORITIES

As noted, there are 2 main objectives in bringing together a multistakeholder group of experts to discuss the scientific merits and limitations of developing and applying an ERA framework to the topic of microplastic particles: 1) to catalyze discussion of the proposed ERA framework (Figure 2) with a specific focus on the potential for the framework to be adopted and applied to microplastic particles, and 2) to identify and discuss the major data knowledge gaps and information needs associated with strengthening the adoption of a risk-assessment tool for microplastic particles, with an emphasis on prioritizing these to inform future research.

Throughout the 1-d symposium that was held to discuss the development and application of an ERA framework proposed in Figure 2, several presentations and expert-led discussion groups covering the material summarized in the preceding sections was presented and discussed. The agenda and list of participants are provided in the Supplemental Data. An important output from the expert elicitation was a positive response to the proposed risk-assessment framework. Consequently, a tool aimed at characterizing and quantifying the potential risks of microplastic particles and used within a regulatory context is seen as providing important value within

an approach that strictly aims at addressing questions of risk. However, it is also stressed that it would be important to additionally consider developing tools that would enable a more robust understanding of exposure and effects to add value to other approaches aimed at assessing the potential environmental impacts of microplastic particles. It is suggested that an improved scientific understanding of factors influencing effects and environmental fate and transport could thus facilitate more accurate communication of the potential impacts associated with microplastic particles to regulators and the public. For instance, the development of tools to acquire data and knowledge to support a risk-based assessment could also help to inform alternative methods used for assessing impact, such as life-cycle impact assessment, ecosystem services, or other similar impact assessment methods.

Regardless of whether the emphasis is on assessing risk or impacts, there remains a fundamental need to strengthen the quality and quantity of data to improve our understanding of the effects and environmental fate and transport of microplastic particles. There is consensus, as evidenced in numerous publications (Connors et al. 2017; Karami 2017; Koelmans et al. 2017a; Burns and Boxall 2018; Ogonowski et al. 2018; Science Advice for Policy by European Academies 2019), that the quality of the data associated with the ever-increasing number of studies is currently insufficient to effectively evaluate and communicate the impact of microplastic particles in the environment. Research that directly addresses the development and application of methods that strengthen the quality of data should thus be given the highest priority.

A key research need identified is access to standardized reference material, defined as being critical toward the development of standardized analytical methods and effect test systems. Access to microplastic particles currently occurs following one of 2 typical approaches: purchase of commercially available microplastic from various suppliers (Browne et al. 2008; Cole et al. 2013; Farrell and Nelson 2013; Setälä et al. 2014; Carlos de Sa et al. 2015; Cole et al. 2015), which has been produced for purposes other than assessing environmental risk, or production of microplastic particles using ad hoc techniques that artificially create microplastic particles, for instance, by grinding or cutting of larger pieces of plastic or artificially aging to simulate microplastic particles that might be encountered in the environment (Au et al. 2015; Watts et al. 2015; Ogonowski et al. 2016; Welden and Cowie 2016; Zhang et al. 2017; Weber et al. 2018). Common to the ad hoc approaches for creating microplastic particles is a lack of characterization and standardization in relation to the materials being tested. Purchased materials, although perhaps providing access to a microplastic particle of uniform shape and type, may or may not contain chemical additives, which can influence interpretation of test results (Connors et al. 2017). Purchased materials also tend to be limited in the polymer type, size, and shape, which does not necessarily reflect the heterogeneous exposure of microplastic particles that may be encountered in the environment (Lambert et al. 2017). In the instance of research groups that create their own microplastic particles, there exist potential issues associated with quality control in the production of the microplastic particles within the laboratory, which may influence both intra- and interlaboratory reproducibility and ability for comparison. Similar challenges exist for groups that acquire their materials directly from the environment.

Providing a suite of standard reference materials for microplastic particles, which would provide access to environmentally relevant microplastic particles as either homogeneous or heterogenous (i.e., with respect to polymer, size, shape, virgin, aged, etc.) from a single source where specifications of the microplastic particles are characterized and certified according to key properties of ecological relevance, should enable a more efficient and effective development and application of analytical method development. In the absence of standard reference materials, the continuing reliance on the use of ad hoc materials will only prolong confusion and frustration associated with scientific advancement. Consequently, support for activities aimed at developing a databank of standard reference materials for microplastic particles is perceived as the research need with the highest priority. Next steps should thus aim at providing multistakeholder agreement regarding the specifics of the standard reference materials that research groups would like access to and identifying a group(s) that could characterize and certify the material accordingly.

With the ability to access standard reference materials for microplastic particles, standard analytical and effects test methods could then be developed and applied within a regulatory risk-assessment process. It is notable that there exists a need to closely align effects test method development with monitoring data, whereby concentrations reported in the environment should be used to help inform exposure concentrations used in effects testing, particularly if the purpose of the testing is to provide an assessment of environmental impact. On the other hand, those conducting effects testing may also wish to elucidate a mode of action associated with exposure. In these instances, communication of results should clearly indicate the purpose for the test and the ecological relevance of the exposure used in the test system.

It is further noted that regulatory decision-making in relation to microplastic particles should be evidence-based, with improvements to the quality of data produced providing invaluable regulatory support; nonetheless, the emotional elements of the issue cannot be ignored. Given the heightened awareness of the public with respect to plastic accumulating in the marine environment and the potential impacts associated with exposure to microplastic particles, there is an opportunity for initiatives that target reductions in the release of mismanaged plastic waste. Consequently, activities that facilitate interdisciplinary scientific and technological innovation will help to address the uncertainties (scientific and socioeconomic) in microplastic particles risk assessment. In this respect, 3 key innovation areas are identified (Figure 5), which are consistent with the implementation of practices associated with a circular economy and the European Union's plastics strategy (European Commission 2018a).

The emphasis of future research is to thus support scientific and technological innovation, a key component of the European Union's plastics strategy (European Commission

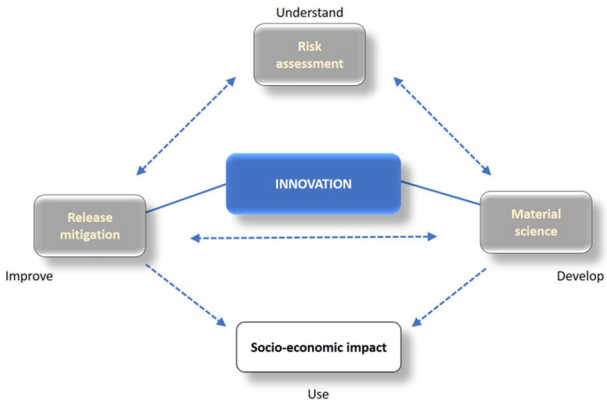

FIGURE 5: Conceptual illustration of innovation benefiting from interdisciplinary collaboration between environmental sciences, waste management, and material sciences.

2018a). Conceptually, current challenges associated with the uncertainties related to the environmental release of microplastic particles can be perceived as opportunities, whereby advances in research can facilitate scientific and technological innovation in assessing risks, material sciences, and release-mitigation strategies, all aimed at addressing concerns related to the potential impact that exposure to microplastic particles may represent. Consistent with sentiments articulated in the European Union's plastics strategy (European Commission 2018a), the adoption of strategically defined activities coordinated with the support of lighthouse projects in each innovation area, the vision of an integrated research strategy could be translated into action in the following ways.

Innovation in risk assessment

This would support the establishment of a databank of standard reference materials for use in the development of analytical methods. Evaluate and further develop analytical methodologies and robust quality assurance and quality control methods to improve standard laboratory and higher-tier procedures; monitoring schemes; as well as environmental fate, transport, and exposure and source modeling. This would be a key requirement to help strengthen our mechanistic understanding of effects and exposure and thus support innovation in risk assessment. Further priorities include the support of higher-tier assessment methods (e.g., mesocosms) that address complex interactions that may influence environmental fate and transport, as well as effects of microplastic particles on the environment and human health under environmentally relevant conditions that enable scientific advances related to degradation/fragmentation processes and which would include the fate and behavior of nanosized particles.

Innovation in waste management and infrastructure development

Provide support in technological innovation activities aimed at improving the removal efficiency of microplastic particles in wastewater-treatment processes of municipal and/or industrial treatment facilities as well as methods targeting storm-water runoff that reduce mass loadings of microplastic particles to the environment and potentially allow for their recapture and/or efficient elimination. Support advances in solid waste management and infrastructure development that help to reduce the release of microplastic particles to the environment as a result of fragmentation of mismanaged releases of plastic articles. Support technological innovation in consumer products that provide capability for particle-capture functionality in products such as domestic washing machines and heating and ventilation air conditioning systems.

Innovation in material sciences

Reduce and eliminate at source through support of material sciences innovation. Depending on application of materials, this can be supported by developing fully (bio)degradable materials via biological and nonbiological processes. Support technological innovation in materials science that helps to significantly reduce the release of microplastic particles at source (such as those associated with consumer products, construction materials, infrastructure). For instance, innovation in the manufacture of polymer-based textiles to reduce the shedding of microplastic particles.

An important element of including an interdisciplinary approach that supports scientific and technological innovation is a recognition of the interconnectedness between each of the key innovation areas. For instance, developments aligned with innovation in risk assessment directly help to identify and prioritize key sources of microplastic particles to the environment, information that can then be used to efficiently leverage activities to support innovation in waste management and materials science, as illustrated in Figure 5.

Lastly, the conceptual relationships illustrated in Figure 5 include a recognition of the importance of assessing impacts aligned with technological innovation and waste management and materials science through the support of socioeconomic impact analysis. The conceptual relationships illustrated in Figure 5 are perceived as being important in helping to inform the regulatory decision-making process and the general public about the potential for physical harm and (eco)toxicological effects in relation to benefits derived through scientific and technological innovation.

SUMMARY

To improve product stewardship and regulatory decision-making, there is a need for stakeholders to collaborate in the development of fit-for-purpose ERA frameworks and tools for microplastic particles. Stakeholder engagement is critical so that diverse perspectives can be considered and used to inform methods and approaches. Challenges identified through the discussions held during the 1-d symposium summarized here represent opportunities that can benefit from lessons that can be transferred between different areas, such as between nanomaterials and microplastic particles. It is thus envisioned

that a series of workshops and research activities should follow from preliminary multistakeholder engagement, the objectives of which would be to maintain communication and to ensure the most efficient uptake of scientific advances within a commonly agreed risk-assessment framework.

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