Microplastics Advance Research and Innovation Initiative (MARII)

Summary of the 2nd Workshop

12 -13 June, 2023

Microplastics: information needs and knowledge gaps

Plastics have been part of our everyday lives for many decades and are often a durable, lighter and cheaper alternative to many other materials. Unless properly recycled or disposed of, however, they can remain in the environment for a long time, breaking down into smaller pieces. Fragments smaller than 5mm are usually referred to as **microplastics**.

Microplastics, whether they are the result of wear and tear of larger pieces or intentionally manufactured for specific purposes, have been found in the environment and have been found in organisms, including humans, drinking water and food.

Concerns have been growing as to the potential threat they may pose to the environment and to our health, boosting the need for further research to fill current knowledge gaps, as indicated for example by reports of SAPEA in 2019 and the World Health Organization in 2022.

MARII: A global platform for scientific exchange to advance research on microplastics

In spite of technological improvements in collecting and identifying microplastics, the lack of validated and standardized methods in the approach to this research still prevents experts from drawing definite conclusions, which are key to informing a sound regulatory response from governments across the globe. Scientists from all stakeholder groups are being called to collaborate and work together to generate this critical information and consistency of observed exposures and effects.

MARII, the Microplastics Advance Research and Innovation Initiative launched by he International Council of Chemical Associations (ICCA), was created as a platform to facilitate the global exchange of information on microplastics research. By bringing together scientists from industry, academia, research institutions and other actors across the world, MARII aims to:

- Exchange information on microplastics research projects, test methods and technologies:
- Organize convenings to discuss, examine and evaluate research and initiatives;
- Foster collaboration and leverage resources to develop relevant data towards a fuller risk assessment of microplastics.

ICCA, through the regional research program of Cefic, JCIA, ACC and Plastics Europe, will support complementary areas of microplastics research to address any critical knowledge gaps and will take advantage of the MARII platform to share initiatives and results with the broader scientific community.

The Seattle Workshop

In June 2023, about 60 researchers from around the globe met in Seattle, WA, USA, for the second MARII workshop to discuss recent progress in the field of microplastics risk assessment as well as associated projects funded by ACC, Cefic, JCIA and Plastics Europe. The goal was to share information and enhance coordination among regions and maximize the use of resources for research towards the development of a holistic quantitative risk assessment for Microplastics. The following sections provide a comprehensive insight on the content and the discussion during the 2nd MARII workshop on Microplastics Risk Assessment.

For further information on MARII, the Microplastics Advance Research and Innovation Initiative launched by ICCA, please visit

https://icca-chem.org/focus/microplastics-advanced-research-and-innovation-initiative-marii/

or contact:

John (Norm) Norman, ACC, john_norman@americanchemistry.com

Blanca Serrano Ramon, ECETOC, blanca.serrano@ecetoc.org

Camilla Carteny, Plastics Europe, camilla.carteny@plasticseurope.org

Felipe Almeida, Cefic, fal@cefic.be

Takashi Mori, JCIA, tmori@jcia-net.or.jp

Joint opening session:

Chair: Blanca Serrano Ramón, ECETOC

The opening session was dedicated to multiple projects and research initiatives related to microplastics and their environmental impact, all of which were part of the projects covered by the Microplastics Advance Research and Innovation Initiative (MARII) platform. The presentations highlighted the ongoing efforts to understand and address the challenges posed by microplastics through innovative modelling, assessment, and risk management approaches.

The session began with a presentation on the UTOPIA project, which aimed to develop an open-source unit world multimedia modelling platform for microplastics. The UTOPIA platform aimed to synthesize knowledge about the fate of microplastics and provide a reference set of equations for screening-level risk assessment and exposure calculations. The model structure, process descriptions, and inter-relationships with other CEFIC-funded projects (ECO57, ECO58, ECO59, and ECO60) were discussed, highlighting the modular design and the potential for ongoing model development as scientific understanding evolved.

Next, the µBETR Global project was presented, which focused on understanding the global-scale fate and transport of micro- and nanoplastics. This mechanistic multimedia mass-balance model evaluated the short- and long-range transport of micro- and nanoplastics, as well as their transformation processes, using high-resolution 3D modelling. The presentation specifically showcased the atmospheric transport within µBETR Global and the influence of physicochemical properties and weather conditions on the particles' residence time.

Emission factors for micro and nanoplastics were addressed in the ECO60 project, known as EMIFACT-MNP. This project aimed to develop a predictive model for environmental emissions factors of plastics across various size ranges and scenarios, covering different life cycle stages. The model parameterization focused on the most widely used polymers in Europe, and the resulting emissions factors would support regulatory risk assessment. The project emphasized the importance of open-source code and documentation to facilitate widespread use and engagement within the scientific community.

The HERA-MP project took a holistic approach to assess the environmental risk of microplastics in the terrestrial environment. By using OECD/ISO standardized test systems, the project evaluated the chronic effects of environmentally relevant microplastics on various terrestrial organisms, including microorganisms, plants, and earthworms. The goal was to establish a comprehensive risk assessment framework by considering the heterogeneous mixture of particles and their specific relevance within agricultural practices.

Another presentation explored the characterization of microplastics in Tokyo Bay, emphasizing the need for quantitative assessments to inform realistic risk-based management strategies. The study utilized a comprehensive review of national and international literature, as well as newly acquired monitoring data, to assess the environmental risk and concentrations of microplastics. Special attention was given to the development of Species Sensitivity Distributions (SSDs) and the correction of MP concentrations.

The focus of a presentation by the University of Rochester was on understanding the exposure and potential health effects of airborne microplastic particles. The study examined the presence of microplastics in indoor and outdoor air samples, particularly those within the human-respirable fraction. By analysing particle size, morphology, and staining techniques, the researchers investigated the inhalability and respirability of microplastics and aimed to determine if they possessed unique toxicological properties.

The development of the Micro/Nanoparticle Health & Environmental Literature Platform (MNP-HELP) was presented as a valuable resource for risk assessment research. This platform acted as a centralized and systematically curated repository of literature, providing a comprehensive database of relevant research on micro- and nanoparticles. The aim was to streamline literature reviews and data gathering for researchers and manufacturers, facilitating evidence-based decision-making.

Lastly, the Brigid project, funded by Plastics Europe, was introduced. This five-year scientific research project evaluates the potential risks to human health of microplastics exposure via ingestion. The project focuses on understanding the fate and behaviour of microplastics in the human body, as well as their potential effects on different organs and systems. The Brigid project aims to generate robust scientific evidence to inform risk assessment and regulatory efforts in managing the potential risks associated with microplastic ingestion.

Throughout the session, there was a particular emphasis on model validation and the potential for interaction with other existing models and databases. The presenters discussed the importance of collaborating with other research projects, regulatory bodies, and stakeholders to ensure the accuracy and reliability of the models and assessments. This collaborative approach aimed to foster a multidisciplinary understanding of microplastic pollution and facilitate the development of effective risk management strategies for the future.

Parallel session on “Reference Materials (RMs) - Status and Needs”

Chair: John Norman, ACC, & Wendel Wohlleben, BASF SE

Ingeborg Kooters (TNO) explained the needs from a tox perspective: need to be able to measure a dose-response, need tiered methods (1: in-vitro/in-chimico; 2: ex-vivo, 3: in -vivo, 4: human and epidemiology). Relevant properties of RM: size, composition, agglomeration, reactivity per surface area, representativeness, non-zero toxicity, ready-to-use. During the Q&A session, the question about negative and positive controls was raised. The complexity of microplastic properties raises some interesting challenges including the need to establish the correct dose metric, the possibility that a different control material may be needed depending on the system being studied (e.g., per organ system), and how much material is actually taken up by the cellular system (i.e., internal dose).

Todd Gouin (TG Environmental Research) presented on reference materials in the current scientific literature. Of critical importance is the need to understand what an environmentally relevant particle is and how the current generation methods alter their properties. Todd emphasized the need to establish a community of practice to share results and develop standard guidelines or methods for generation.

Christie Sayes (Baylor Uni.) Presented results from simulated aging to produce more realistic RM, using mechanical stress (l-N2 in food blender), bacterial stress, enzymatic stress, oxidation stress (Fenton, Mohr’s salt). Terminology was clarified during discussion to differentiate from solvent-non-solvent processes (which would be termed as precipitation).

Luke Parker (TNO) presented progress from MOMENTUM project, using sequential cryogenic micronisation. Extensive micronisation produces a significant fraction of submicron particles (in number count), but very polydisperse across many orders of magnitude in size (number vs. volume metrics). Issue of contamination is addressed. Issue of polydispersity to be resolved in Brigid.

Wendel Wohlleben (BASF) presented progress in LRI C10: the generated submicron materials are sufficiently monodispersed to be submicron in both number and volume metrics measurements. Issue of available mass (gram scale for many, kg scale for one material). Extensive testing of chemical (molecular) properties and physical (particle) properties to address representativeness. A joint summarizing overview by TNO and BASF was given on different routes to RM. Also, a joint table of available materials in MOMENTUM, BRIGID, C10 was given, for each size range (<1µm, 1-10µm, >10µm).

Discussion clarified terminology: The currently available materials should be termed "representative test materials", and it should be clearly communicated, which scenario is to be represented (pristine plastic e.g. in air of production facilities, or aged plastics e.g. in aquatic environment, etc). The range of polymer types within one chemical name was also discussed as an important to factor when manufacturing a representative test material. Only when also the biological behavior is known, the material should be considered as RM.

Parallel session on "Microplastic effects testing with relevance for environmental modelling and risk assessment"

Chair: Albert A. Koelmans, Wageningen U

In her talk about the ECO49 project, Vera de Ruijter discussed the need for improved methods in plastic research due to current limitations in quality assurance and harmonization, which hinder our understanding of the true effects of microplastics in the environment. The authors conducted a review of 105 microplastic effect studies with aquatic biota and proposed a method to assess the quality of such studies. They developed 20 quality criteria in four main categories: particle characterization, experimental design, applicability in risk assessment, and ecological relevance. The average score for the studies was 44.6% of the maximum score, indicating a significant need for better quality assurance. Consequently, urgent recommendations for improvement were proposed, including avoiding and verifying background contamination and enhancing the environmental relevance of exposure conditions. The authors found a mismatch between the sizes of particles tested and those targeted in environmental samples. Many studies proposed mechanisms without sufficient support from study design and data reporting, posing a problem for decision-makers and requiring improvement in future research. Three effect mechanisms related to food assimilation, internal physical damage, and external physical damage were identified as high-priority in risk assessment.

In his presentation, Bart Koelmans presented a recipe for preparing environmentally realistic microplastic particles for use in effect tests. Current tests often use less diverse particles than those found in nature, limiting their relevance. The authors provide practical guidance on designing and preparing these microplastics, which can also be used for non-polymer particles. This approach enables comparisons of the intrinsic toxicities of different environmentally realistic particle types.

Leah Thornton Hampton discussed the recent surge in microplastic research driven by legislative mandates to develop environmental management strategies. The State of California is specifically active in addressing microplastic pollution, standardizing methodologies, and developing health-based thresholds. Efforts are underway to evaluate collection methods, sample processing, and analysis for microplastics in various matrices. Preliminary health-based thresholds have been derived for ambient water and drinking water, and critical research needs have been identified for the next phase of microplastic research and environmental management in California.

Paula Redondo-Hasselerharm emphasized the need to assess the impacts of nano- and microplastics on aquatic and terrestrial species at the community level under ecologically realistic conditions. While most studies focus on single species in controlled laboratory settings, data on the long-term implications of nano- and microplastics on communities in natural environments are limited. Paula presented a literature overview and the results of a 15-month outdoor experiment where a freshwater community was exposed to nano- and microplastics. Guidance is provided on how community effect thresholds can be used in risk assessment.

Lastly, Todd Gouin acknowledged the substantial growth in microplastic research but highlighted the challenge of interpreting the environmental relevance of results. Adverse effects reported suggest that exposure to elevated concentrations of microplastics can lead to various responses, such as inflammation, oxidative stress, and effects on behavior, growth, and reproduction. Recent research proposes innovative strategies to address these challenges and move the field forward. The presentation aimed to reflect on recent advances, identified areas that still need to be addressed, and assessed the overall progress in microplastic research.

Parallel session on “Degradation Processes of Microplastics”

Chair: Kara L. Law, Sea Education Association, & Jing Hu, Dow

Kara Lavender Law opened the session by level setting the definitions of plastics and degradation that would be used in this session. Plastics are the synthetic polymers with chemical additives. Degradation refers to changes in material properties resulting in reduced performance and/or loss of function. Law then emphasized the importance of studying the degradation process of plastics to inform the lifetime/timescale of plastics in the environment, and their consequent interactions of plastics with biota. Several polymer characteristics (chemical composition, polymer microstructure and plastics properties) affecting degradation were also pointed out, and she provided a high-level overview of the four presentations in this session, which were deeper dives on different aspect of degradation.

The first presentation was given by Anthony Andrady from North Carolina State University on the topic of microplastics in the ocean. Andrady first pointed out the similarities and differences in environmental conditions between ocean (sea surface) and land (air) exposures (e.g., similar solar UV radiation, decreased temperature and dissolved oxygen and potentially increased water sorption in seawater compared to air). Andrady highlighted his research on the comparison of degradation and fragmentation processes of plastics in air and seawater under accelerated weathering testing in the laboratory. Findings suggest diffusion-controlled oxidation of the polymer results in localized degradation in a thin surface layer, and plastics tested did not result in a large accumulation of particles that are < 2000 nm.

The second presentation was given by Bryan D. James from Woods Hole Oceanographic Institution on the topic of linking formulation to the fate and impacts of plastics in sunlit surface waters. James pointed out that plastics are engineered complex mixtures: polymers plus additives, and the talk focused on the role of inorganic additives in the fate of plastics. Findings indicate that inorganic additive formulation could control photochemical fate and also biofouling of plastics. Further, leachates from shopping bags were subjected to a

zebrafish developmental bioassay to evaluate toxicological effects. The findings indicate toxicological effects could be attenuated by product formulation.

The third presentation was given by Melissa Duhaime from University of Michigan on the topic of processes of environmental plastic weathering and biodegradation in natural systems. Duhaime pointed out that microbial species in nature live in consortia, not in isolation, and mechanisms and rates of microbial cooperation in polyethylene biodegradation are unknown. The talk centered around four approaches to holistically study UV- and bio-weathering of polyethylene in the environment: laboratory UV accelerated aging, field exposures, and experiments with microbial isolates and microbial consortia, utilizing analytical chemistry and environmental microbiology. Findings from this research are being used to develop new metabolic models of polyethylene-degrading microbes and multi-species consortia that can be used to predict outcomes for different polymer formulations and environmental conditions.

The last presentation was given by Sam Harrison from UK Centre for Ecology & Hydrology on the topic of predicting plastic fragmentation in the environment (Cefic LRI ECO59 project). The talk centered around developing a mechanistic fragmentation model and building an experimental database to populate the model with data from photodegradation and mechanical abrasion studies. The goal is a model with pragmatic input requirements that predicts the time evolution of plastic size distribution in environmental compartments. The model will strive to provide realistic fragmentation rates and particle size distributions to fate and exposure models and may also be integrated with an additive release model.

During the general discussion, participants identified as a research priority the need for quality data linking product formulation to plastic degradation processes under relevant environmental conditions, which can then be fed into model development. In addition, they discussed the need for follow up workshops to consolidate and further advance our knowledge of degradation processes of microplastics.

Parallel session on “IVIVE in human toxicology assessment of microplastics”

Chair: Robert Ellis-Hutchings, Dow, & Tanja Hansen, Fraunhofer ITEM

The WHO 2022 human health assessment highlighted that there is insufficient information to assess the bioavailability of MNPs and that in vitro MNP biokinetics cannot currently be extrapolated to in vivo. In vitro model approaches predominate in MNP research; however, all of these models lack the ability to fully recapitulate intact in vivo barrier function. With these limitations in mind the session focused on identifying opportunities to incorporate in vitro to in vivo extrapolations early in the planning and generation of microplastics bioavailability data. Through presentations by Justin Teeguarden (Pacific Northwest National Laboratory), Gunter Oberdoerster (University of Rochester), Tanja Hansen (Fraunhofer Institute), and Leah Johnson (RTI International), and subsequent discussion the following key takeaways were identified:

Key takeaways

- It is critical to establish a clear quantitative understanding of human exposure. Knowledge of exposure should drive prioritization of which NP and MP should be studied.

        - It is important to predict (via modelling?) microplastic pollution out into the future (e.g. 20 years) not just current exposures. Same goes for predictions of microplastics degradation.
    - It is important to set community standards for determination of “relevant” and interpretable exposures in in vitro studies.
    - Correct dosimetry is often neglected in in vitro studies:
        - Sedimentation behavior of microplastic particles should be considered in in vitro systems.
        - Concentration doses given in submerged in vitro studies often do not reflect cell surface doses, particularly for microplastic particles less dense than water. The ISDD and VCM-ISDD models can be used to model cell surface doses.
        - For ALI experiments, the P.R.I.T.®ExpoCube® provides a useful tool to enable relevant and controlled dosing and the determination of surface doses.
    - It is imperative to only use well characterized MNP test materials in experimental studies. This includes particle and non-particle characterization and ensuring the biological studies are solvent and endotoxin-free.
    - Other important parameters include: agglomeration state, physicochemical properties, reactivity, and dissolution potential. Optimal dose metric needs to be determined but all should be documented in studies.
    - Non-particle substances, either inherent to the particle source or adhered to from environmental exposures, need to be considered.
    - Model selection: Selection of in vitro models, i.e. simple vs complex, needs to be discussed along with their limitations (e.g. lack of cell types, barrier function differences).
    - Biokinetics and Hazard
        - Physiologically-based Pharmacokinetic (PB(P)K) models are suitable to model particle retention in the lung and particle uptake.
        - Modeling alone though is insufficient for MNPs given out limited scientific understanding. Measured data are needed using both in vitro and in vivo approaches.
- While typically in vitro should precede in vivo, with novel test materials in vivo biokinetics might be considered as a prioritization approach to define the in-vitro testing strategy (e.g. selection of cell models).
- Particle uptake is size dependent, therefore size is an important descriptor.
- A size cut-off should be defined for microplastic uptake. Least is known about the ingestion route. Plastics Europe sponsored testing is planned to examine 1, 10 and 100 µm distributions for various reference materials in in vitro and in vivo test systems.
- Visualization and quantification of particles is challenging when studying microplastic uptake
- As part of the Cefic LRI C10 project, Stimulated Raman Scattering (SRS) has been identified as a promising method to measure cellular uptake of microplastic particles providing 3D visualization of particle distribution inside cells.
- Air liquid interface (ALI) testing with pulmonary cells is relevant and predictive for acute local toxicity
- Ultrafine particles can cross the BBB, potentially causing neurological effects. This has not been explored for plastic particles and is a new aspect to consider.
- Outstanding question: can grouping and/or read-across approaches derived for (nano)particles be useful for microplastic materials?

Joint session on “A risk assessment framework for microplastic particles”

Chair: Jens C. Otte, BASF SE, & Todd Gouin, TG Consulting

The first presentation was given by Bart Koelmans von Wageningen University, Netherlands, entitled “Risk assessment of Microplastic particles for human health and environment, a probabilistic view”. He explained that microplastic risk assessment is a complex task and as a result, many assessments to date have compared apples to oranges, with exposure and effect assessments not aligning. Recently, QA/QC and standardization methods have been developed to alleviate some of these problems, although some degree of uncertainty always remains. In his presentation, he summarized the essentials of recent methods for performing a consistent risk assessment with the use of probability density functions (PDFs). Examples of new risk assessments for microplastic effects were given in marine systems, freshwater, sediment, and soil, and microplastic effects on humans.

The second presentation was given by Holger Kress, University of Bayreuth, Germany on “Lost in parameter space – Can we reduce the complexity in microplastic research?”. He presented the challenge to investigation of potential harmful effects of microplastic on organisms due to the huge parameter space in microplastic research. He laid out that it would be very helpful to reduce the complexity in microplastic research. One approach to achieve this is to search for a small set of key parameters that are crucial for the interactions between microplastic particles and organisms and proposed to do so with cells. For some particular materials, the interactions between microplastics particles and cells strongly depends on the surface of the particles. Therefore, he and his team investigated the influence of the surface properties of microplastics particles on their adhesion to cells and their internalization into cells. He showcased that a single physical parameter – which varies drastically between different particles – strongly influences the interactions between particles and cells.

Scott Coffin, California State Water Resources Control Board, highlighted in his talk the assessment of risks of microplastics in drinking water and the aquatic environment to inform risk management strategies in California. State legislation requires the local agencies to develop standardized analytical monitoring methods, to assess risks to humans and to aquatic ecosystems, to perform monitoring to determine exposure to humans and contamination in the environment, and to recommend policy strategies to reduce further contamination. Fulfilling these policy and regulatory goals requires research to fill scientific gaps in this rapidly emerging field. He laid out that health impacts of microplastics in aquatic organisms have been relatively well-documented, literature on potential impacts to humans are limited but rapidly emerging. An expert workshop developed frameworks for assessing microplastics’ risks to humans and ecosystems and applied this framework to the available literature. While the team was able to derivate a preliminary human health-based threshold for microplastics, while the value is highly uncertain due to incomplete data. Similar work was done for microplastics in aquatic organisms.

The final talk was given by Raymond Pieters, Utrecht University, Netherlands, on “Human health risk frameworks - needs for human health microplastics risk assessment”. The work that he presented is part of the EU funded project POLYRISK which aims to establish a fit-for-purpose risk assessment framework for assessing human health risks of micro- and nanoplastic particles (MNPs). The major focus in the POLYRISK project is the inhalation

exposure route. The conceptual framework proposes to distinguish micro/nano-sized fibers, polymers and particles and will make use of effect data of MNP on inflammation-related key events (cell stress, release of proinflammatory mediators, and activation of immune cells) and of human exposure and effect data from real world human scenario studies.

The overall discussion on risk assessment for microplastics focused on the prioritization of research needs. High quality studies were identified as being impactful also towards applicability in a risk assessment framework. However, uncertainty remains and brings up the questions on where to focus with upcoming research. Meeting participants brought up the question of whether to focus on relevant compartments for research towards the environment. Regarding human health, such targeted research would focus on the relevant impact and exposure pathway. Studies and /or models indicating the relevant exposure route would be helpful to guide such studies towards potential impacts of microplastics. Finally, and in combination, such studies would then serve the need to perform risk assessment for both the environment and for human health aspects.

The final presentation to the workshop was given by Veronica Padula from Seattle Aquarium. She presented a case study on “Microparticle monitoring at the Seattle Aquarium: Life before and after Covid-19”.