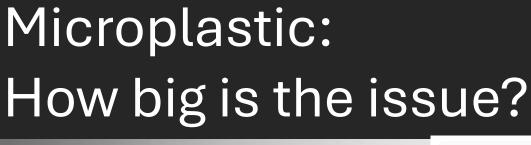
The potential hazards of microplastics to human health and the complexity of assessing risks

Dr Todd Gouin

Dr Stephanie Wright | Imperial College London



Updated 2038 GMT (0438 HKT) June 5, 2019

INTERNATIONAL

Interview on Microplastics

SPIEGEL ONLINE SPIEGELE

Interview Conducted by Philip Rothgo **

'Never Good News Having Particles in Your Brain

the human body. British toxicologist Rosemary Waring warns our oceans will be inundated with the stuff.

You could be swallowing a credit card's weight in plastic every week

Google News f

Immune System

Ancient Galaxy

Understanding

PLASTIC

CRISIS



health Food Fitness Wellness Parenting Vital Signs





A modern health crisis: microplastics



Communication is key

- Comment published in Nature draws attention to the reliability and relevance of data reporting plastic/microplastic particles in human tissues, including concerns related to:
 - Sampling and analysis
 - Exposure and plausibility



Microplastics have been found in oceans, lakes, rivers, soils, food and air.

Are microplastics bad for your health? More rigorous science is needed

Jun-LI Xu, Stephanie Wright, Cassandra Rauert & Kevin V. Thomas

Micro- and nanoplastic particles: what are they?

 Broadly defined nano- and microplastic particles are plastic particles <5mm



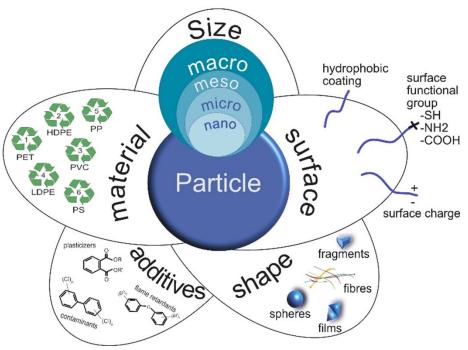


Image source: Visual Capitalist

Image source: WHO, Geneva, 2022

Emission sources and (environmental) routes of exposure

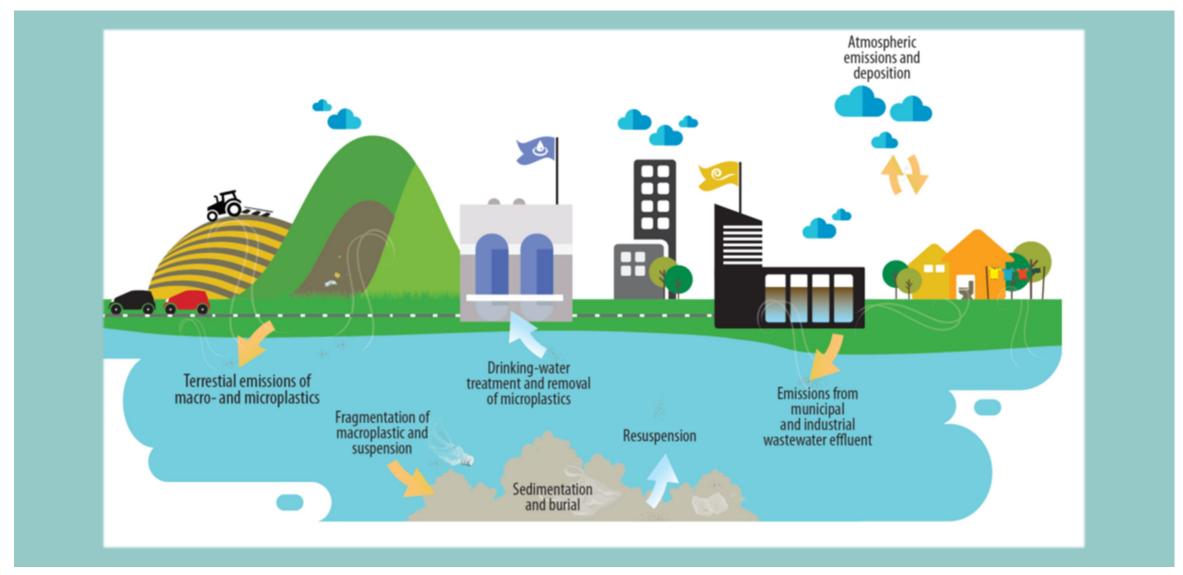


Image source: WHO, 2019

Human exposure to micro- and nanoplastic particles

- What we know
 - Ubiquitous
 - Water
 - ► Air (indoor/outdoor)
 - Oral
 - ► Particles_{>10µm}
 - Food, beverages and drinking water
 - Max. daily intake (fish-based diet + glass bottled water)
 - 221 MP/kg bw (Zuri et al., 2023)
 - ▶ Inhalation
 - ► Max. inhaled dose (outdoor and indoor environments)
 - ▶ 195 MP/kg bw (Zuri et al., 2023)
 - ► TDI (worst case)
 - ► Max 417 MP/kg bw (Zuri et al., 2023)
 - ▶ 32,588.55 MP per day (average)

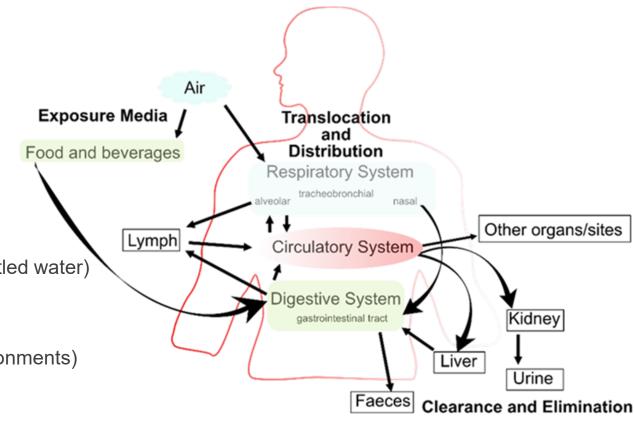


Image source: WHO, Geneva, 2022

Human exposure to micro- and nanoplastic particles



32,588.55 MP per day (average)

Size (and other properties) influence particle fate and internal exposure

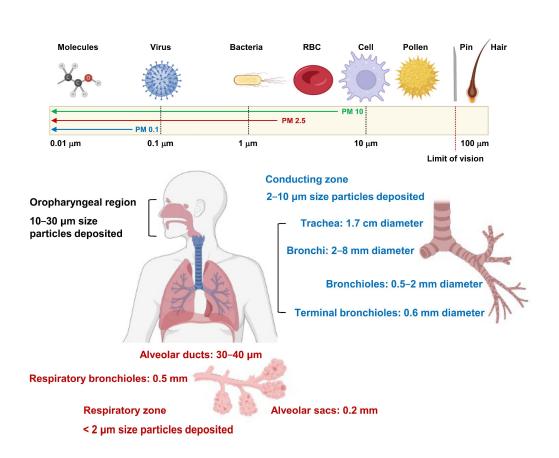


Image source: Lim and Kim, 2024

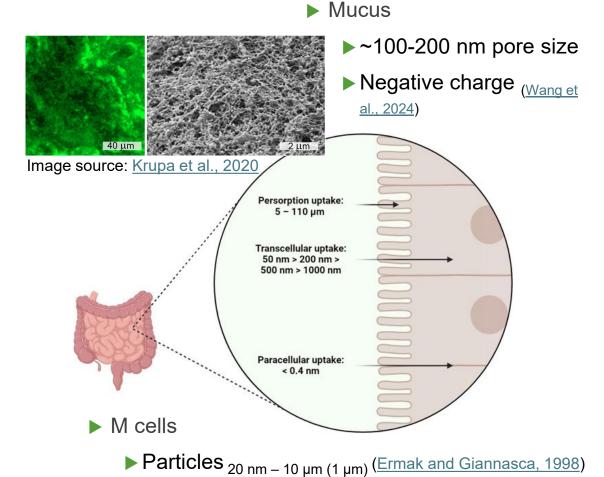


Image source: Mok, 2024

Potential hazards of micro- and nanoplastic particles

- Direct and indirect
- Localized effects

Potential hazards at the cellular level

Oxidative stress

- Too many free radicals (Reactive Oxygen Species, ROS) and not enough antioxidants to neutralise
- Free radicals on surface of weathered microplastics (<u>Hu and Palic, 2020</u>)
- Intracellular ROS as part of innate immune system defence (Hu and Palic, 2020)

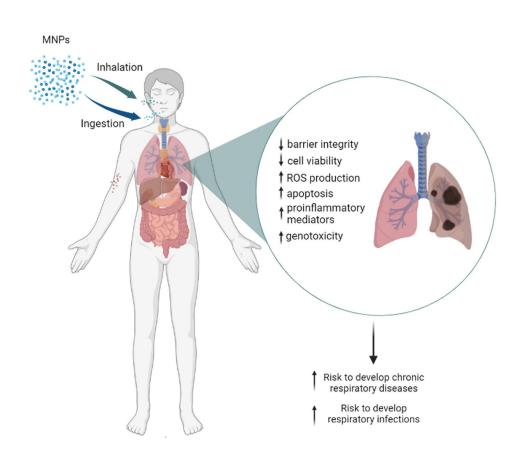
Inflammation

- Response to injury or infection: remove cause of damage, clear debris and repair tissue
- Microplastics are foreign bodies
- Oxidative stress may lead to inflammation

Metabolic disruption

- Normal processes are altered, leading to impaired function or cell death
- MNP can disrupt mitochondrial function
- Oxidative stress can disrupt energy metabolism

Localized hazards in the airways



Source: Romero-Andrada et al., 2023

DIRECT EFFECTS

When in contact with cells, MNPs can:

- Lead to ROS formation
- Reduce cell viability and metabolic activity
- Increase membrane permeability
- Activate inflammatory pathways

Pathology includes:

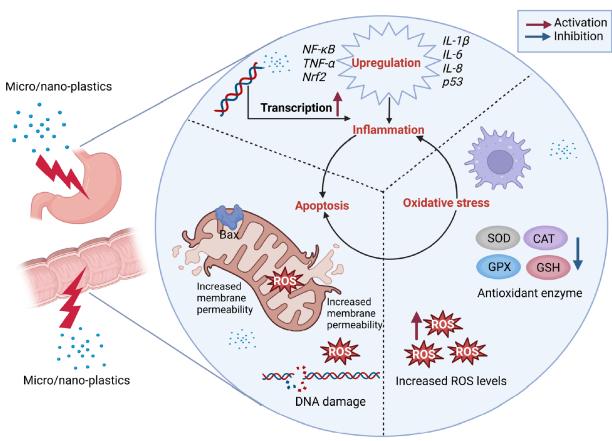
Fibrosis

Influential factors include:

- Particle shape > irregular more toxic than spherical
- Size > smaller = more toxic
- Surface charge > positive = more toxic
- Plastic material
- Model cell line or organism

Source: Zhao et al., 2024

Localized hazards in the gastrointestinal tract



DIRECT EFFECTS

When in contact with cells, MNPs can:

- Stimulate cells to produce reactive oxygen species (ROS) resulting in oxidative stress.
- Stimulate cells to produce inflammatory cytokines or induce an inflammatory response through oxidative stress.
- Common endpoints reported across studies (both in vitro and in vivo) include:
 - Apoptosis (programmed cell death)
 - Upregulation of cytokines and ROS
 - Downregulation of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) and glutathione (GSH)

Source: Wang et al., 2024

The case of nylon – clinical observations

- Interstitial lung disease nylon (most commonly 66), acrylic, PP, PE, PET, synthetic textiles
- Flock Worker's Lung (nylon flock industry)
 - Lymphocytic bronchiolitis and peribronchiolitis with lymphoid hyperplasia represented by lymphoid aggregates
- IR all interstitial lung disease = 48 (95% CI 23-88)
- IR IPF = 258 (95% CI 104-530)
- PE (Spain), PP (Turkey), Rayon (USA)

~2.2 mg/m³ exposure

Kern et al. 1998, 2000, 2003; Barroso et al., 2002; Atis et al., 2005; Antao et al., 2007; Burkhart et al., 1999.

Risk Assessment



"All substances are poisons; there is none which is not a poison."

The right dose differentiates a poison."

What are the human health risks? RISK = EXPOSURE x HAZARD

KEY QUESTIONS

Are the data reliable and relevant – Is there a dose-response relationship?

EXPOSURE

- What are the main sources of nano- and microplastic particles in air, food and beverages?
- Are the analytical methods currently used sufficient to characterize and quantify exposure?

HAZARD

- What is the primary endpoint of toxicological concern?
- Are there intrinsic properties of microplastic that are more 'toxic' than others?

WHAT WE KNOW

- There are negative effects
- non-standard mammalian in vivo and in vitro lab-based studies
- Occupational epidemiology
- There is exposure

ARE THE DATA FIT-FOR-PURPOSE?

Are the data fit-for-purpose?

- Toxicity testing to date is represented by:
 - The use of very high concentrations, which are understood to be inconsistent with typical ambient exposure.
 - Limited number of studies reporting dose-response relationships that include environmentally relevant exposure.
 - Studies using a single type of particle (e.g. shape, size, polymer composition)





Discussion

On the need to avoid apple-to-orange comparisons in microplastic research

Albert A. Koelmans 💇, Todd Gouin⁶, Alvine C. Mehinto⁶, and Scott Coffin⁶

^aAquatic Ecology and Water Quality Management Group, Wageningen University, Wageningen, the Netherlands; ^bTG Environmental Research, Sharnbrook, Bedfordshire, UK; ^cSouthern California Coastal Water Research Project Authority, Costa Mesa, CA, USA; ^cCalifornia State Water Resources Control Board, Sacramento, CA, USA

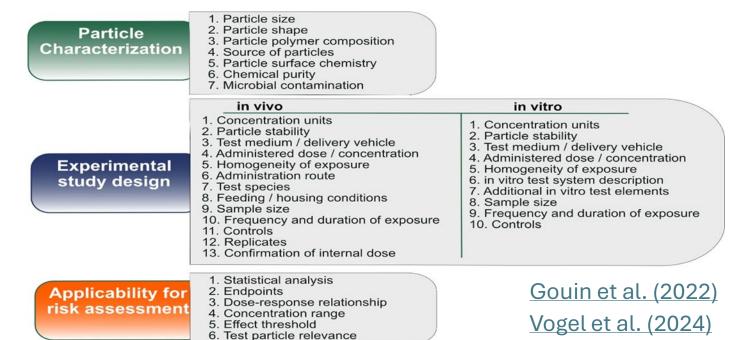
Corresponding author: Albert A. Koelmans (email: bart.koelmans@wur.nl)

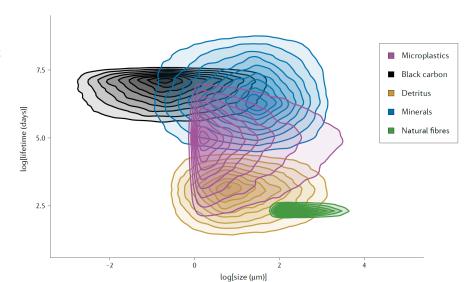
Aligning the dose to the microplastic continuum space

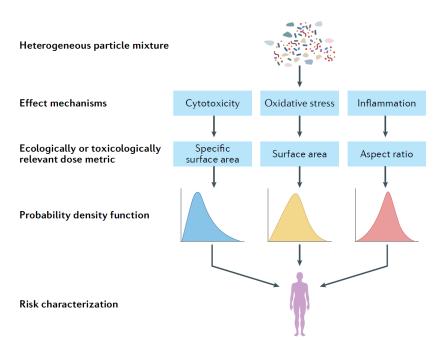
 Recognizing similarities between the properties of microplastic and other types of particles opens opportunities to advance our ability for risk assessment.

Koelmans et al. (2022)

Particle and Fiber toxicology fundamentals – Best practices







Microplastic and chemicals Is there an intrinsic risk?

RISK = EXPOSURE x HAZARD

KEY QUESTIONS

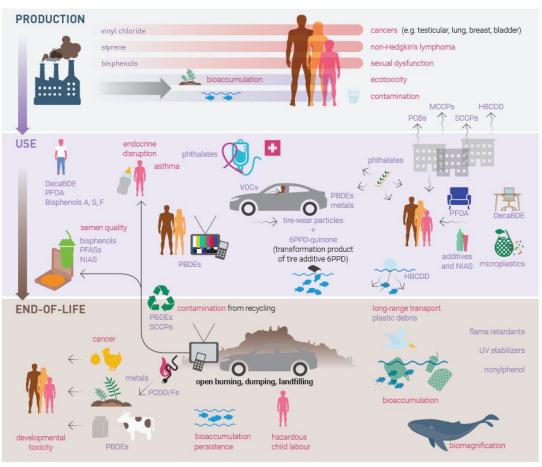
Do we data that provide use with a reliable and relevant dose-response relationship?

"All substances are poisons; there is none which is not a poison.

The right dose differentiates a poison."

Plastic and plastic associated chemicals: Exposure pathways





Estimating chemical exposure and potential risk in relation to ingesting microplastic particles

Calculating exposure and risk requires estimates of the mass of microplastic ingested, mass of chemical in the microplastic and a toxicological threshold value

Microplastics in

Table 3.3 Upper-bound daily intake estimates of chemicals from microplastics, maximum levels of contaminants associated with microplastics, and corresponding MOE

Chemical ^a	Upper bound concentration in microplastic (μg/g)	Maximum daily intake (ng/kg bw/day) ^b	Point of departure (μg/kg bw/day)				
Bisphenol A	0.7297	0.001	609	Margin of exposure	Adequacy of MOF	Conclusion	Chemical
Cadmium	3390	5.0	0.8	(MOE)	Adequacy of MoL	Conclusion	Circinical
Chlordane	0.0144	0.00002	50	5.9 × 10 ⁸	MOE of at least 100	No safety concern	Bisphenol A
Di(2-ethylhexyl)phthalate	0.0699	0.0001	2500	1.7×10^2	MOE of at least 10°	No safety concern	Cadmium
Dichlorodiphenyltrichloroethane	7.1	0.0001	1000	2.5×10^{9}	MOE of at least 100	No safety concern	Chlordane
Hexachlorobenzene	0.0587	0.00002	50	2.5×10^{10}	MOE of at least 100	No safety concern	Di(2-ethylhexyl)phthalate
Polyaromatic hydrocarbons	119	0.06	100	1.0×10^{8}	MOE of at least 100	No safety concern	Dichlorodiphenyltrichloroethane
· · ·				6.0×10^{8}	MOE of at least 100	No safety concern	Hexachlorobenzene
PBDEs	9.9	0.01	100	6.0×10^{5}	MOE of at least 10 000	No safety concern	Polyaromatic hydrocarbons
PCBs	18.7	0.03	5	7.2×10^{6}	MOE of at least 100	No safety concern	PBDEs
				1.9 × 10 ⁵	MOE of at least 1000d	No safety concern	PCBs

WHO, Microplastics in drinking-water, World Health Organization, Geneva, Switzerland, 2019.

Estimating exposure to chemicals in microplastic requires quantification of the mass of microplastic ingested

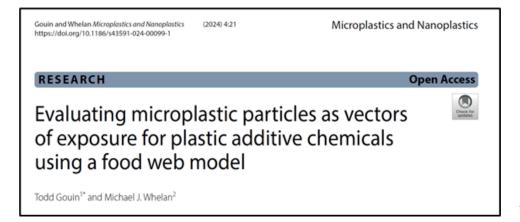
Ingestion = egestion (number of MPs per day)

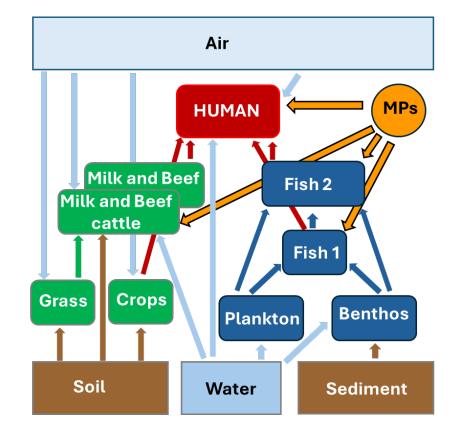
 $I_P = E_P = mc_F \cdot n_F = n_H$

Steady state number of MPs in the human

Mass of food and beverages consumed by humans (kg d⁻¹)

Number of MPs per kg food and beverages



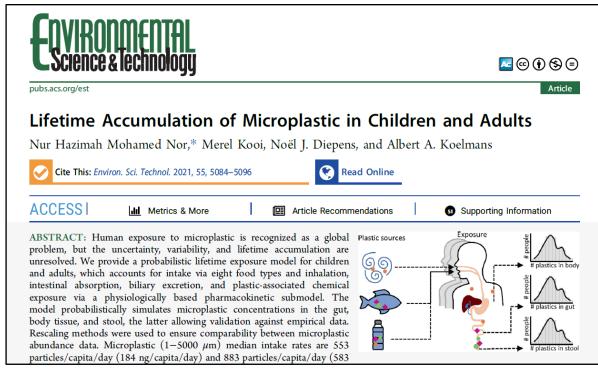


EU Horizon 2020





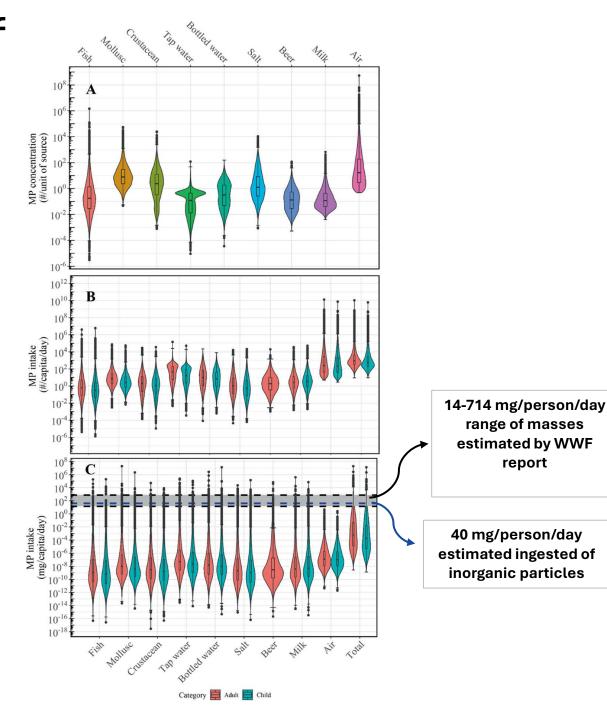
Estimating human ingestion of microplastic particles



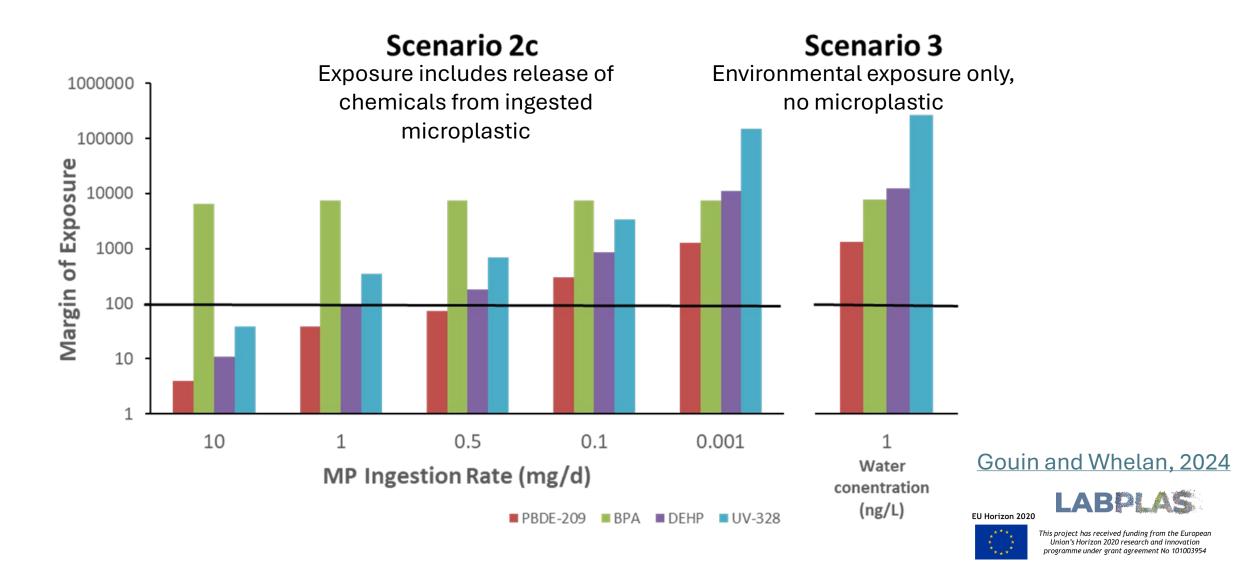
Mohamed Nor et al., 2021

Estimates of human exposure to microplastic particles varies by >20 orders of magnitude, ranging from 10^{-16} mg/person/day to 10^{6} mg/person/day.

• The median values are 184 ng/person/day for children and 583 ng/person/day for adults



Estimating human health risks related to chemicals leaching from ingested microplastic



Several outstanding research needs

EXPOSURE

- Standard and harmonized methods:
 - Sampling and analysis of NMP in air, water, food and beverages require robust, quality-assured methods, supported by the availability of nano- and microplastic particles representative of environmentally relevant human exposure
- Sources of contamination:
 - The contributions of different factors would guide strategies for mitigating exposure.
- Uptake and fate for both inhalation and oral ingestion exposure:
 - More information is required on the absorption, distribution and elimination of NMP.
- Particle characterization:
 - Quality-assured environmental monitoring studies should be conducted to characterize the distributions of size, shape and composition of NMP in the environment for studies of the effects of exposure on human health and to prepare reference standards for environmentally relevant testing of toxicity.

HAZARD

- Toxicology
 - Quality-assured experiments suitable for risk assessment should be conducted, with adequate characterization of exposure to the types of NMP to which humans are most commonly exposed.