PlasticsFatE: Lessons from microplastics research for standardisation, policy and regulation

Short overview

Rudolf Reuther (ENAS)

MAELSTROM webinar 20 March 2024

PlasticsFatE has received funding from the European Union's Horizon 2020 Research and Innovation programme, under the Grant Agreement number 965367

PlasticsFatE a nutshell

PlasticsFatE = **Plastics** Fate and **E**ffects in the human body

Consortium: 28 partners from 11 European countries

- 7 private-public research organizations (ISTEC-CNR, CSIC, ITENE, UFZ, FHG, IGB, GAIKER),
- 4 national governmental agencies (STAMI, BAM, NRCWE, UBA),
- 2 medical research centers (UMCU, FAU),
- 9 universities (WFSR, ULEIDEN, UL, BOKU, UBT, UNITO, URTV, UP, NTUA),
- 5 SMEs (ENAS, ERS, INNOSIEVE DIAGNOSTICS, OPTIMAT, DECHEMA),
- and 1 large company (ECAMRICERT)

Management team

- Scientific coordination: Rudolf Reuther, ENAS (DE)
- Project coordination: Mark Morrison, OPTIMAT (UK)
- Project management: Nadine Bresch, ERS (DE)
- Dissemination management: Lesley Tobin, OPTIMAT (UK)
- Data management: Damjana Drobne, UL (SI)

Duration: 1 April 2021 – March 2025

Budget: 6 million EUR

Advisory Board:

- Philip Demokritou, Harvard School of Public Health, Boston (USA)
- Tobias Stöger, Helmholtz Zentrum (DE)
- Thava Palanisami, University of Newcastle (AUS)
- Chunying Chen, Chinese Academy of Science (CAS) (PRC)
- Antoine Ghanem, Solvay (BE)
- Peter Krüger, Covestro Deutschland AG (DE)
- Hans Schweisfurth, IPR Cottbus (DE) (ethical advisor)

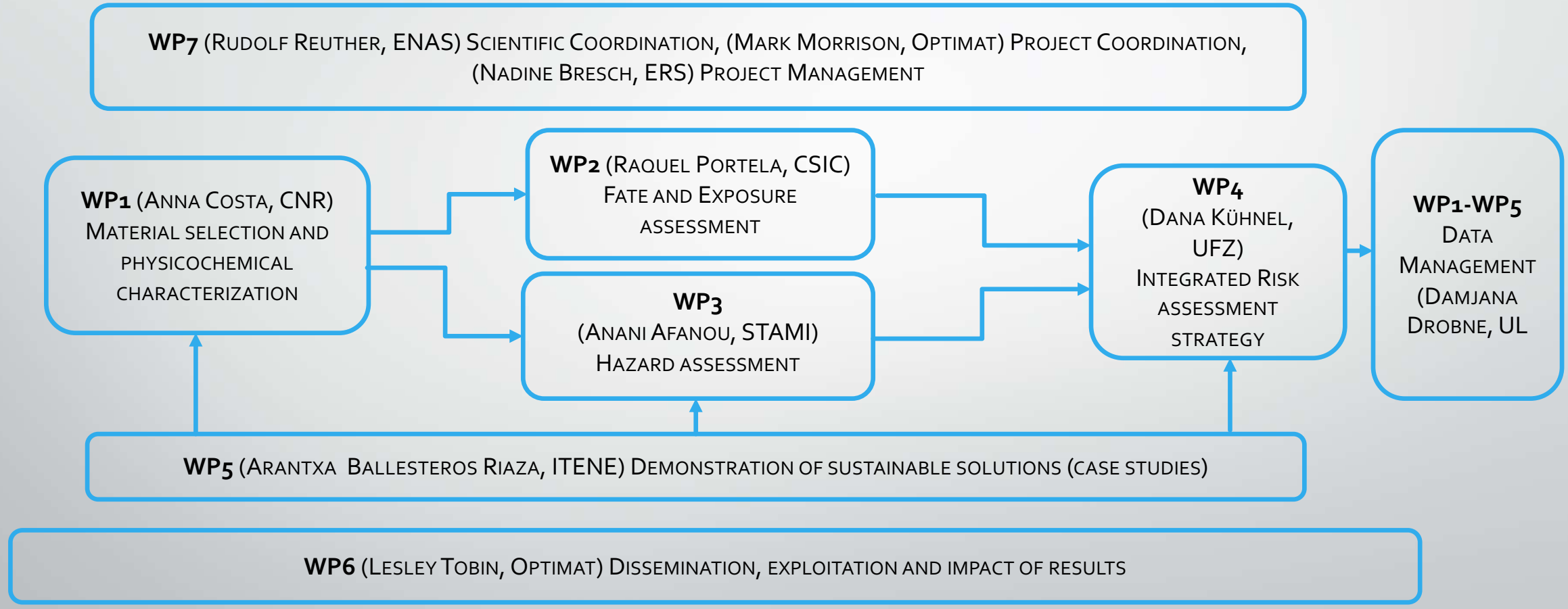
Main goal, approach and results

Our goal: Improve current understanding of fate and effects of MNP and associated chemicals in the human body

Our approach: Establish reliable methods for **(1)** detection, identification and quantification of MNP in complex human health relevant matrices and for **(2)** assessing exposure, fate and effects of MNP in the human body through *in vitro*, *in vivo*, *in silico* and *field studies*

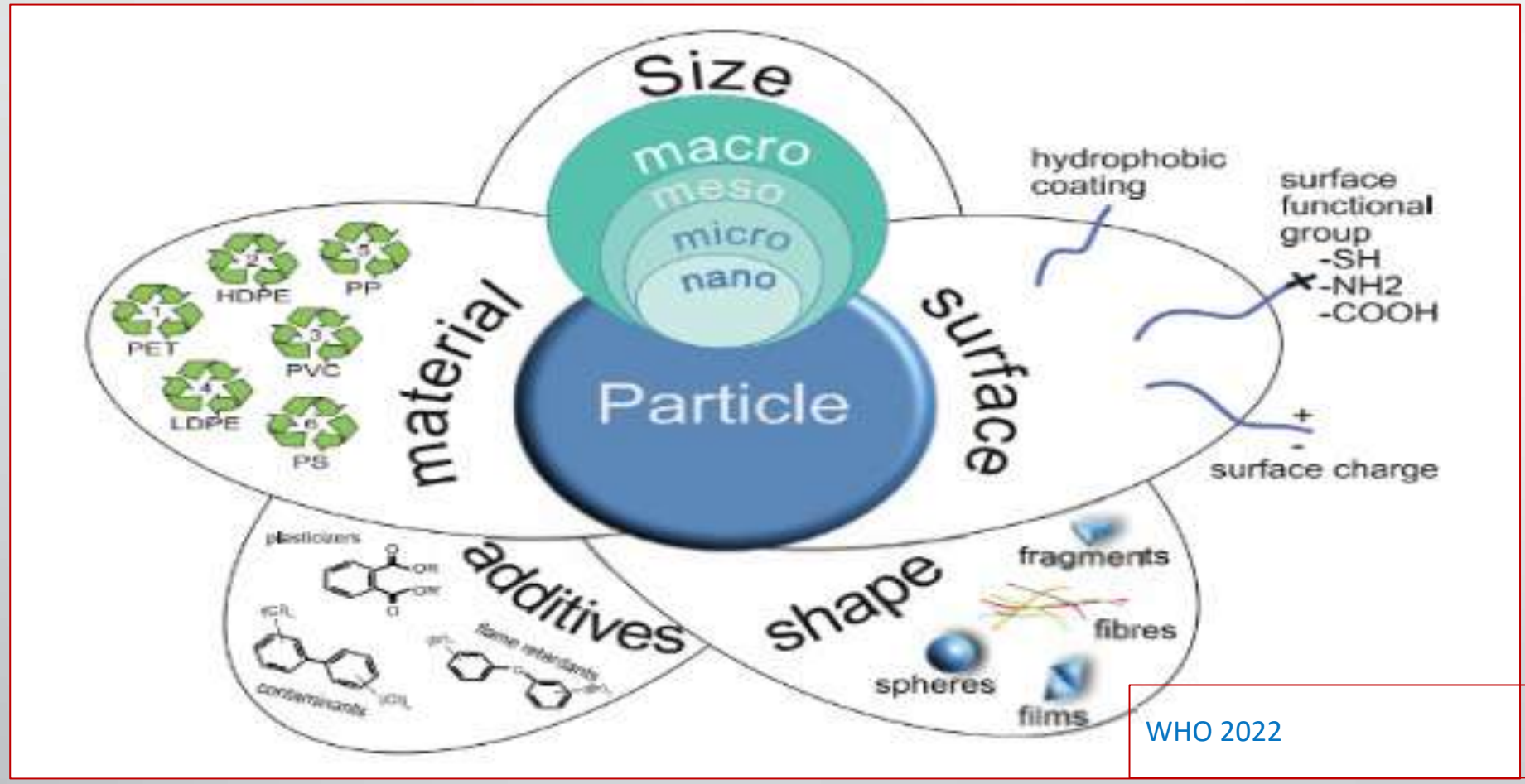
Our results: **(1) create new data and insights** on the impact of MNP on human health, **(2)** a **new integrated human health and environmental risk assessment strategy** based on validated data and methods, **(3)** to ultimately **support future policy, research, regulation, and standardisation**

PlasticsFatE workplan



Relevant characteristics of MNP that affect human exposure + hazard*

* WHO (2022) Dietary and inhalation exposure to nano- and microplastic particles and potential implications forhuman health



WHO 2022

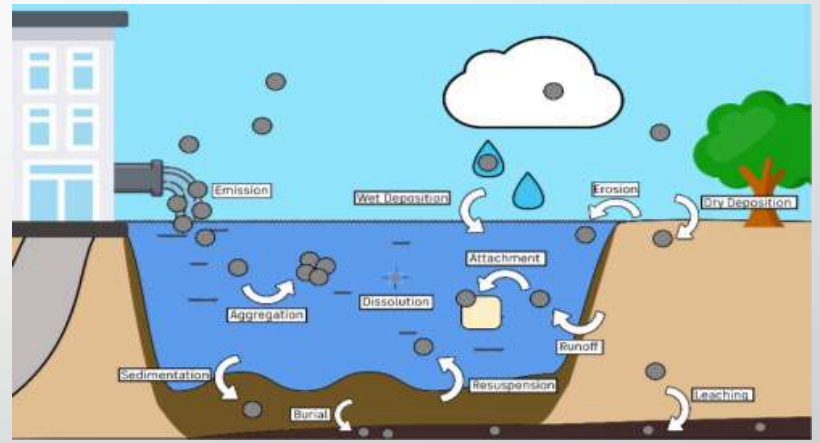
Starting point: establish relevant MNP test materials with various properties to validate methods for characterization and exposure and hazard assessment

Material	Batch identification		Characterisation information							Synthesized ...	
Name of material/ Polymer type	Material code no. (e.g. HDPE_21181_S-MP_W)	Producer	Particle size (D50)	Particle shape	Powder/ Dispersion (conc.)	surfactant/ dispersant	Origin: primary/ secondary	Labelled	Aged	Internal Supplier to Consortium	Aliquot size available
(Nano) PS	PS_9347072001 0350_NE_L-Eu	Distrilab	0,3 µm	spherical	Dispersion (10000 µg/ml)	Na-Azide (0,05%) - Carboxylate modified	Primary	yes	no	STAMI, NO	
(Micro) HDPE	HDPE_296_P-MP_F	Ceridust 3610 (Clariant)	4-5 µm	round	Powder	no	Primary	no	no	BAM, DE	1-50 g
(Micro) PE	UHMWPE_1619 1_P-MP_P	BAM	145 µm	round (cloud shape)	Powder	unknown	Primary	no	no	BAM, DE	1-10 g
(Micro) PE	UHMWPE_1618 6_P-MP_P	BAM	57 µm	round (potato shape)	Powder	unknown	Primary	no	no	BAM, DE	1-10 g
(Micro) PE	UHMWPE_1619 0_P-MP_P	BAM	22 µm	round (popcorn shape)	Powder	unknown	Primary	no	no	BAM, DE	1-10 g
(Micro) LDPE	LDPE_16242_P-MP_P	BAM	<75 µm	round	Powder	unknown	Primary	no	no	BAM, DE	1-10 g
(Micro) HDPE	HDPE_21181_S-MP_W	BAM	60 µm	irregulat, flat	Powder	almost no	Secondary, Cryo milled	no	yes	BAM, DE	<1 g
(Micro) PET	PET_21180_S-MP_F	BAM	44 µm	irregular	Powder	almost no	Secondary, Cryo milled	no	no	BAM, DE	<1 g
(Micro) PET	PET_21182_S-MP_F	BAM	130 µm	irregular	Powder	almost no	Secondary, Cryo milled	no	no	BAM, DE	<1 g
(Micro) PET	PET_21183_S-MF_F	BAM	70 µm	irregular	Powder	almost no	Secondary, Cryo milled	no	no	BAM, DE	<1 g
(Nano) PE	PE_490_P-NP_W	BAM	350 nm	irregular	Dispersion (82 µg/ml)	no	Prymary	no	no	BAM, DE	10 ml
(Nano) PP	PP_491_P-NP_W	BAM	180 nm	irregular	Dispersion (41 µg/ml)	no	Prymary	no	no	BAM, DE	10 ml
(Micro) PET	PET_001_S_MP_F	CSIC (José)	300 - 500 µm	irregular	Powder	no	Secondary, Cryo milled	no	no	CSIC (Josè)	1-20 g
(Micro) PET	PET_001_S_MP_F _sterile	CSIC (Josè)	300 - 500 µm	irregular	Powder	no	Secondary, Cryo milled	no	no	CSIC (Josè)	1-20 g
(Nano) PET	PET_002_S_NP_F	CSIC (Josè)	50-2000 nm	irregular	Dispersion (2,5 mg/ml)	no	Secondary, Cryo milled	no	no	CSIC (Josè)	1-5g/100 ml
(Nano) PET	PET_b001_P-NP_F	CSIC (Raquel)	Dv50= 69 nm	spherical	Dispersion (4.9 g/L)	no	Primary	no	no	CSIC (Raquel)	10 ml
(Nano) PET	PET_c000_P-NP_F	CSIC (Raquel)		spherical	Dispersion (2.4 g/L)	no	Primary	no	no	CSIC (Raquel)	10 ml
(Nano) PET	PET_c001_P-NP_F	CSIC (Raquel)	Dv50=77 nm	spherical	Dispersion (1.6 g/L)	no	Primary	no	no	CSIC (Raquel)	10 ml
(Nano) PET	PET_c002_P-NP_F	CSIC (Raquel)		spherical		no	Primary	no	no	CSIC (Raquel)	10 ml
(Micro fiber) PLA	PLA_7.001_S-MF_F	CSIC (Raquel)	D=3.5 µm, 20µm long	fiber	Dispersion (5 g/L)	no	Secondary (electrospun)	no	no	CSIC (Raquel)	10 ml

- **Panel of > 20 well-defined test materials** with dispersion protocols
- **2 Technical Data Sheets** (TDS) for well-characterized MP and NP particles
- **Various relevant polymers** (PET, PE, PS, PLA and PP, as particles or fibres)
- **pure relevant polymers** (PET, PE, PS, PP, PLA) **and derived from plastic items** (packages, bottles), with and w/o additives or contaminants (phthalates, BaP, microbes), aged/weathered or not etc.
- **Material testing strategy** built on 6 different characteristics: polymer types, sizes, shapes, additives, contaminants, aging/weathering
- **Two Interlaboratory comparisons** (ILCs) performed to validate reproducibility of methods for size measurement and detection (also within **VAMAS**), and **1 ILC on NP** size measurement still planned (DLS)

Fate and exposure assessment of MNPs

- **To get an overview: a Critical review on the occurrence of MNP in humans**
- **Exposure concentrations of MNP analysed in real world samples**:
  - **Bottled water** from some European countries with 3 exposure scenarios: environmental contamination, opening + closing + mechanical damage
  - **Food** (vegetables, fruits, meat etc., packaged/unpackaged)
  - **Air** (indoor, outdoor, workplaces) preliminary results: suburban > remote = indoors
  - **Personal care products** (face creams, toothpaste, shampoo)
  - **Human tissues, blood and excretion** (GIT, RT, liver, spleen, kidney, lymph nodes, EBC, urine, feces)
  - **Analytical methods** included MuScan, µ-FTIR, µ-Raman, TED- or Py-GC/MS
- **Developed 3 models** for **fate** (SimpleBox4MNP), **exposure** (2Box4MNP), **toxicokinetics** (PBPK) of MNP in tissues and organs



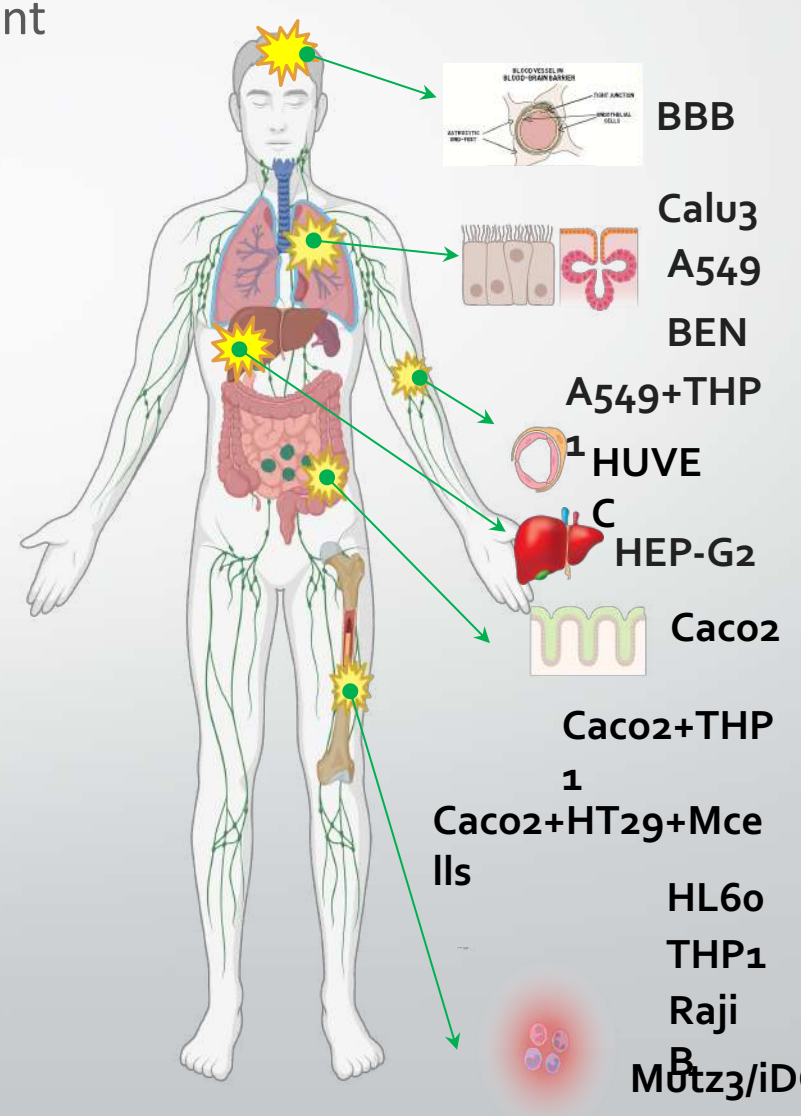
Assess human health hazards of MNP + AC

Test materials included various MNP (PS, PE, PET, PLA) of different size, shape, with and w/o aging, additives/contaminants, and leachates

Test assays included different simple + more complex 2D/3D *in vitro* cell models and biomarkers that simulate main exposure routes (RT and GIT) and target organs, tissues, biological barriers and the immune system

Measured effects after acute/subacute exposure included:

- cell viability
- Cytotoxicity
- metabolic or organelle activitiy
- barrier integrity + permeability
- cellular uptake, internalizaton + bioaccumulation
- immune effects



Simulation of fate and effects of MNPs in human gastrointestinal tract

Science of the Total Environment 902 (2023) 166003

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/scitotenv

Simulated gastrointestinal digestion of polylactic acid (PLA) biodegradable microplastics and their interaction with the gut microbiota

C. Jiménez-Arroyo [a], A. Tamargo [a], N. Molinero [a], J.J. Reinosa [b,c], V. Alcolea-Rodriguez [d], R. Portela [d], M.A. Bañares [d], J.F. Fernández [c], M.V. Moreno-Arribas [a,*]

Simulated gastrointestinal digestion and colonic fermentation

scientific reports

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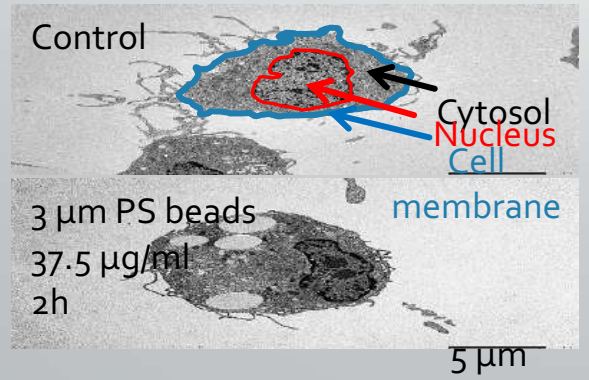
Open Access | Published: 11 January 2022

PET microplastics affect human gut microbiota communities during simulated gastrointestinal digestion, first evidence of plausible polymer biodegradation during human digestion

Alba Tamargo, Natalia Molinero, Julián J. Reinosa, Victor Alcolea-Rodriguez, Raquel Portela, Miguel A. Bañares, Jose F. Fernández & M. Victoria Moreno-Arribas

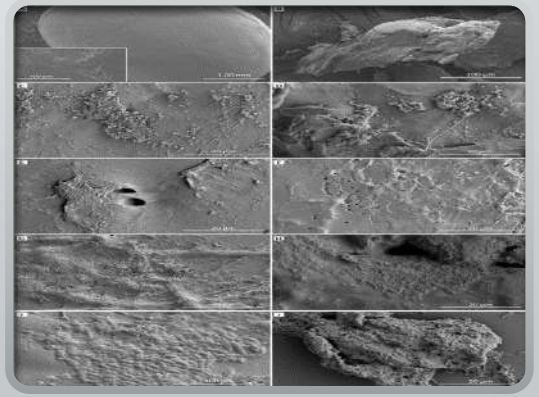
Results: MPs are transformed by and alter the human microbiota and and a biofilm formed on MPs surface

MNPs (PS) taken up in human macrophages



MNP (PLA) biodegradation in GIT

Pristine
Oral
Gastric
Small Intestine
Colonic phase



Preliminary results based on in vitro models show:

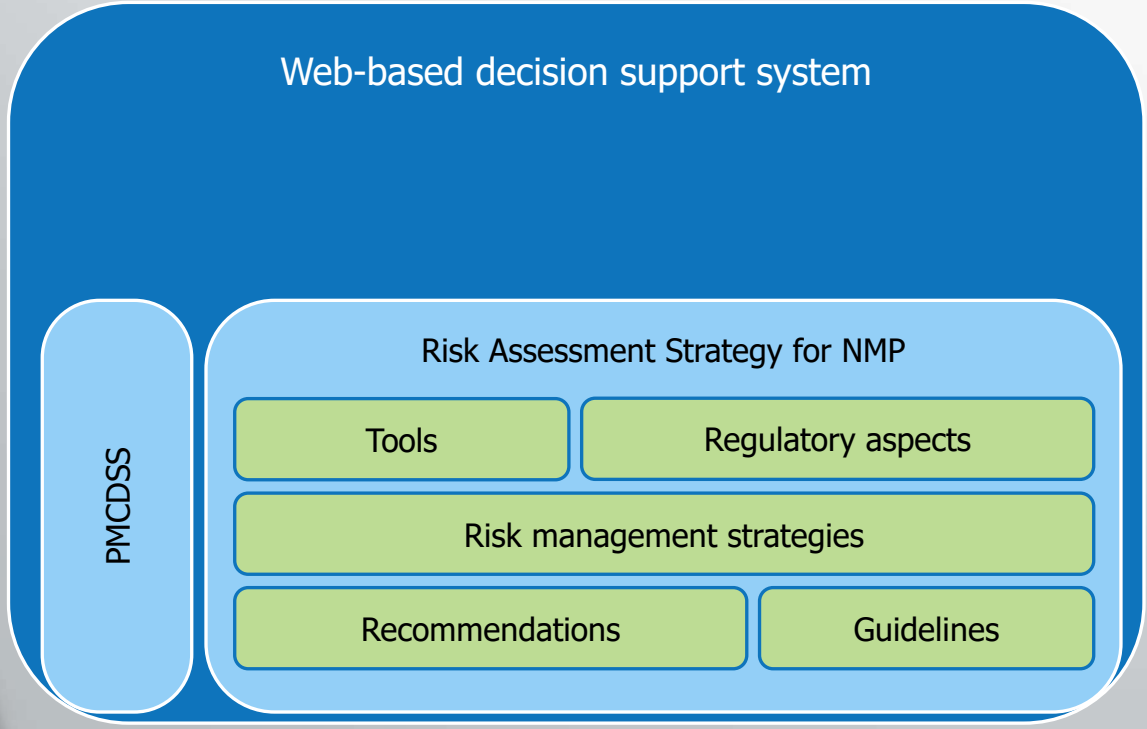
- **no significant effects on cell viability + cell membran integrity** (unless particles have a microbial biofilm or are coated by biofilms, contaminants or simlated digestive fluids)
- **minor inflammatory responses of the immune system** and **no oxidative stress** in granulocyte like cells (white blood cells), still to be confirmend for lung and GIT cells
- **MPs changed gut microbiota and are transformed and a biofilm formed on MPs surface** (planned to compare gut microbiome of healthy and unhealty patients)
- **MNP was taken up + bioaccumulated**, e.g., in RT and GIT cells but not in THP1 cells (immune system), also depending on biofilms, eco-corona etc.

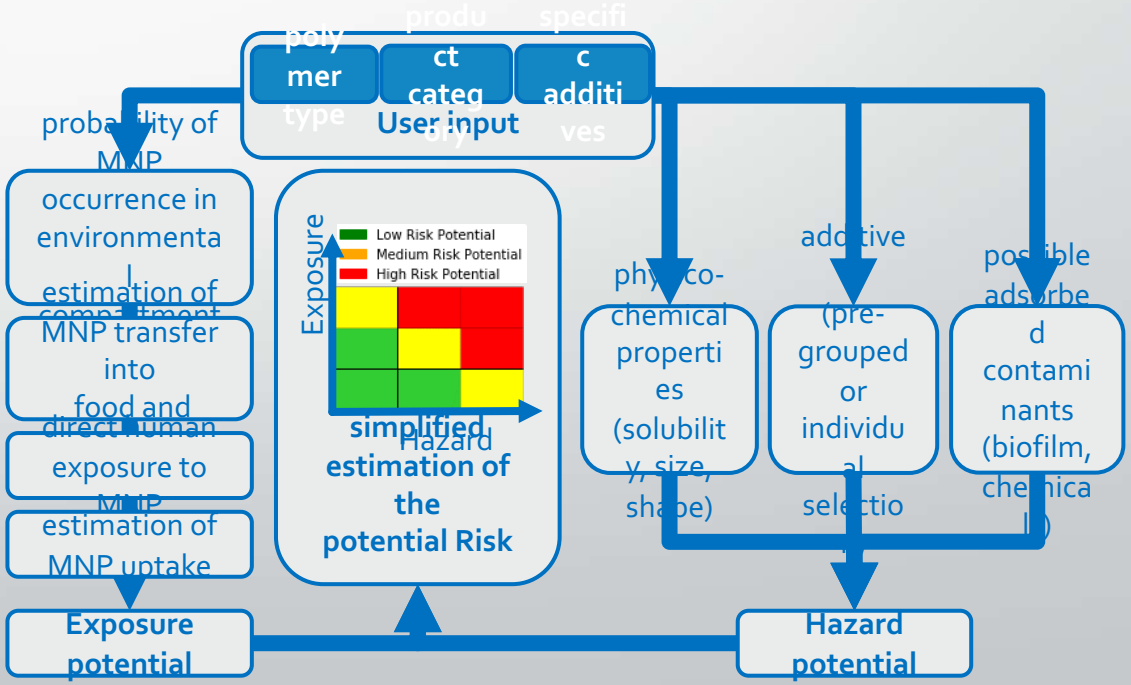
Still need to verify the *in vitro* by in vivo (mice) studies, **and look into** long-term exposure effects, more real-world plastics, leaching of additives and contaminants, mixture effects, effects of biofilms, mucus and ecocorona, realistic exposure concentrations, dosimetry etc.

Integrated risk assessment strategy for MNPs and A/C

Integrating the newly developed data and methodology into a **novel human and environmental risk assessment strategy** that is based on:

- **MNP and A/C specific IATAS**
- **web-based platform with decision trees**
- **PMCDS system to guide end-users during early design and production**

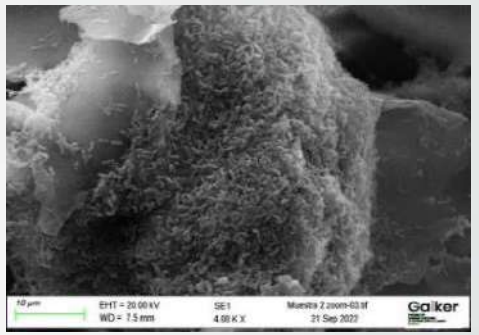




Case studies to assess feasibility of developed methods

Case study on occupational exposure monitoring

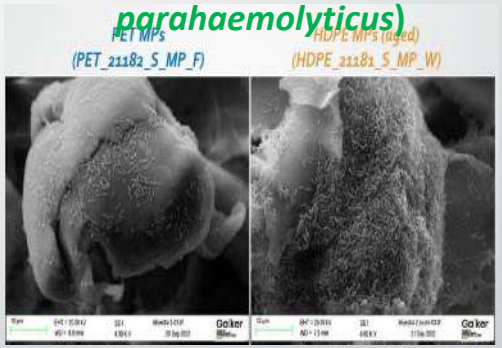
- **8 air collection campaigns at various plastic production, use, recycling and packaging sites, and a water treatment plant**



Case study on microbial colonisation of MNP as vectors for potential pathogens

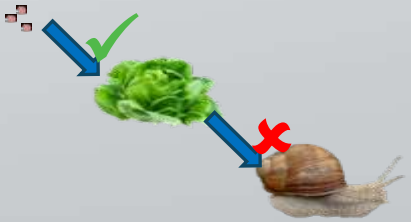
- **Various types of MNPs and bacterial strains (marine, fresh and wastewater) used for colonization:** biofilm formation + antibacterial resistance gene transfer observed in bacteria growing on MPs

Marine water (*V. parahaemolyticus*)



Case study on long-term effects after exposure to food and air

- **PS uptake in lettuce showed no further transfer to snails**
- **Occupational exposure and human biomonitoring studies at workplaces using MNP-specific biomarkers for inflammation and oxidative stress** to study human health effects at realistic conditions



PlasticsFatE

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CUSP

The European research cluster to understand the health impacts of micro- and nanoplastics

These projects have received funding from the European Union's Horizon 2020 research and innovation program.

Who are we and what are we doing?

- **5** Large-scale EU funded research projects 2021 – 2024/5
- **75** Organisations from **21** Countries
- contribute to human health-relevant policies, regulation and standardization of micro- and nanoplastics:
  - European Strategy for Plastics in a Circular Economy and the
  - Bioeconomy Strategy, as well as
  - New REACH restrictions on intentionally added MNPs to products,

by providing a **robust and comprehensive scientific database** and **new scientific-based evidence for better preventive policies** to ensure **safe and sustainable handling, use, and disposal of plastic products**

Focus of the 5 CUSP projects

AURORA: Health impacts of MNP related to **early human life (placenta, fetus)**

IMPTOX: Health effects of MNP related **asthma and allergic diseases**

PlasticHeal: Health impacts **of MNP** related to **mode of action and genotoxicity**

PlasticsFatE: Human exposure to MNP related to **fate and effects in the human body**

Polyrisk: Human exposure and hazard of MNP related to **immune effects**

CUSP Working Groups (WG)

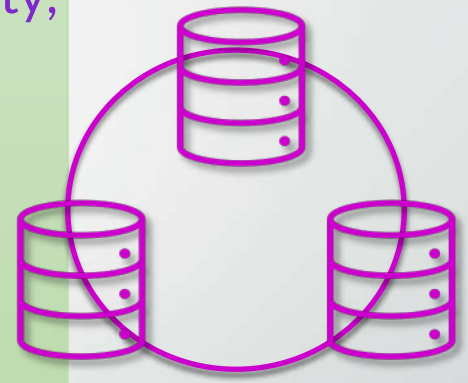
Cross-project cooperation and coordination:

- WG1 Methods and materials
- WG2 Data sharing and management
- WG3 Interlaboratory studies (ILS)
- WG4 Exposure assessment
- WG5 Risk assessment
- WG6 Communication and dissemination
- Sub-WG on human biomonitoring
- Sub-WG on in vitro, ex vivo, and in vivo testing

Standardisation relevance of CUSP research

Make obtained exposure and hazard data open and FAIR for end-users (policy and decision makers, industry, regulatory bodies, scientific community, standardization, NGOs)

- enable prediction of health outcomes based on particle characteristics
- or the identification of the properties linked to human health effects
- or for human biomonitoring, clinical and epidemiological studies



Perform Interlaboratory studies (ILS) for method validation, harmonization of protocols and standardization within VAMAS TWA 45, to contribute to ISO 24187:2023 Principles for the analysis of microplastics in the environment, or ISO/CD 16094-3:2023 on analysis of microplastic in water

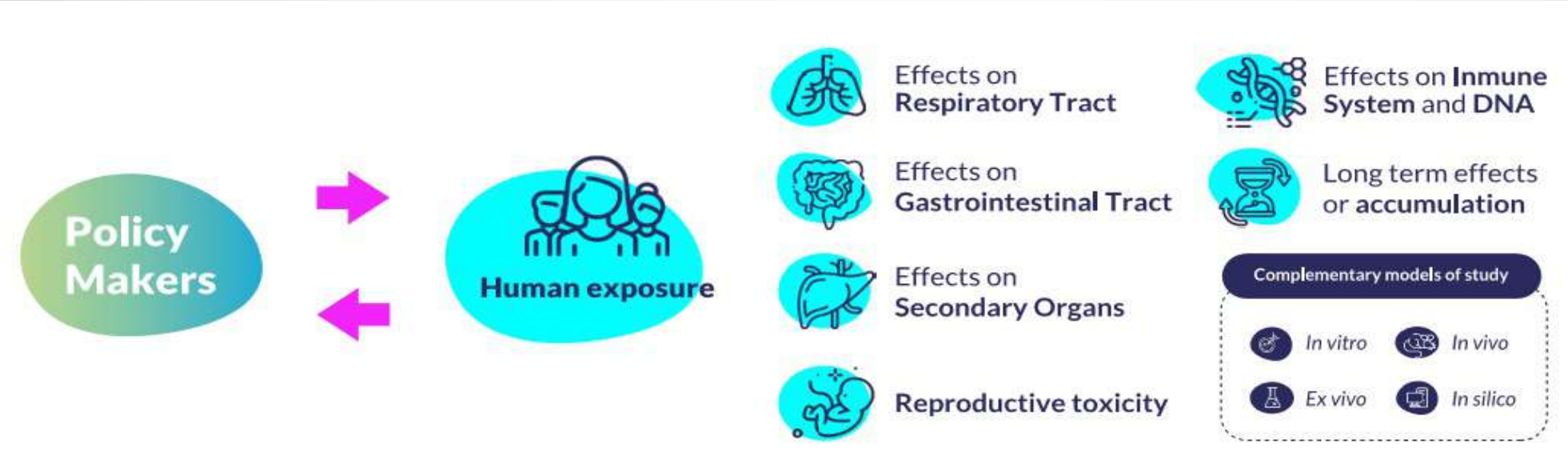
Largest ILCs on MPs organised under VAMAS TWA 45 on standardized methods for characterisation of microplastics (over 85 participants from over 20 countries)

Regulatory relevance of CUSP research

Support regulations addressing environmental concerns of plastic use and disposal:

- the Single-use Plastics Directive
- the Restriction of microplastics intentionally added to products
- REACH Chemicals Directive
- the EU Drinking Water Directive
- The Urban Wasterwater Treatment Directive

→ to ultimately reduce environmental emissions and the impact of MNP on human health



Visual summary of the data generated in CUSP

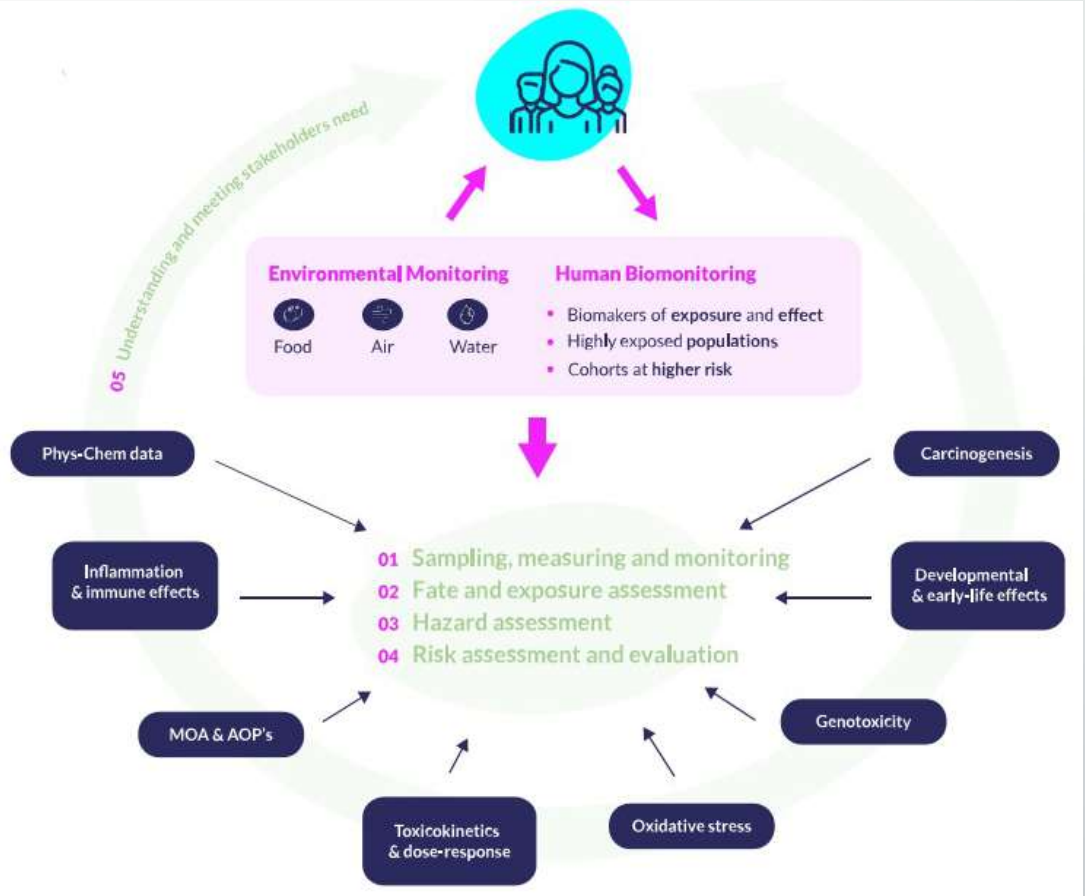
Policy relevant of CUSP research

CUSP contributions to policy are grouped across these areas:

1. Sampling, measuring, and monitoring;
2. Fate and exposure assessment;
3. Hazard assessment;
4. Risk assessment and evaluation and
5. Understanding and meeting stakeholder needs

CUSP's findings inform these main EU policy and legislative areas:

1. Chemicals
2. Plastics
3. Food
4. Water



CUSP

The European research cluster to understand the health impacts of micro- and nanoplastics

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