plasticheal

Development of Framework for Risk Evaluation

DTU
Steffen Foss Hansen

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 965196

Framework For Risk Evaluation

Aim: Innovative tools to study the impact and mode of action of micro and nanoplastics on human health: towards a knowledge base for risk assessment

Tasks:

- T 7.1 Stakeholder consultation for problem identifcation refinement and question formulation (Jul. 2022)
- T 7.2 Gap analysis (Mar. 2023)
- T 7.3 Scientific input (from WP16) to MNPLs risk assement (Mar. 2025)
- T 7.4 Risk assessment framework development (Mar. 2025)

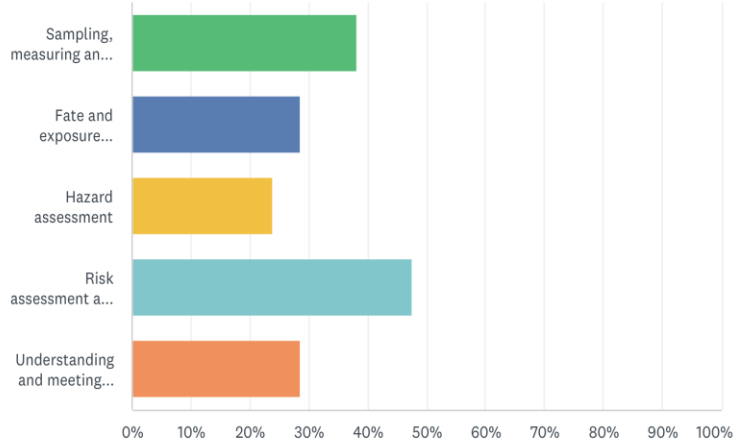
Task 7.1 Problem refinement through Stakeholder survey

- Reached out to stakeholders
  - Online survey
  - Followup interviews
- Key questions
  - Most important knowledge gaps
  - Most important research needs from a regulatory perspective?
  - Regulatory gaps?
- Next activities
  - Follow interviews
  - Open online survey

https://www.surveymonkey.com/r/3DSRJVZ

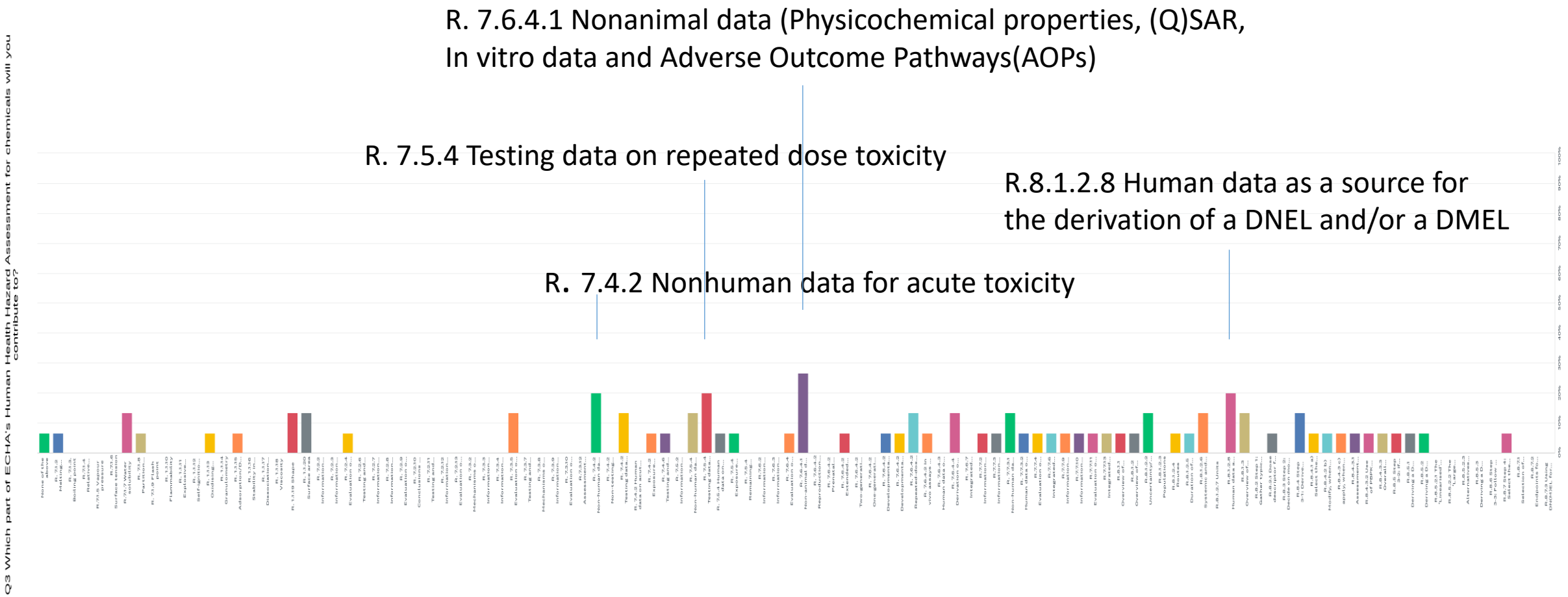
What do you consider to be the most important knowledge gaps when it comes to plastic pollution?

Answered: 21 Skipped: 6



ANSWER CHOICES	RESPONSES	
Sampling, measuring and monitoring	38.10%	8
Fate and exposure assessment	28.57%	6
Hazard assessment	23.81%	5
Risk assessment and evaluation	47.62%	10
Understanding and meeting stakeholder needs	28.57%	6
Total Respondents: 21		

CUSP Survey: Which part of ECHA's Huamn Health Hazard Assessment for Chemicals will you contribtube to?



What was no one looking at initially?

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R. 7.1.3. Boiling point	R. 7.2.2 Information requirements on skin corrosion/irritation	R.8.1.2.3 Populations
R.7.1.5 Vapour pressure	R. 7.2.3 Information sources on skin corrosion/irritation	R.8.1.2.7 Units
R.7.1.6 Surface ten	R. 7.2.6 Testing and assessment strategy for skin corrosion/irritation	R.8.3 Step 2: Decide on mode of action (threshold or non-threshold) and which next step(s) to choose
R. 7.1.9 Flash p	R. 7.2.7 Information requirements for seri eye damage/eye irritation	R.8.5.2.1 The 'Linearised'
R. 1.1.10 F	R. 7.2.8 Information sources on serio nage/eye irritation	R.8.5.2.2 The 'Large Factor' approach ("EFSA
R. 1.1 e properties	R. 7.2.9 Evaluation of information eye damage/eye irritation	R.8.5.2.3 Al the conven polation procedures
R -ignition temperature	R. 7.2.10 Conclusions on ser nage/eye irritation	R.8.5. g a DMEL for a non-thresho carcinogen/mutagen, without adequate cancer data
R. Granulometry	R. 7.2.11 Testing and as tegy for serious eye damage/eye irritation	R.8.6 Step 3-3: Follow a more qualitative approach when no dose descriptor is available for an endpoint
R. 1.1.17 Dissociation constant	R. 7.2.12 Informatic n respiratory tract corrosion/irritation	R.8.7.1 Selection of the critical DN(M)EL
R. 1.1.18 Viscosity	R. 7.2.13 Evaluation o rmation on respiratory tract corrosion/irritation	R.8.7.2 Endpoints for which no DNEL/DMEL can be derived
	R. 7.3.2 Mechanisms of skin sensitisation	R.8.7.3 Using DN(M)EL for human exposure patterns
	R. 7.3.3 Information requirements for skin sensitisation	
	R. 7.3.4 Information sources on skin sensitisa n	
AURORA	R. 7.3.7 Testing and assessment strategy nsitisation	
	R. 7.4.2 Non-testing data for acute t	
	R.7.6.2 Information requiremen g approaches for reproductive toxicity	
	R. 7.6.3 Information so roductive toxicity	
	R. 7.6.4.2 Reprod pmental toxicity screening test	
	R. 7.6.4.2 Prenata pmental toxicity study	
	R. 7.6.4.2 Two-gene ation reproductive toxicity study	
	R. 7.6.7 Integrated Testing Strategy (ITS) for reproductive toxicity	

Basic properties

Skin and Eyes

MoA and DNELs

Reproductive tox

Plasticheal

Task 7.2 Key risk assessment and regulatory issues and gaps identified

- Application and appropriates of definitions
- Relevance of existing tonnage thresholds
- Suitability of current information requirements
- Limitations of existing decision support tools e.g., risk assessment
- Appropriateness of risk management procedures
- Adequate monitoring requirements and reliable monitoring methods

Policy Brief # 1: How can Plasticheal and CUSP address Gaps?

CUSP

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

www.cusp-research.eu
hello@cusp-research.eu
https://doi.org/10.5281/zenodo.7101443

Policy brief

REGULATORY RELEVANCE OF THE EUROPEAN RESEARCH CLUSTER TO UNDERSTAND THE HEALTH IMPACTS OF MICRO- AND NANOPLASTICS (CUSP)

Micro- and nanoplastics: substances of public health concern?

The presence of micro and nanoplastics (MNPs) is part of our everyday life and they find their way into our bodies through the air we breathe, the water we drink and the food we eat. It is not known how MNPs might be affecting human health. Policymakers and regulatory authorities around the world are increasingly implementing regulatory measures to address this concern. For instance, policymakers in the EU have adopted the Single-use Plastics Directive to reduce the environmental impact of certain forms of plastics used once or for a very limited period of time, such as straws, cutlery, plates, cotton swabs and balloon sticks[1].

1 Directive (EU) 2019/904

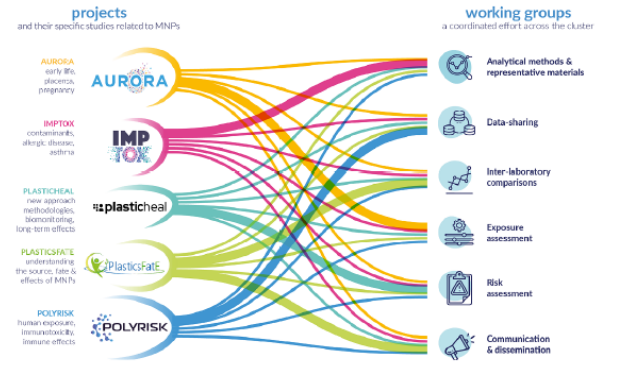


Figure 1: The five large-scale research projects united under CUSP and the CUSP working groups.

These projects have received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreements AURORA nº 964827, IMPTOX nº 965173, PLASTICHEAL nº 965196, PLASTICFATE nº 965367, POLYRISK nº 964766.

Chemicals

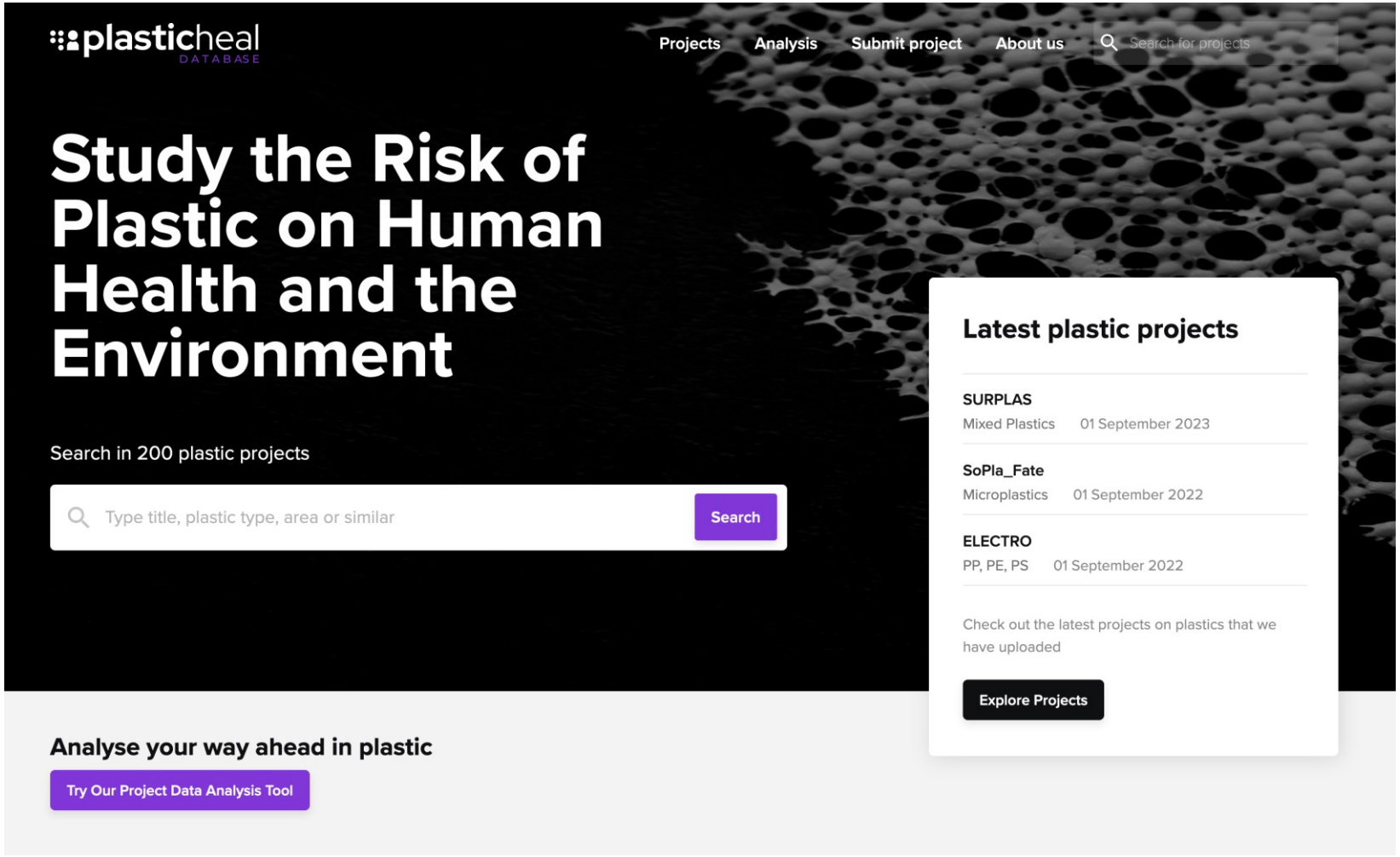
Zero pollution action plan	CUSP will establish whether there are any potential human health risks associated with MNPs and absorbed/desorbed/adsorbed contaminants. This will help in the identification and elimination of pollution sources and reduce consumer and occupational exposure to e.g., carcinogenic and endocrine disrupting substances.
Chemicals Strategy for Sustainability	CUSP will develop methodologies for chemical risk assessment that consider the whole life cycle of substances, materials and products and develop risk evaluation frameworks that can facilitate the development of safe and sustainable alternatives.
REACH Regulation (EC) No 1907/2006	CUSP will assist in the operationalization of a practical definition of a synthetic polymer and guidance on how to complete human risk assessment of MNPs. CUSP will furthermore assist regulators in specifying the information requirements that should apply to MNPs under REACH in the future. Analytical methods will be developed to determine the presence and risks of synthetic polymer microparticles (≤ 5 mm in size) intentionally added to products including cosmetic products, detergents and maintenance products, paints and coatings.
Classification labelling and packaging (CLP) Regulation (EC) No 1272/2008	Data and information on human health risks of MNPs generated in CUSP will be compared to current CLP criteria and Regulation
Horizon Europe Mission on Cancer	CUSP will help establish potential cancer risks associated with MNPs and absorbed/desorbed/adsorbed contaminants.
Chemical Agents Directive (98/24/EC) EU Strategic Framework on Health and Safety at work 2021-2027	The data on occupational exposure and health effects of MNPs generated in CUSP may be utilised when considering occupational exposure control plan e.g., by setting occupational exposure limit values.
Carcinogens and Mutagens Directive (2004/37/EC)	The data generated on potential genotoxicity and carcinogenicity of MNPs in CUSP may be utilised to conclude whether these materials should be considered as mutagens or carcinogens.

Plastics

EU Plastic Strategy COM 2018/028	CUSP will help address the unknown impacts on human health of microplastic noted in the EU Plastic Strategy, as well as the effect of littering and leakage from plastic waste as possibly affecting human health through the food chain.
Single Use Plastics Directive (EU) No 2019/904	CUSP will help in assessing the risks stemming from environmental exposure of MNPs e.g., seafood, sea salt.
Bioeconomy Strategy	CUSP will assess applications where the use of eco-friendly, biodegradable or compostable plastics and nanocelluloses can be considered less harmful compared to HDPE, PP, PET and PA. Harmonised methods will be developed to measure unintentionally released MNPs and increase our capability to observe, measure and monitor progress made towards a sustainable plastics bioeconomy.

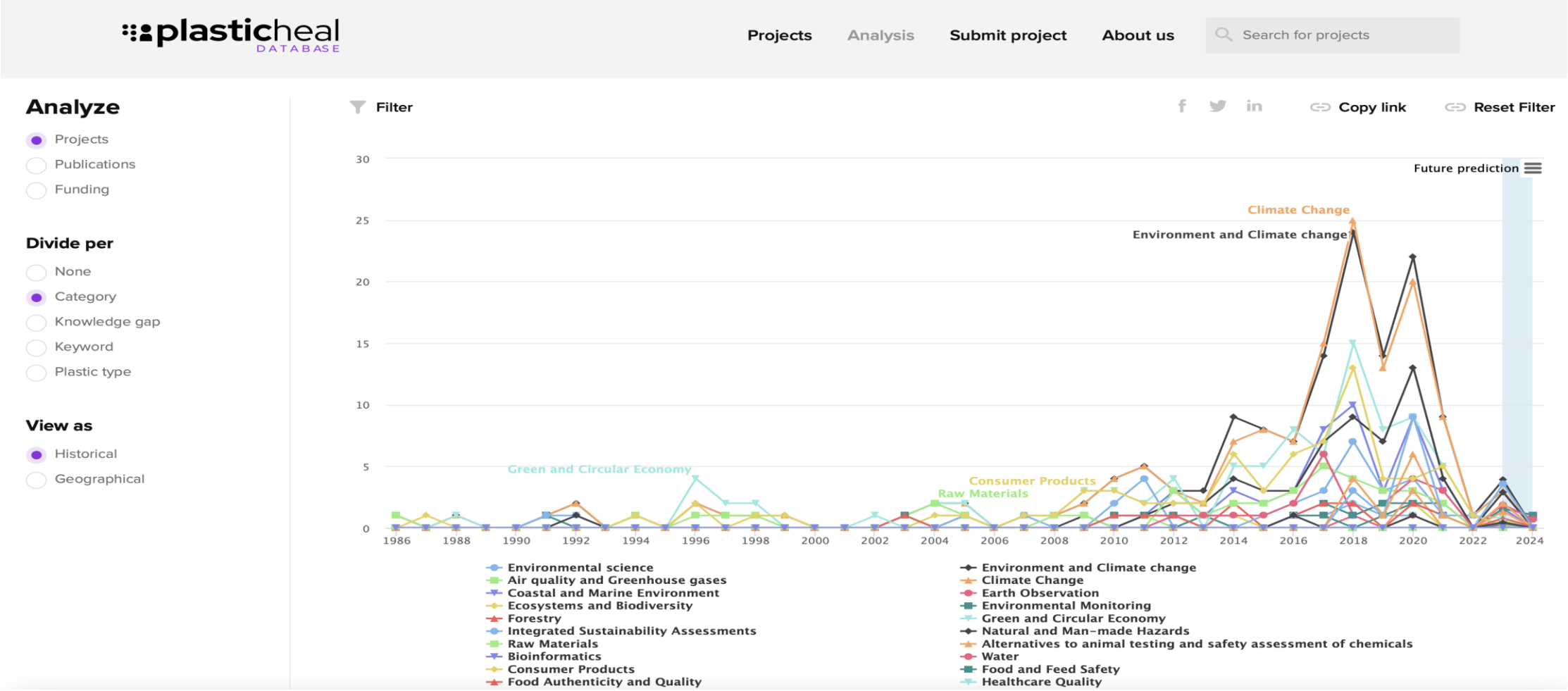
Find it at https://cusp-research.eu/resources/

Ensuring Policy Relevance throughout - Plasticheal database

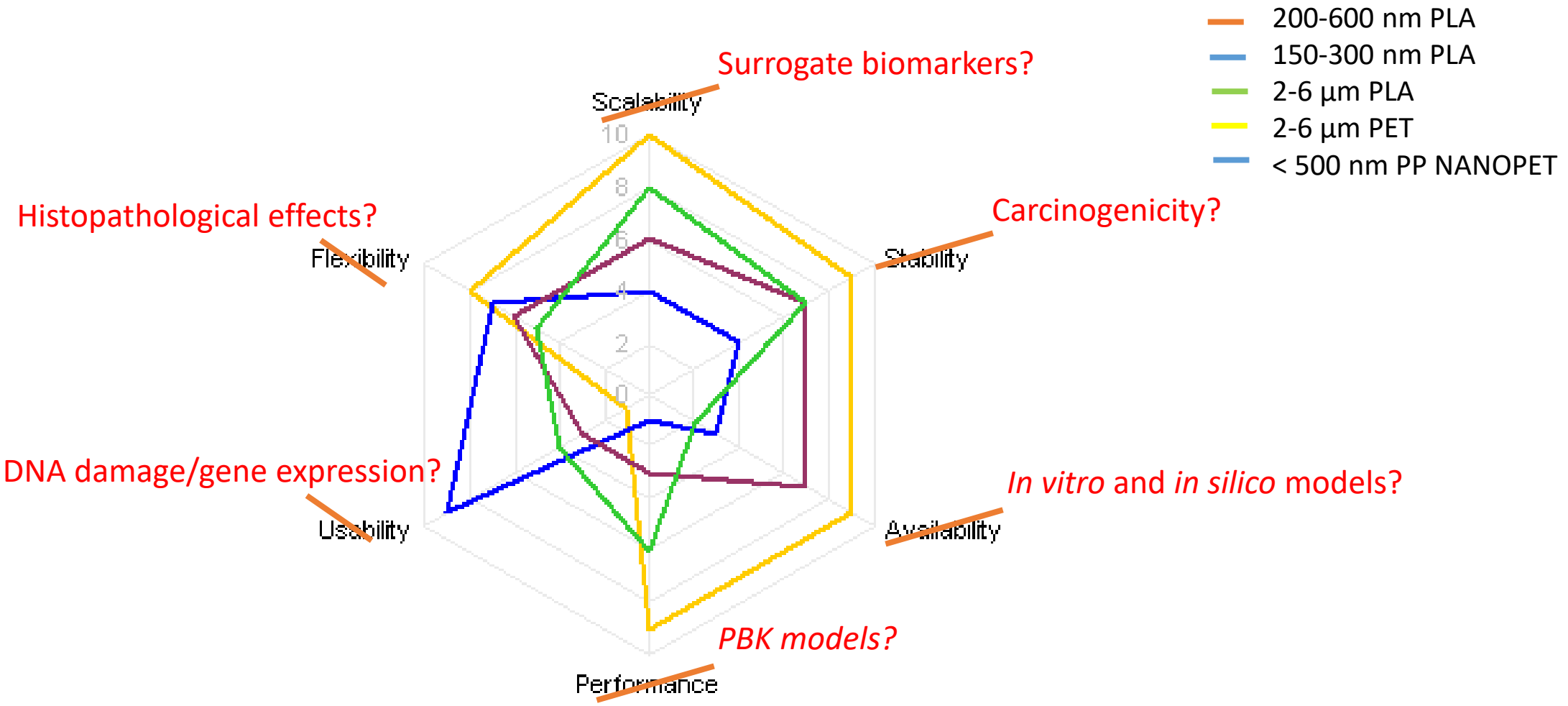


www.plasticheal.dk

Work in Progress



How do we display the wealth of PlasticHeal information? Preliminary idea



Twitter
Instagram
LinkedIn
YouTube

@plasticheal

Thank you
for your attention!

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www.plasticheal.eu

Actionable European Roadmap for Early-life Health Risk Assessment of Micro- and Nanoplastics

Virissa Lenters, Assistant Professor

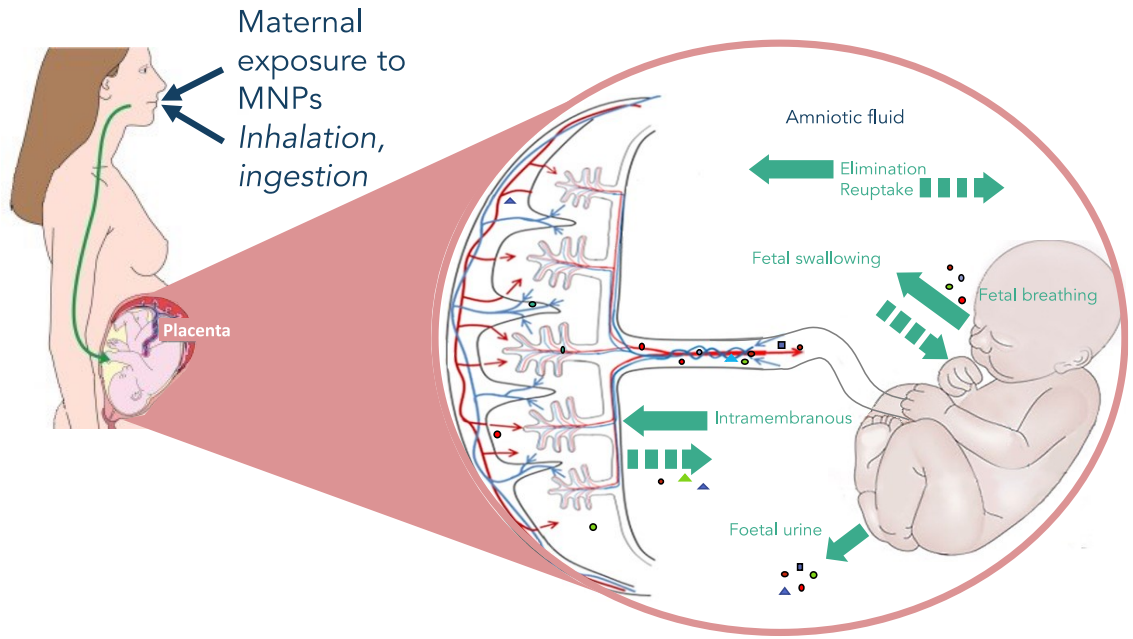
On behalf of Prof. Roel Vermeulen, UMC Utrecht / Utrecht University

And the AURORA consortium

This project has received funding from the European Union's Horizon 2020 research and innovation programme under AURORA grant agreement No 964827

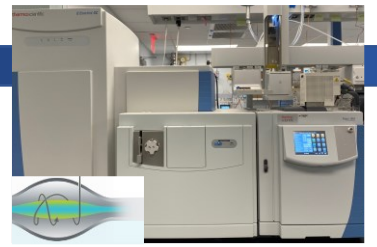
AURORA project

- Focusing on
  - Vulnerable periods of **pregnancy & early-life**
  - Advancing **analytical methods** for measuring MNPs in human tissues
  - Developing **roadmap for** human health **risk assessment**: early-life

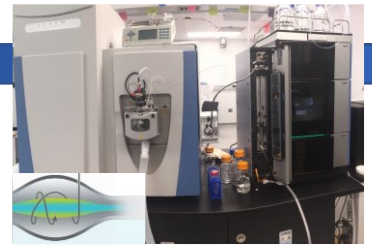


Advancing exposure assessment

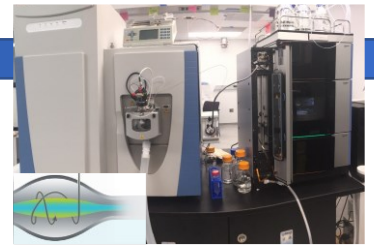
Population biomonitoring



Pyrolysis GC-HRMS



DP LC-HRMS

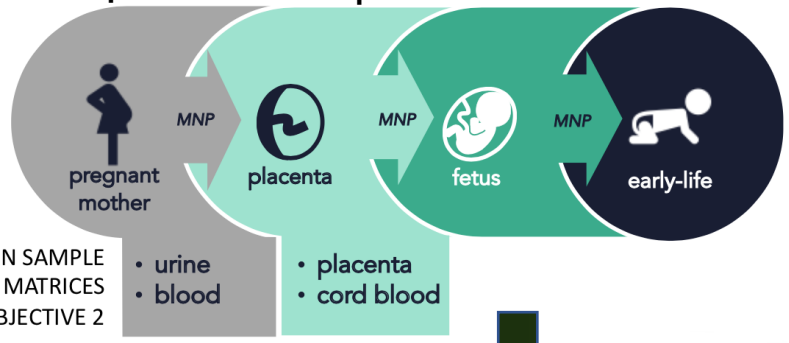


SM LC-HRMS

Population exposure burden and distribution

Maternal Exposures

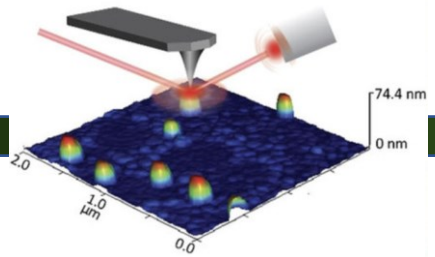
Fetal Exposures



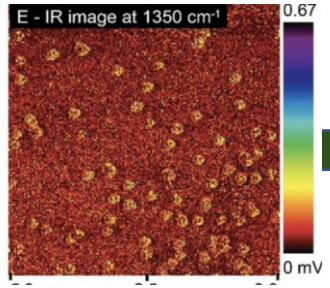
HUMAN SAMPLE MATRICES OBJECTIVE 2

- urine
- blood
- placenta
- cord blood

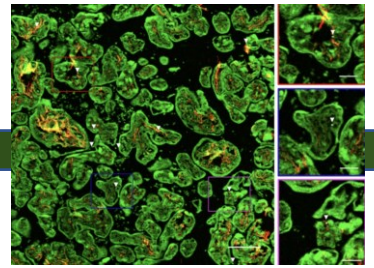
Deep MNP characterization



Forced microscopy



AFM-IR

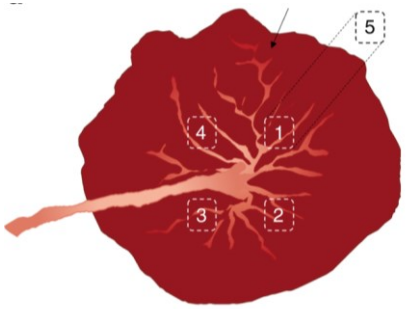


In-situ MNP imaging

Tissue localization and MNP morphology

Slide courtesy of Douglas Walker

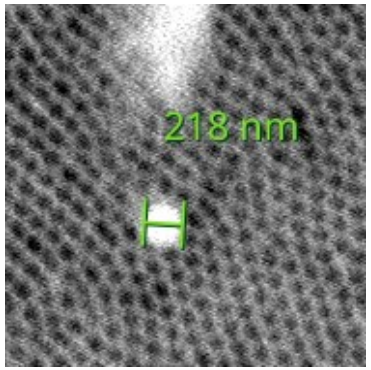
Characterisation & mass-based quantification in placenta

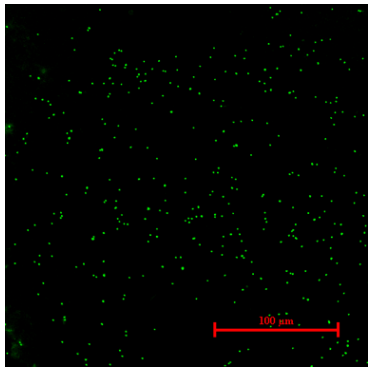


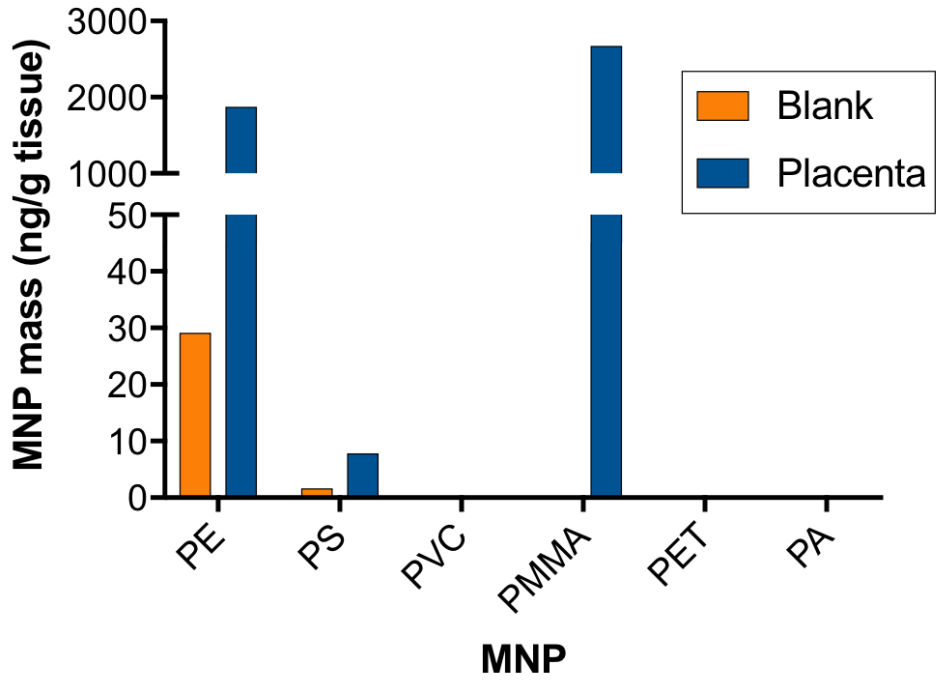
Sample collection and preparation

→

Morphology
Chemical composition
Surface chemistry
State of degradation
Quantity



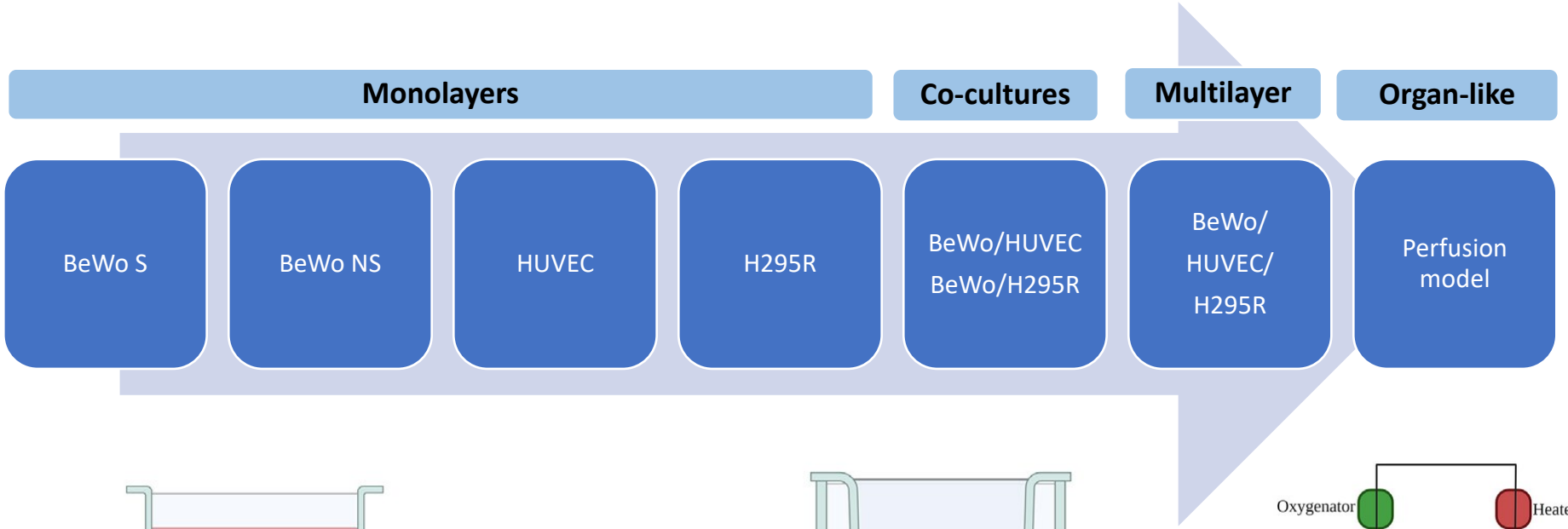


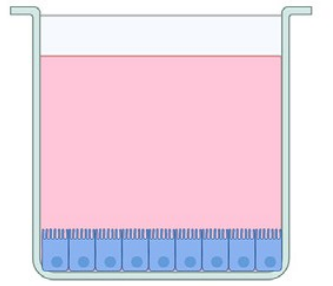


Double-shot pyrolysis with nontargeted GC-HRMS

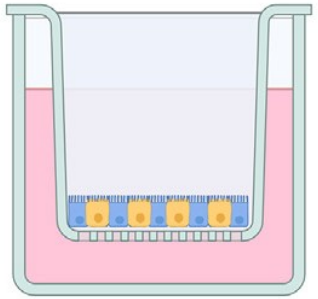
Laura Zoutendijk, Laurens Mandemaker, Florian Meier (Utrecht University, in preparation)
Anna Robuck, Brooklynn McNeil, Zoe Coates-Fuentes, Douglas Walker (Emory University, in preparation)

Toxicology: placental models of increasing complexity

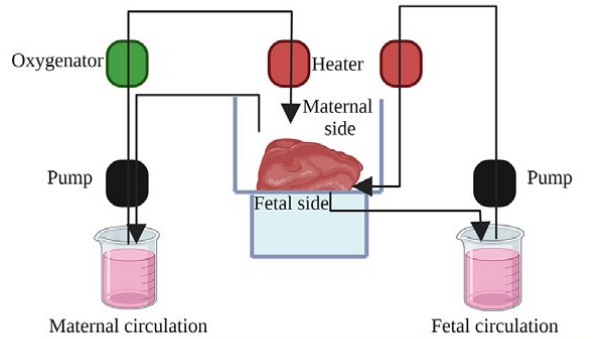




Mono-culture



Transwell co-culture
(direct)



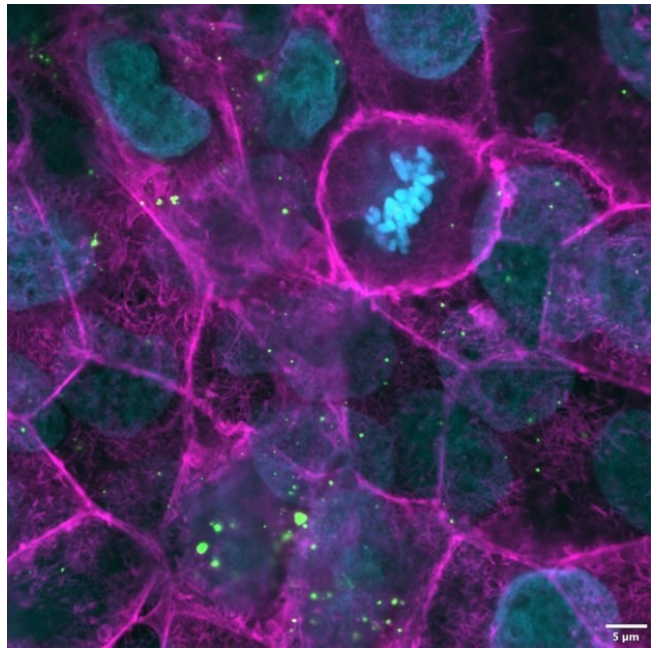
Dually perfused placental cotyledon

MNP uptake/transport, effects on placental integrity/function:

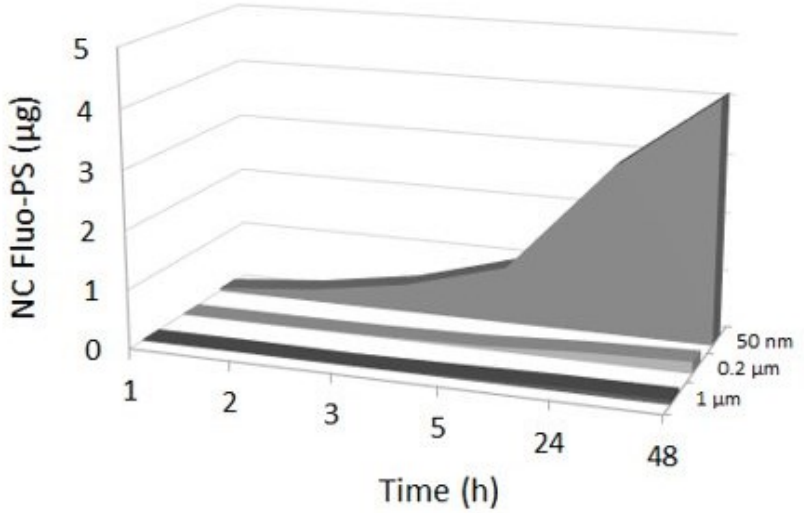
endocrine function, metabolism, immune responses, premature aging...

Toxicology: placental models of increasing complexity

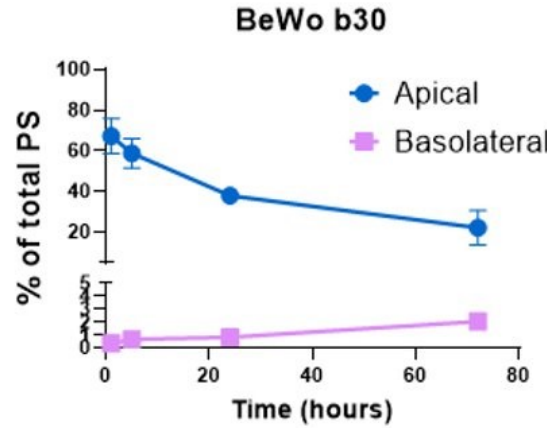
Uptake: PDI-PVC
avg. 0.15 µm (100 µg/mL)



Transport over BeWo
monoloayer (Fluo-PS)



Barrier integrity
(72 h 10 ug/Ml Fluo-PS)

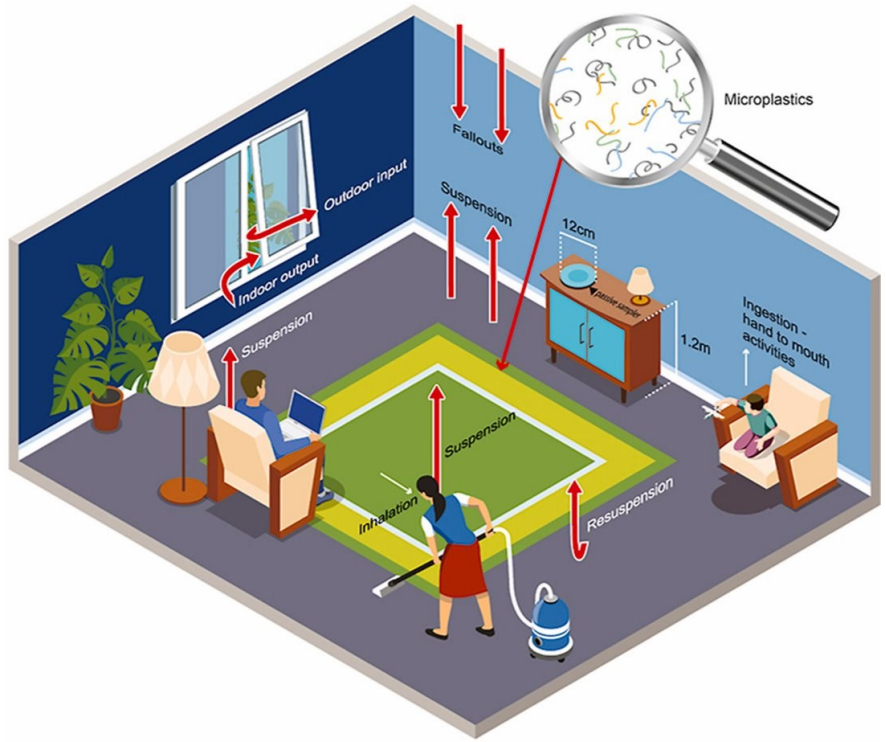


Hanna Dusza, Prof. Juliette Legler (Utrecht Uni.), Jeske van Boxel, Majorie van Duursen (VU Amsterdam), Markus Forsberg (Uni. Eastern Finland)

Human observational epidemiological studies

- **Birth cohorts (BE, ES): associations with health outcomes**
  - Placenta & cord blood: MNP levels
  - Associations with
    - Placental function, blood flow
    - Immune-inflammatory responses, oxidative stress
    - Accelerated aging, endocrine function
    - Metabolomics
    - Fetal growth, metabolic disorders, development

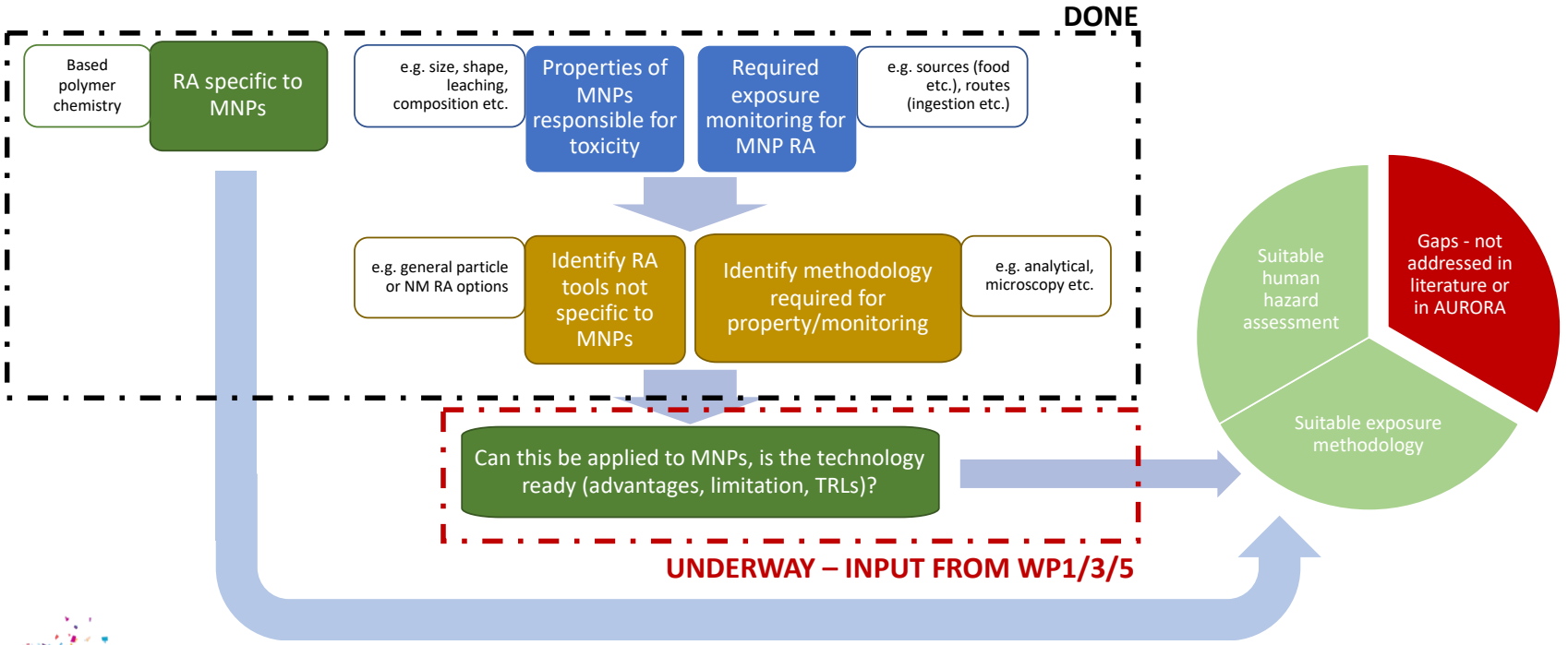
- **Adult women: determinants of exposure (NL)**
  - Women 18-45 years of age, questionnaire on home environment, food preparation/packaging, etc.
  - Repeat sampling: dust, blood, urine

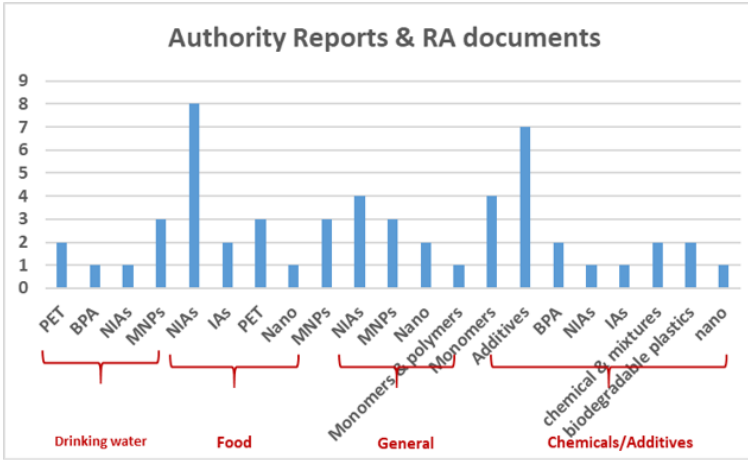


Soltani et al. Quantification and exposure assessment of microplastics in Australian indoor house dust. *Environ Pollution* 2021

Roadmap to risk assessment

- Systematic evidence mapping: adequacy of available regulatory risk assessment tools
- End of project: recommendations to advance risk assessment & management of MNPs





Consortium

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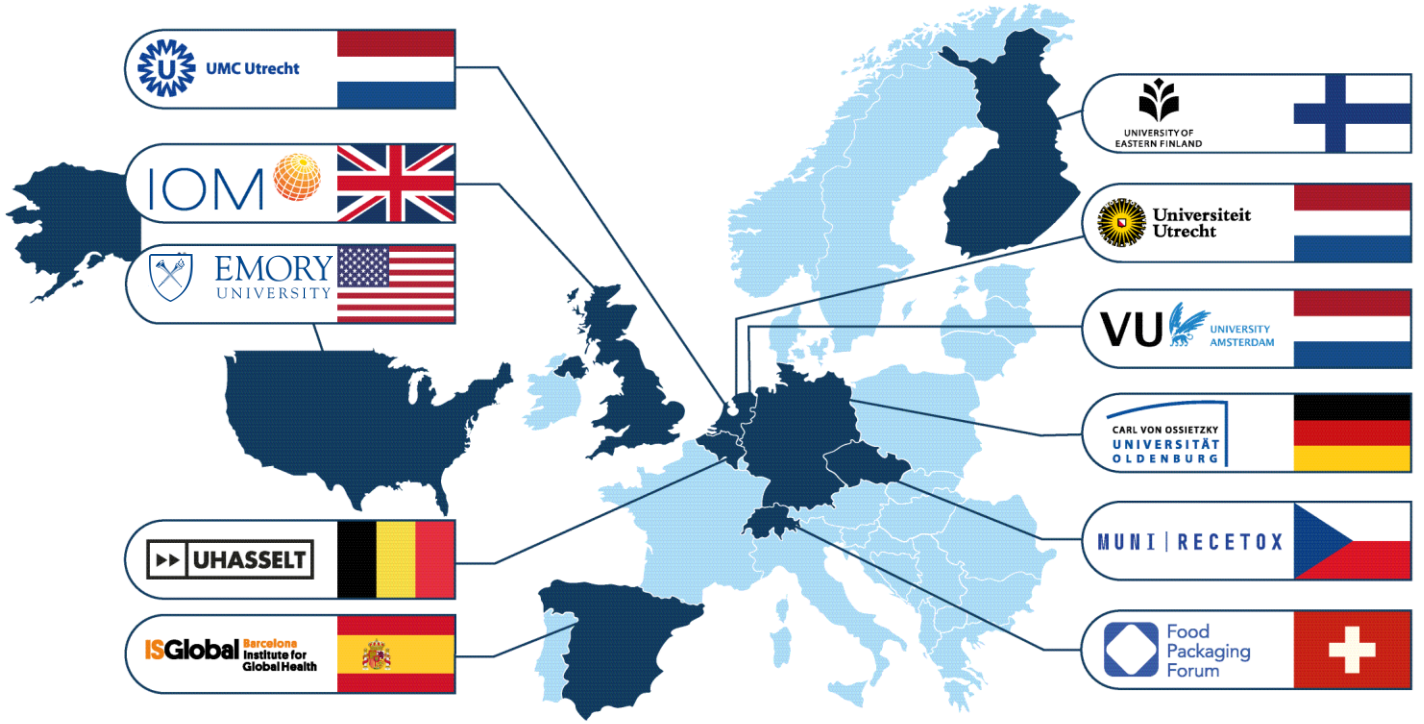


The AURORA project has received funding from the European Union's Horizon 2020 research and innovation program under AURORA grant agreement No 964827.

CUSP thematic workshop on risk assessment and regulation

7 February 2023

Relevant PlasticsFatE activities and contributions

Rudolf Reuther (ENAS), Dana Kühnel (UFZ) and Lesley Tobin (OPTIMAT)

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

PlasticsFatE in a nutshell

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)

Duration: 1 April 2021 – March 2025

Budget: 6 million EUR

Overview of the flow of work towards risk assessment

WP7 (Rudolf Reuther, ENAS) **Scientific coordination,** (Mark Morrison, OPTIMAT) **Project Coordination,** (Nadine Bresch, ERS) **project management**

WP1 (Anna Costa, CNR) **Material selection and physicochemical characterization**

WP2 (Raquel Portela Rodriguez, CSIC) **Fate and Exposure assessment**

WP3 (Anani Johnny Komlavi Afanou, STAMI) **Hazard assessment**

WP4 (Dana Kühnel, UFZ) **Risk assessment and management**

WP5 (Arantxa Ballesteros Riaza, ITENE) **Demonstration of sustainable solutions (case studies)**

WP6 (Lesley Tobin, Optimat) **Dissemination, exploitation and impact of results**

WG1. Analytical methods and representative materials

WG2. Data sharing

WG3. Inter-laboratory comparisons

WG4. Exposure assessment

WG5. Risk assessment

WG6. Communication and Dissemination

CUSP cluster

PlasticsFatE test material repository established: First and second set of MNP particles (PS, PE, PP, PET) ➔ **different sizes, shapes and compositions** (18 test materials)

Basic physicochemical characterisation of representative test materials performend (particle size and morphology, particle composition, surface chemistry, specific surface area, density, crystallinity) and **Technical data sheets** established.

Dispersability of test materials examined by preparing **stock + working dispersions** and **testing synthetic** (Sodium Surfactin, Tween, Triton) and **natural surfactants** in biological relevant fluids (simulated lung or gastrointestinal tract surfactants, human/bovine albumin or human/calf serum) **mimicking real matrices**.

Applicability of different methods tested to detect, identify and quantify MNPs in real matrices: to **understand their behaviour and influence of their properties on effects in the human body**

Two internal inter laboratory comparison (ILC) studies in preparation within VAMAS **to validate MNP size measurement** by diffraction laser (MPs) and DLS (NPs also at CUSP level ➔ **contribution to method standardization** (e.g. ISO/CEN, OECD, VAMAS)

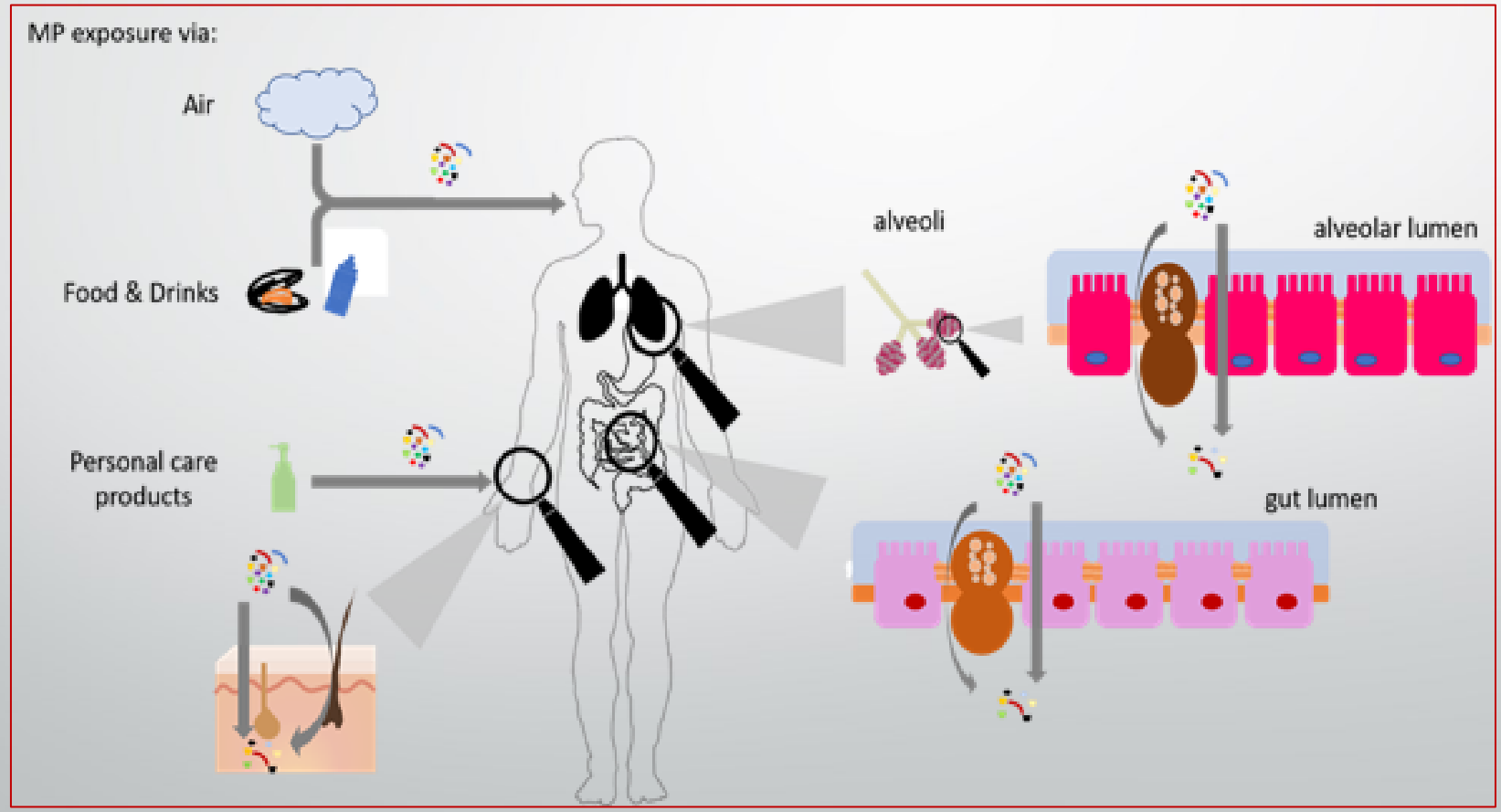
First and second set of MNP test materials of different sizes, shapes and compositions

	Polymer type	CODE	Supplier	Storage (Aliquot)	Polymer size (D50)	Polymer shape	Powder (P) / Dispersion (D)	Aged
Benchmark	PS	PS_93470720010350_NE_L-Eu	Thermofisher by Distrilab*	now at STAMI	0,3 µm	Spherical	D (1%)	no
Primary	UHMW-PE	UHMWPE_16191_P-MP_P	BAM	BAM (1 -50g)	145 µm	round (cloud shape)	P	no
	UHMW-PE	UHMWPE_16186_P-MP_P	BAM	BAM (1 -50g)	57 µm	round (potato shape)	P	no
	UHMW-PE	UHMWPE_16190_P-MP_P	BAM	BAM (1 -50g)	22 µm	round (popcorn shape)	P	no
	LD-PE	LDPE_16242_P-MP_P	BAM	BAM (1 -50g)	< 75 µm	round	P	no
	HDPE	HDPE_296_P-MP_P	Ceridust by Clariant*	1 Kg BAM/ 1 kg ISTEC	5 µm	round	P	no
Secondary	HDPE	HDPE_21181_S-MP_W	BAM	BAM (< 1g)	60 µm	irregular, flat	P	yes
	PET	PET_21180_S-MP_F	BAM	BAM (< 1g)	44 µm	irregular	P	no
	PET	PET_21182_S-MP_F	BAM	BAM (< 1g)	130 µm	irregular	P	no
	PET	PET_21183_S-MF_F	BAM	BAM (< 1g)	70 µm	irregular	P	no

	Polymer type	CODE	Supplier	Storage	Polymer size (D50)	Polymer shape	Powder (P) / Dispersion (D)
Primary (synthetic route)	Nano-PE	PE_490_P-NP_W	BAM (10 ml)	BAM	180 nm	Round	D (30 µg/ml)
	Nano-PE	PP_491_P-NP_W	BAM (10 ml)	BAM	180 nm	Round	D (75 µg/ml)
	Nano-PET	PET_b001_P-NP_F	CSIC* (10 ml)	CSIC	69 nm	Spherical	D (4,9 mg/ml)
	Nano-PET	PET_c001_P-NP_F	CSIC* (10 ml)	CSIC	77 nm	Spherical	D (1,6 mg/ml)
Secondary (milled/sieved)	Micro-PET	PET_001_S_MP_F	CSIC** (1-20g)	CSIC	300 - 500 µm	Irregular	P
	Micro-PET	PET_001_S_MP_F _sterile	CSIC** (1-20g)	CSIC	300 - 500 µm	Irregular	P
	Nano-PET	PET_002_S_NP_F	CSIC** (100 ml)	CSIC	50-2000 nm	Irregular	D (2,5 mg/ml)
	Nano-PET	PET_002_S_NP_F_sterile	CSIC** (100 ml)	CSIC	50-2000 nm	Irregular	D (2,5 mg/ml)

Assess main exposure sources, levels and routes of MNP in the human body:

Air → lung, food/water → gut and PCP → skin



Screeening of exposure levels of MNP in food and drinking water from several European countries initiated

Protocols developed to assess fate of MNP in GI tract after oral exposure by a **static (infogest) and a dynamic (simgi®) model**

Investigating of human tissues from medical programs: if and how MNP translocate from primarily exposed organs (GI, lung, skin) **into surrounding tissues and secondary organs** (kidney, lymph nodes, liver, etc.)

Follow-up of MNP excretion (faeces and urine)

Air sampling and analysis of MNP in different working environments by different air sampling devices **resembling human inhalation** and **the inhalable and respirable fraction** of nanoplastics

Fate modelling ("SimpleBox4MP&NP"), **Physiologically Based PharmacoKinetic (PBPK)** and **Compartmental modelling** to **determine fate and effects of MNP entering the body** by ingestion and inhalation

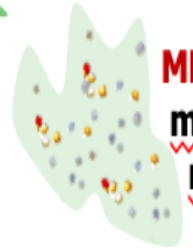
Assess relevance of PCP and different exposure routes: **dermal** (liquid eyeliner and face cream), **ingestion** (lipstick/lip care and toothpaste) and **inhalation** (make-up powder and deodorant spray)

Test materials:

Bottom-up and top-down MNP
PS, PE, PP, PET, PLA

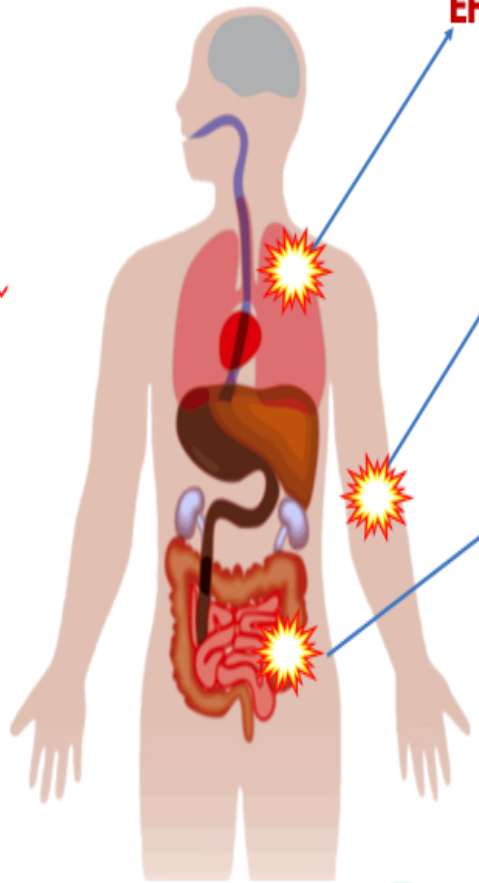
MNP with adsorbed contaminants
PAHs, metals, pharmaceuticals

Additives leaked from MNP
leaching of toxic substances



MNP coated with eco-corona
microorganism biofouling,
microbial contaminants

Target systems:



EFFECTS ON THE RESPIRATORY SYSTEM

STAMI · Universität Bayreuth · Paris Diderot

EFFECTS ON THE IMMUNE SYSTEM

STAMI · Universität Bayreuth · Paris Diderot · Gaiker

EFFECTS ON THE DIGESTIVE SYSTEM

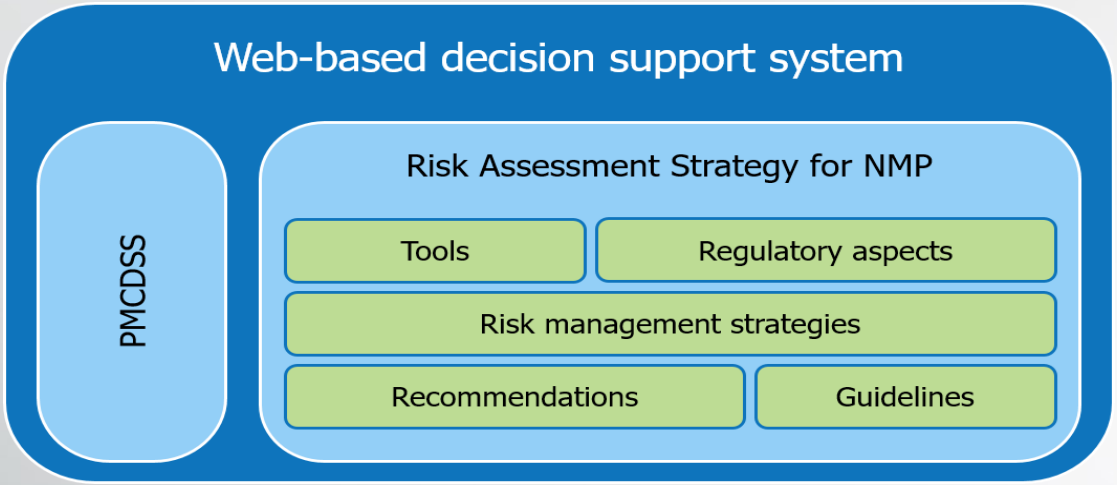
STAMI · Universität Bayreuth · Paris Diderot · Gaiker

Università degli Studi di Torino · Det Nationale Forskningscenter for Arbejdsmiljø · Wageningen University & Research · Univerza v Ljubljani

Fraunhofer · Ecam Ricert · Helmholtz Zentrum für Umweltforschung UFZ · Universiteit Leiden The Netherlands · CSIC

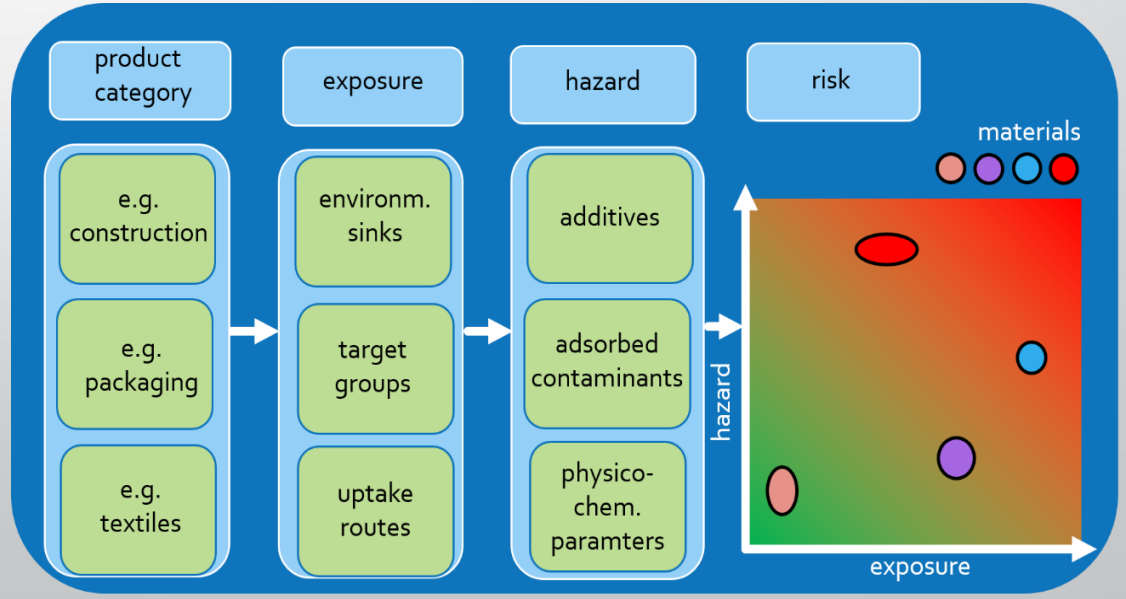
- **Studies on acute effects of MNPs on cell viability** from respiratory and gastro-intestinal tract, liver and immune system ➔ **no significant effects**
- **Studies on acute effects of MNPs on membrane integrity** of cells from respiratory, gastro-intestinal tracts, liver and immune system ➔ **no significant effects**
- **Tests of immune effects** (IL8, IL6, RANTES, MCP-1, TNF alpha, TGF beta) **at gene level** of MNPs (HDPE296 and PS934Eu) on Calu3 in ALI exposure system ➔ **no significant effects** for doses up to 45µg/cm2
- **Tests of immune effects** (IL6 and IL8) **at protein level** of MNP (PET002) on Caco2 and Hep-G2 in submerged exposure system ➔ **dose dependent release of IL6 and IL8.**
- **Study on impact of two different particle sizes of PET on GI tract** after **digestion and colonic fermentation**

- **Requirements defined** for developing a **novel human risk assessment strategy** applicable to MNP by **integrating both human and environmental risks**
- **Compilation of existing regulatory documents** applicable **to microplastic particles of various origin, overview on scientific state-of-the-art and gaps in MNP risk assessment, restrictions for microplastic**
- **Development of decision trees** to support the **development of IATAS** by using a case study on plastics as food contact material (oral exposure) and of a **prospective multi criteria decision support (PMCDS)** system
- **First draft for a web-based platform for stakeholders** prepared to **integrate all WP4 results** and **guide users to select proper analytical, testing and/or modelling approaches** as part of the risk assessment of MNP particles and associated chemicals
- **Build up of the PlasticsFatE central project database** available on TEAMS and **eNanoMapper** to make all data **FAIR and compatible with the IPCHEM** including newly developed SOPs



Structure for the **web-based platform for stakeholders integrating achieved results** and **informing users** on up-to-date relevant guidelines, regulations and recommendations, but also to run own risk analyses by employing the PMCDS or other specific tools.

Basic structure of the **Prospective criteria descisoin support (PMDS) system for MNP:** for early risk assessment of plastic applications. Screening based on prospective risk indicators, considers polymers, additives, material fate: green boxes include a selection of relevant criteria as decision trees ➔ **to estimate and compare risk of plastic materials (**materials represented by the pink dot would pose a lower risk as materials represented by the blue dot)



Pilot field monitoring campaigns at industrial sites (plastic packaging and plastic bags producing plant)

Human biomonitoring to quantify **MNP particles in biological media of workers** and assess a **panel of biomarkers of inflammation and oxidative stress in** possible target organs, including collection of **exhaled breath condensate** (EBC) and **urine**.

Study of potential of plastic particle surfaces to act as vectors of pathogens: assess **toxicity of metals from tyre MP to bacteria**; **transfer of antibacterial resistance genes** (ARG); and **effects of different aged MNP on bacterial growth**

Studies on longterm exposure to MNP contaminated food, through **quantification of uptake via aquatic organisms** that are a significant part of the human diet

Thank you for your attention

PlasticsFatE

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

IMPTOX

A SCIENTIFIC PROJECT TO UNDERSTAND THE HEALTH EFFECTS OF MICRO- AND NANOPLASTICS, WITH A FOCUS ON ALLERGIC DISEASE

- Tanja Cirkovic velickovic, UBFC, Serbia

- CUSP RA workshop, February 07, 2023

The Imptox project has received funding from the EU's H2020 framework programme for research and innovation under grant agreement n. 965173. Imptox is part of CUSP, the European MNP cluster on human health.

THE PROJECT

Understanding the Complex Role of

Micro- and Nanoplastics

combined with

Environmental Contaminants

on Human Health

Focus:

Allergy and Asthma

RISK ASSESSMENT

Exposure studies

Exposure to MPs from seafood

Exposure to MNPs from sea spray aerosols

Human exposure (paediatric population)

Hazard assessment

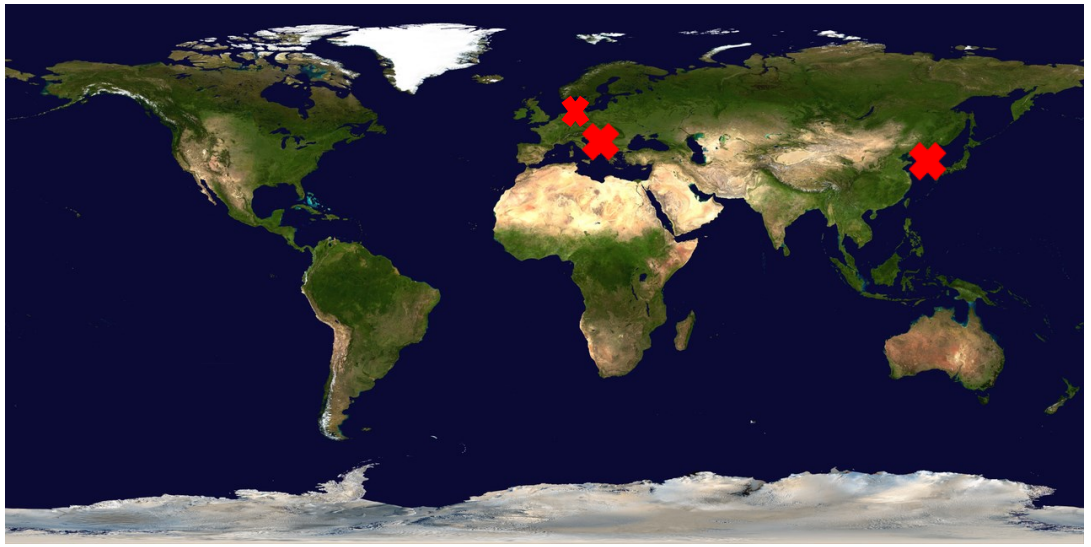
In vitro cytotoxicity – first responder line

In vivo - Immunotoxicity and immune response modulation

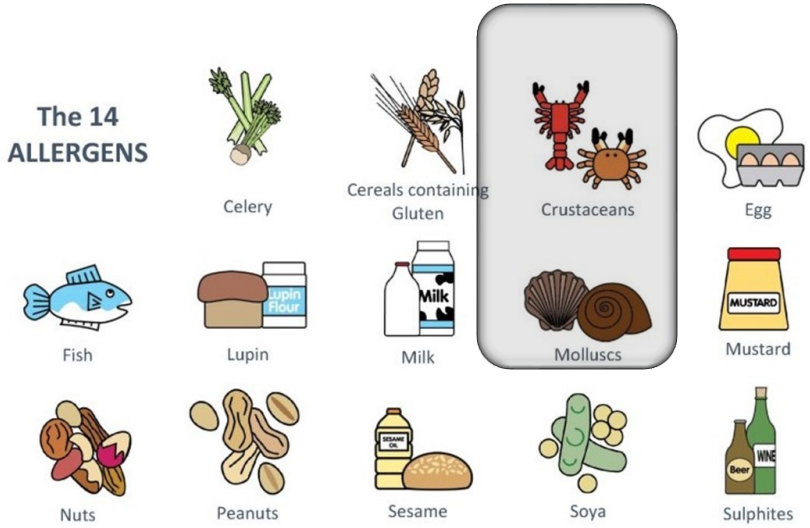
Gastrointestinal tract

To determine links between MNPs and food allergy by **assessing exposure and clinical data** of a population of **allergic children.**

CO-EXPOSURE TO MPS AND ALLERGENS



Credit: NASA Goddard Space Flight Center Image by Reto Stöckli (land surface, shallow water, clouds).



- Market origin of seafood: South Korea, Croatia, Belgium
- Crustaceans (shrimms), molluscs (clams, mussels)

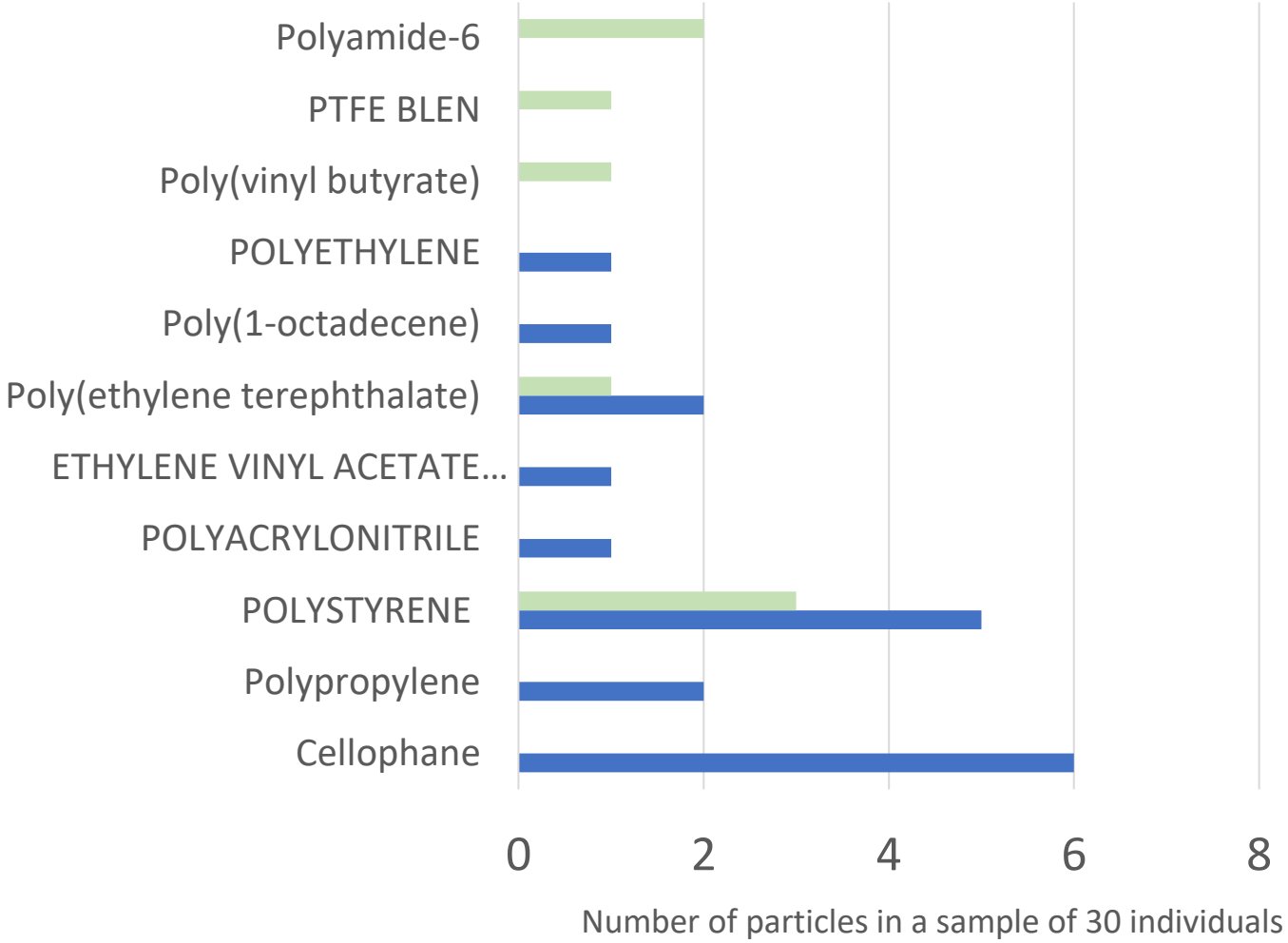
Major allergen – tropomyosin quantification

MP quantification

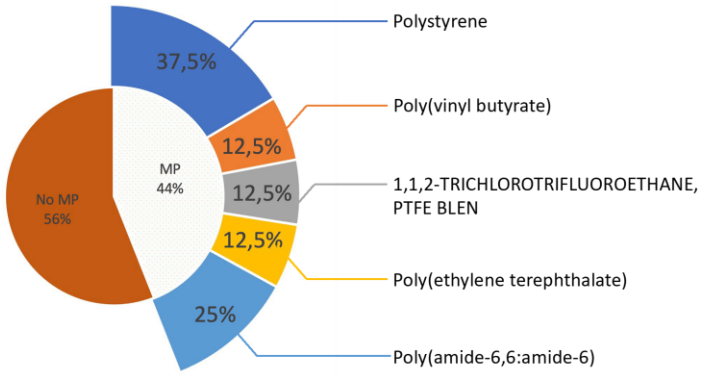
Processing

Co-exposure studies

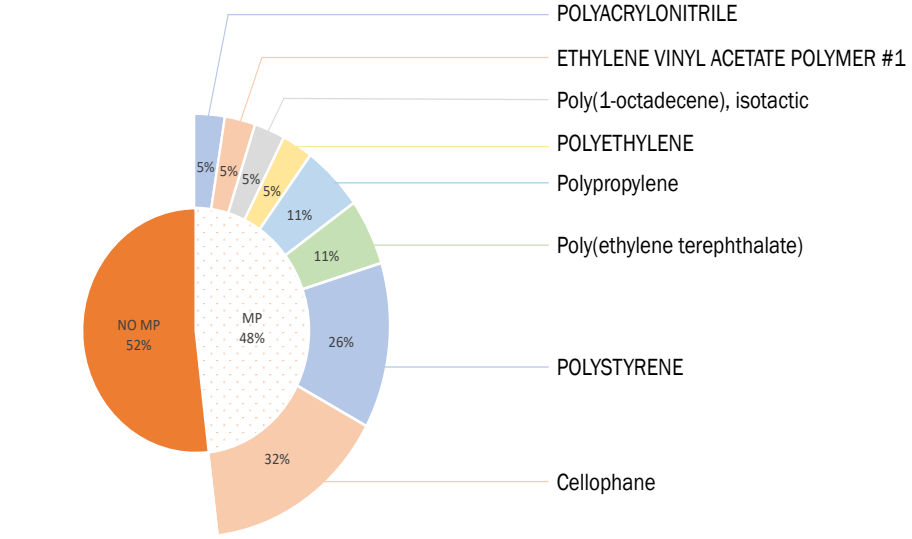
MP IN MUSSELS



Mussels from Belgium



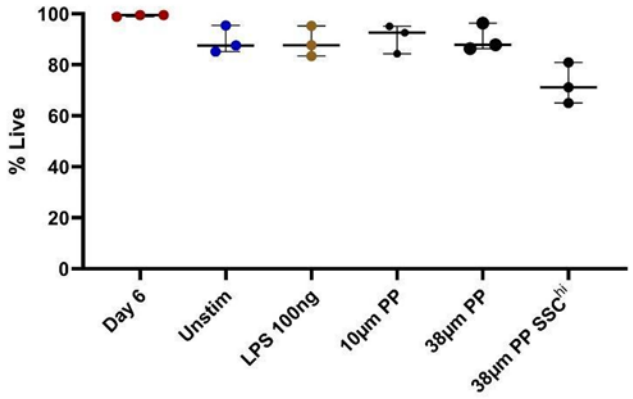
Mussels from Croatia



EFFECTS RELATED TO THE MNP/CONTAMINANTS INTERPLAY AT THE FIRST RESPONDER LINE

- Model gut epithelium cells, primary immune cells
- PP and PET (small MPs)
- No effect was observed on the viability of primary cells (peripheral blood mononuclear cells).
- no effect on the maturation and activation status of the MDDCs by PP
- no differences in IgE binding between the milk allergen lactoferrin in the presence of PP MPs.

MDDC viability testing



EFFECTS ON INTESTINAL AND HEPATIC CELLS

- Testing the toxicity of polystyrene nanoplastics (PSNPs) and their combined effect of with cyanotoxins (microcystin-LR) on intestinal and hepatic cells have shown

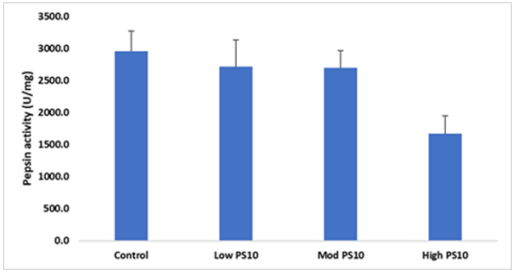
- (1) short term exposure of Caco-2 cells to PSNPs disrupts the bioenergetic status at subtoxic doses;
- (2) synergetic toxic effect of PSNPs and MC-LR exists and depends on the concentrations;
- (3) As MC-LR is a potent tumour promoter, long-term of exposures in combination with several types of NPs need to be further investigated to assess the health impact in real life.

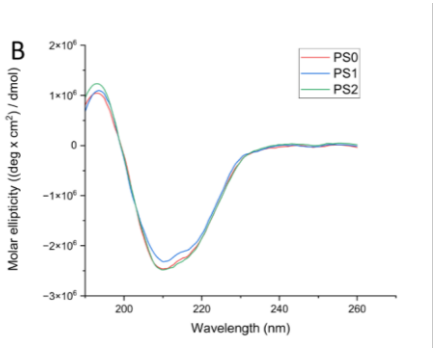
GASTROINTESTINAL TRACT

- Many food allergens are resistant to pepsin digestion
- Allergenic proteins are processed to generate MHCII peptides
- MPs binding to food allergens *in vitro*
- Digestive enzymes activity in the presence of MPs *in vitro* (trypsin, pepsin)
- Protein digestibility in the presence of MNPs in simulated fluids
  - Focus on allergens: tropomyosin, ovalbumin, beta-lactoglobulin
  - Insight into allergens conformational and functional changes affected by binding to MPs

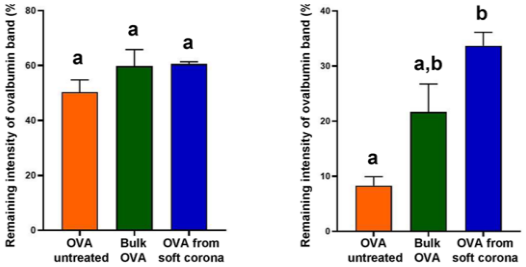
EXPOSURE RELEVANT CONDITIONS

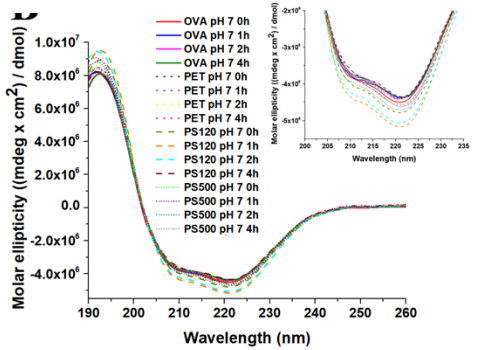
PS/pepsin





OVA/trypsin/PS





CLINICAL STUDIES

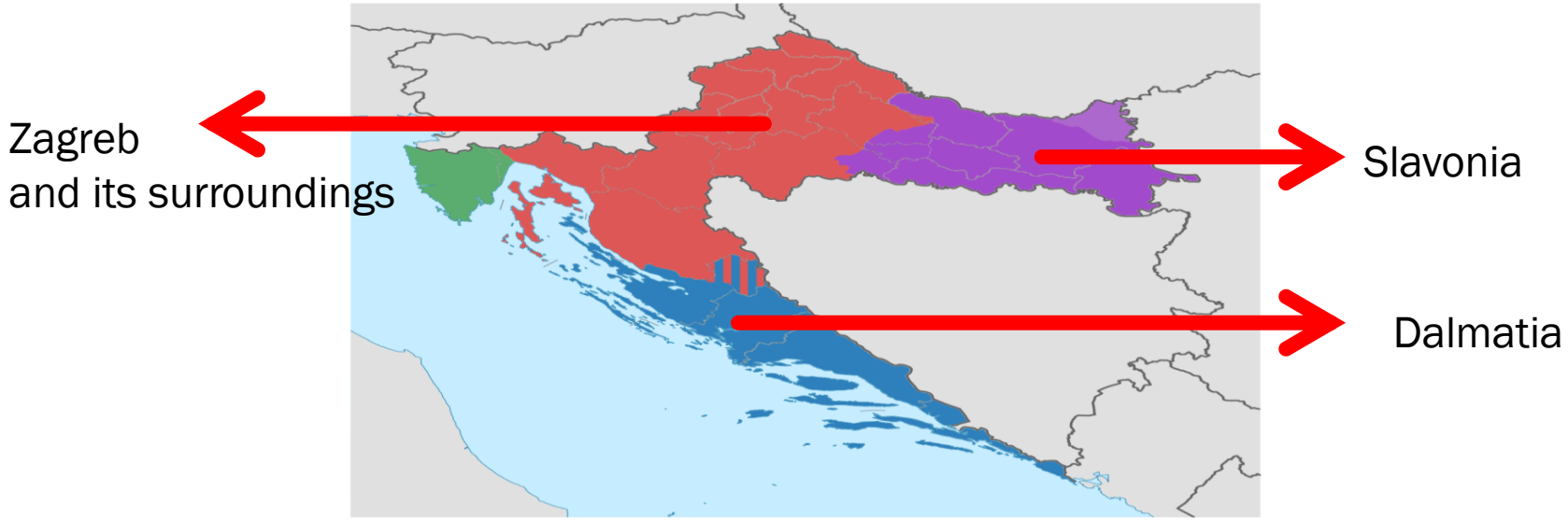
Understand fate and estimate the potential risk of MNPs on the development and the severity of allergic disease:

- By identifying and recruiting a population cohort of allergic and healthy children based on differential environmental exposure, food and water consumption and nutrition (from 3 different urban and rural Croatian regions).
- By analysing excretions (stool), exhaled breath and samples of induced sputum.

- To assess the level of exposure to MNPs in food and water and its impact on human health
- Special focus in the extent of the health impact of MNPs to the immune system and allergy
- Children- a vulnerable population, developing immune system- “window of opportunity” (up to 5 yrs of age)

IDENTIFICATION AND RECRUITMENT OF A POPULATION COHORT BASED ON DIFFERENTIAL EXPOSURE AND SUSCEPTIBILITY (PAEDIATRIC POPULATION, ALLERGIC VS. HEALTHY SUBJECTS)

- Work plan- recruit 210 schoolchildren in 3 different geographical regions in Croatia (70 children with FA, 140 healthy, non-allergic)
- Regions differing in lifestyle and environmental factors



EXPOSURE ASSESSMENT (ORAL ROUTE) AND TOXICOKINETICS (EXCRETION) MONITORING

- standardized and detailed nutritional questionnaires (emphasizing questions regarding potential plastic exposure, gum chewing, cosmetics, PET bottle usage)
- detailed food logs at least 7 days prior to stool sampling (twice, at baseline and after 6 months)
- blood specimens collection (biochemical analyses, BAT).
- Dietary, epidemiological, clinical, biochemical, anthropometric, and lifestyle data
  - using Principal Component Analysis (PCA) as an explorative approach.
- assessment of allergic sensitization will be performed using ISAC platform
  - >100 allergic components of food and/or inhaled allergens

SAMPLING FOR THE PRESENCE OF MNPS

- **Stool samples** together with the selected number of will be collected from the investigated population,
  - analysis in accordance to SOP developed within Imptox for digestion of the samples, chemical characterization by μFTIR
- Samples of **induced sputum and exhaled breathe condensate** only in Mediterranean area

- The effect of MNPs on will be analysed by expression of co-stimulatory markers (CD80, CD86, CD40) and MHC II in blood samples.

ALLERGY STATUS, INFLAMATORY MARKERS AND EXPOSURE DATA WILL BE CORRELATED

THANK YOU

- Tanja Cirkovic Velickovic

The Imptox project has received funding from the EU's H2020 framework programme for research and innovation under grant agreement n. 965173. Imptox is part of the European MNP cluster on human health.

POLYRISK

Understanding human exposure and health hazard of micro- and nanoplastic contaminants in our environment

Raymond Pieters
Institute for Risk Assessment Sciences (IRAS)
Faculty Veterinary Medicine
Utrecht University

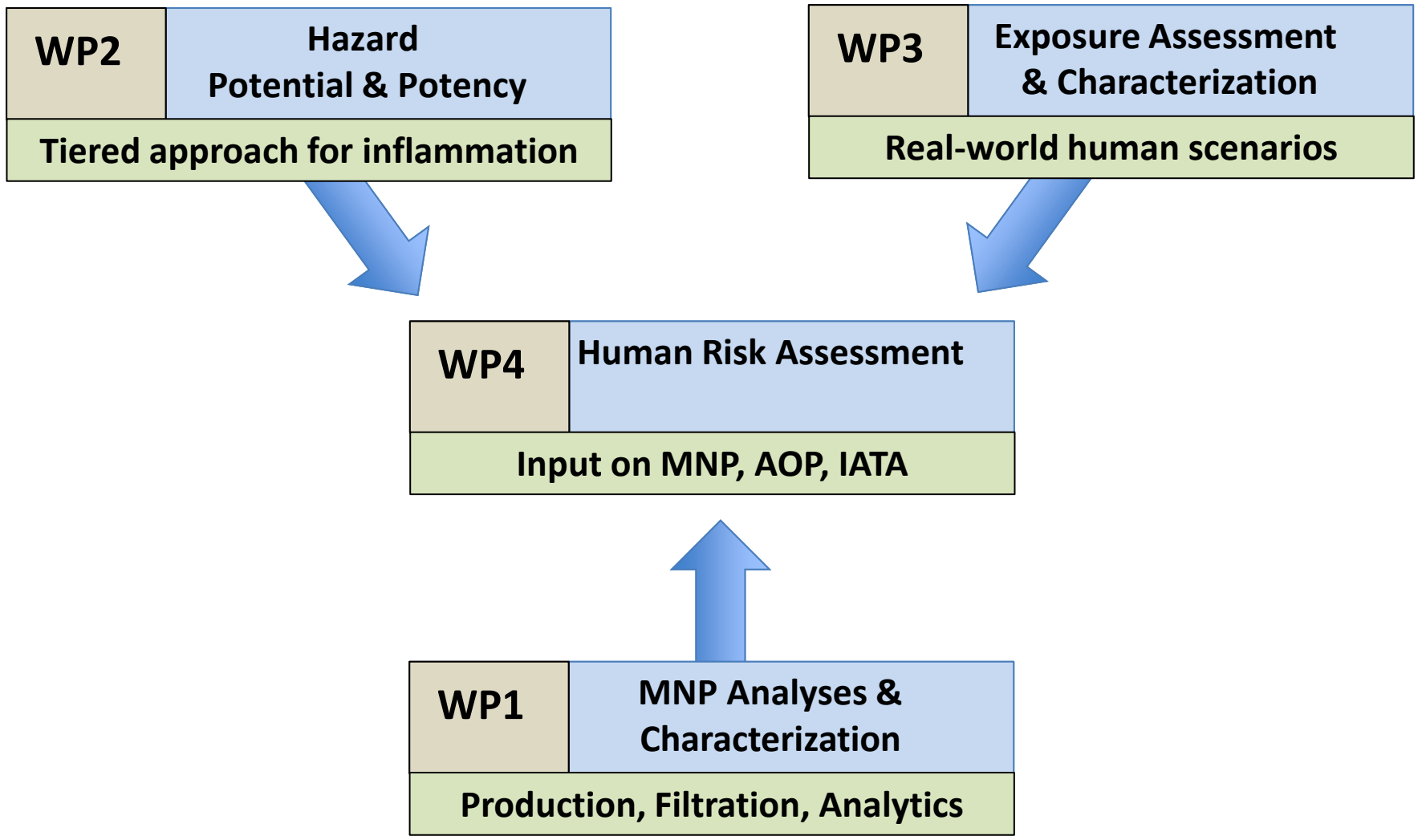
Overall Aim

With POLYRISK, we propose to lay the foundation for a novel approach to human risk assessment for micro and nanoplastics (MNP), taking into account MNP's complex composition.

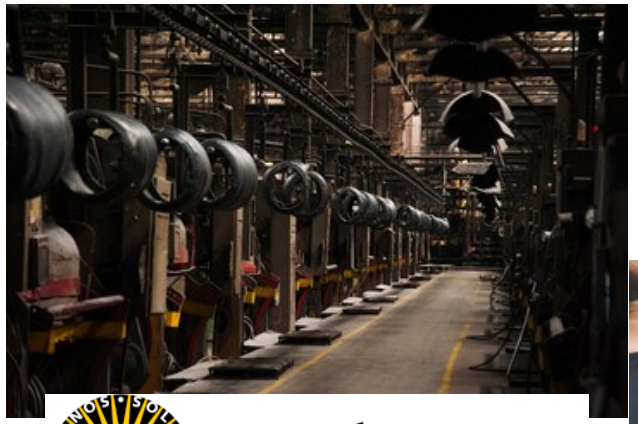
We will combine methodologies for **exposure** and **hazard** assessment into an iterative, tiered approach according to principles of the **Integrated Approach to Testing and Assessment (IATA)**

POLYRISK Objectives

1. Assess **exposure** and biological **effects** of MNP in **real-life scenarios**
2. Develop and apply **innovative sampling, sample preparation and analytics** to assess internal (human matrices) and external (abiotic) exposure to MNP.
3. Develop and apply a **human-based in vitro toolbox for testing** epithelial transfer and immunotoxicity of MNP
4. Establish a **risk assessment strategy** and **execute HRA** for MNP
5. To **manage data** for **current use** in developing MNP risk assessment strategy and for **future *in silico* predictions**
6. **Exchange and communicate** information and knowledge **to stakeholders**


WP2
Hazard
Potential & Potency
Tiered approach for inflammation
WP3
Exposure Assessment
& Characterization
Real-world human scenarios
WP4
Human Risk Assessment
Input on MNP, AOP, IATA
WP1
MNP Analyses &
Characterization
Production, Filtration, Analytics

WP3: Human exposure and effects in real-world exposure scenarios



Utrecht University

INCDTP

NIPH
Norwegian Institute of Public Health

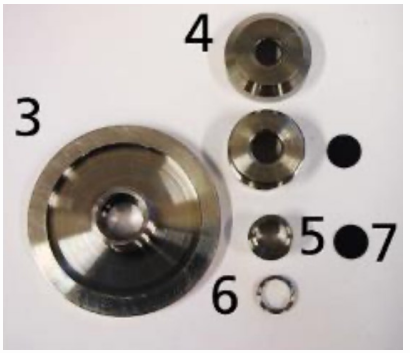
POLYRISK

WP1: Sampling and analytical method development

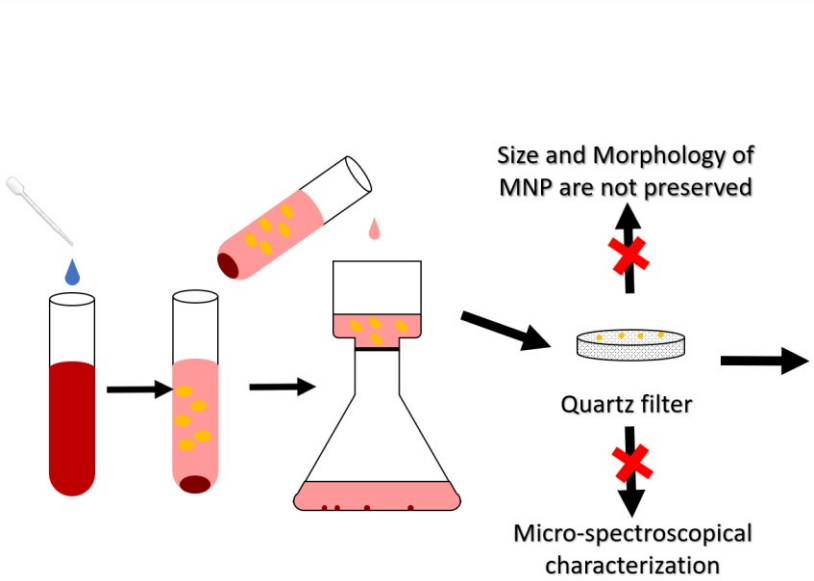
Protocols for:

1) blood analysis
2) analysis of air samples
3) liquid sample filtration

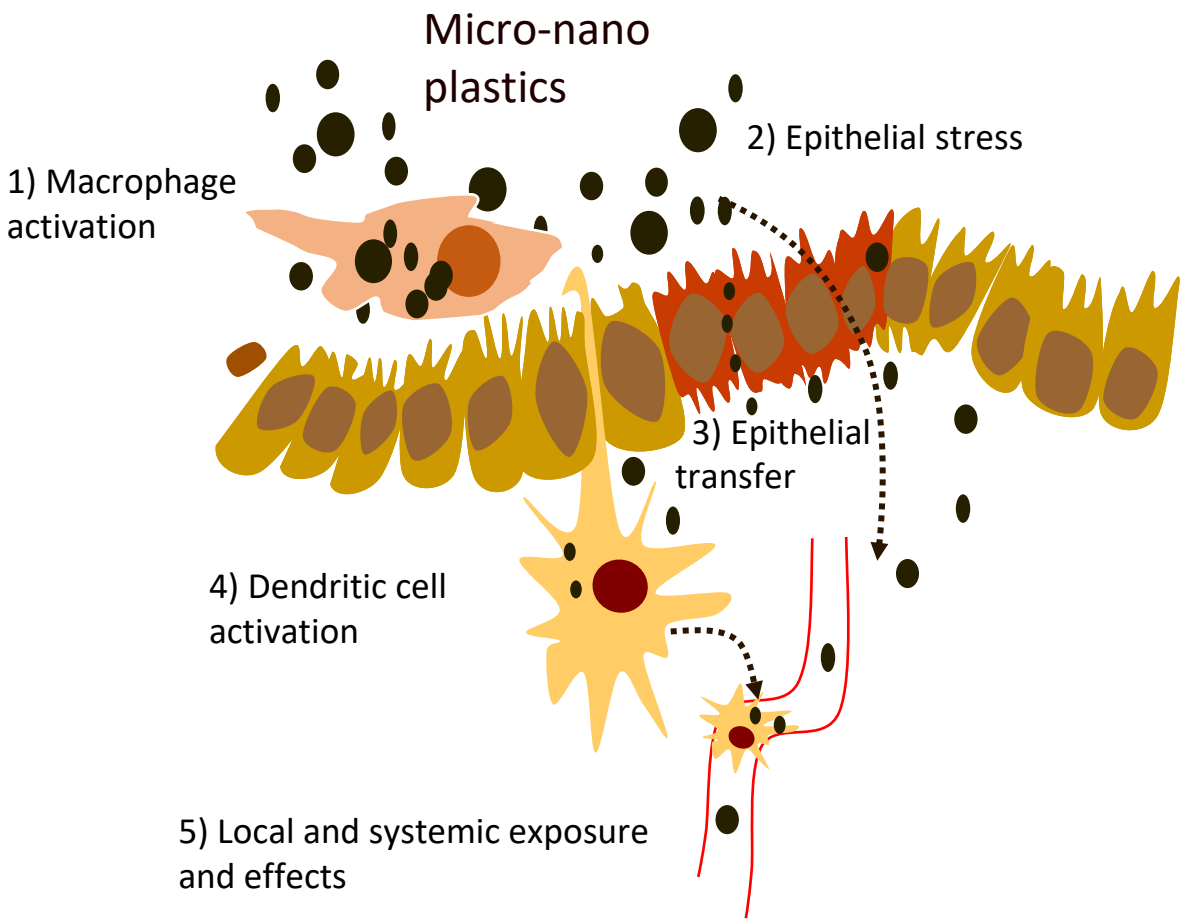
(using different types of filtration)



Digestion and filtration protocol for blood analysis.
Based on:
Leslie et al., Environment International, 163, 2022, 107199.



WP2: Tiered approach of in vitro testing



TIERs:
-Cell-lines
-Human-derived cells
-Co-cultures/organoids
-Tissue models (skin)
-Air Liquid Interface

POLYRISK

WP4: Risk assessment

Exposure route dependent;
(inhalation is focus of POLYRISK scenarios, but POLYRISK also considers oral route (drinking water, swallowing)

Dependent on **size**, **shape** (e.g. fibre or not) and **surface** chemistry (e.g. weathering, and leaching) of MNP.

Dependent on solubility and amount of toxicity of MNP.

Focus on immunotoxicity (e.g. inflammation-KE of AOP

Grouping is foreseen (e.g. as fibres, PLC, or specific MNP)

Announcement

March 14, 2023

from 12.30 to 17.00 (CET)

Human Health Risk Assessment Frameworks

for Micro- and Nanoplastic (MNPs)

Consortium Partners

15 partners in 7 countries

Utrecht University (UU)

Netherlands

Vrije Universiteit Amsterdam (VUA)

Netherlands

Amsterdam UMC – Location VUmc

Netherlands

German Federal Institute for Risk Assessment (BfR)

Germany

Bundesanstalt für Materialforschung und -prüfung (BAM)

Germany

Federal Institute for Occupational Safety and Health (BAuA)

Germany

Norwegian Institute of Public Health (NIPH)

Norway

University Medical Centre Utrecht (UMCU)

Netherlands

The Research Development National Institute for Textile and Leather (INCDTP)

Romania

Italian National Agency for New Technologies, Energy and Sustainable Economic Development (ENEA)

Italy

Ideaconsult Ltd. (IDEA)

Bulgaria

Health and Environment Alliance (HEAL)

Belgium

Fraunhofer-Center für Silizium-Photovoltaik (CSP)

Germany

European Research Services (ERS)

Germany

Umweltbundesamt (UBA)

Germany