Human exposure and health effects of micro- and nanoplastics

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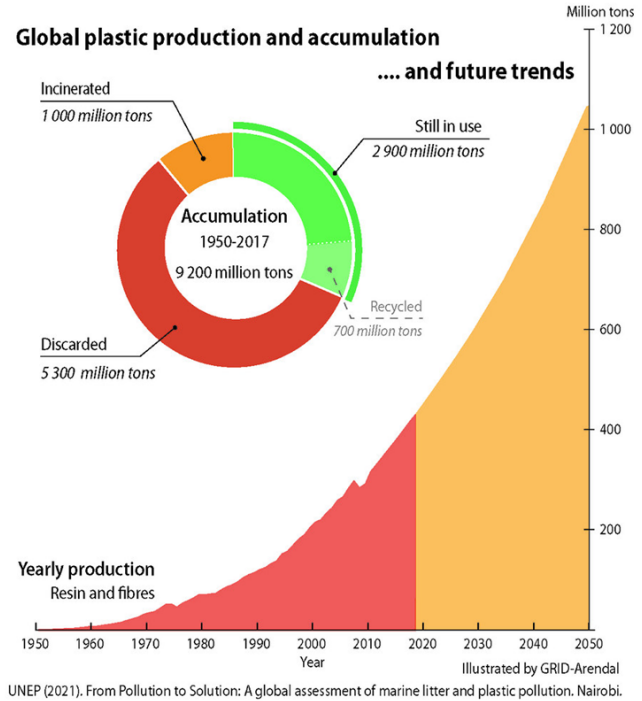
Plastics – Production and disposal



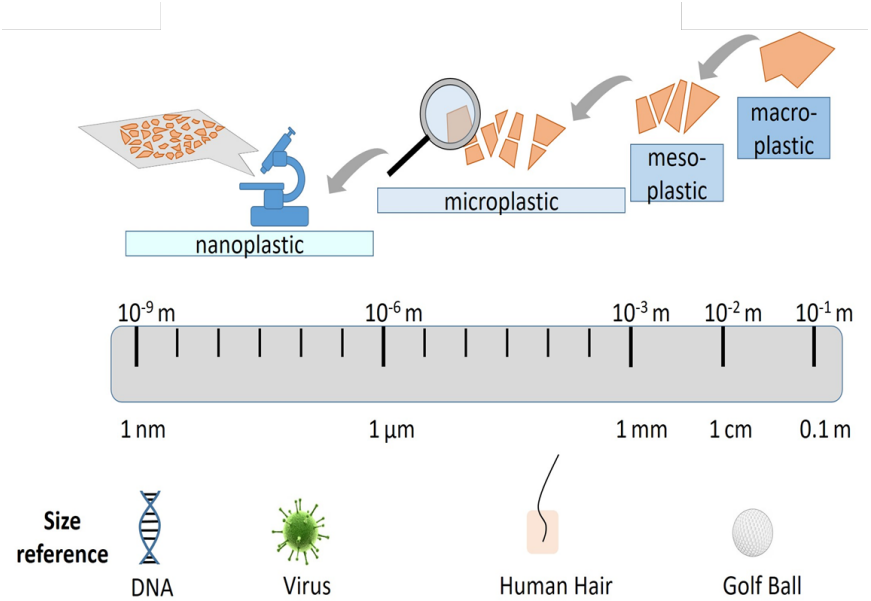
UNEP (2021). From Pollution to Solution: A global assessment of marine litter and plastic pollution. Nairobi.

- Without interventions the production of plastics will be doubled in 2050
- Approximately 10% of plastics is recycled
- The majority of the plastics produced is still in use or discarded (disposed in landfills or released in the environment)

Plastics – Widespread uses

Chemicals in plastics – a technical report (UN)

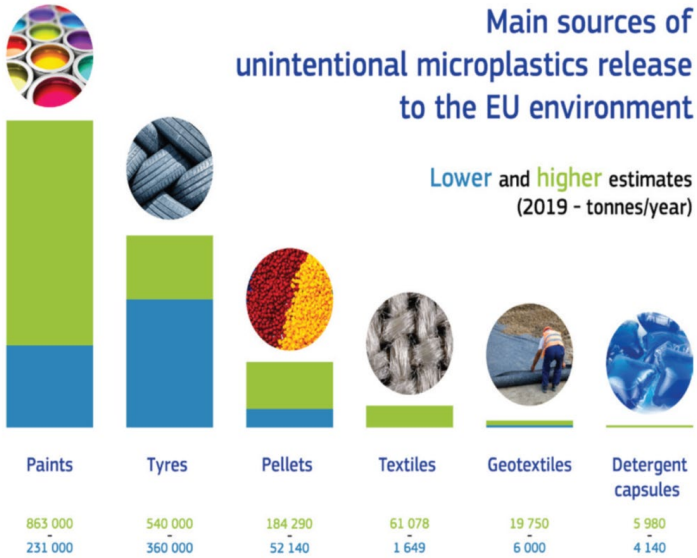
Micro and nanoplastics - sizes



- Microplast: ≤ 1 mm (≤ 5 mm)
- Nanoplast: ≤ 1 µm

Classification of plastic particles by their size and size references, definition of nanoplastic by Hartmann et al. [3] © Andreas Mattern/ UFZ: Nanoplastic in the environment – Wissensplattform nanopartikel.info

Sources of microplastics



- Breakdown of plastics in the environment
- Microplastics are intentionally added to products like cosmetics, detergents, paints, fertilisers, plant protection products +++
  - REACH restriction in place in Europe on microplastics in products

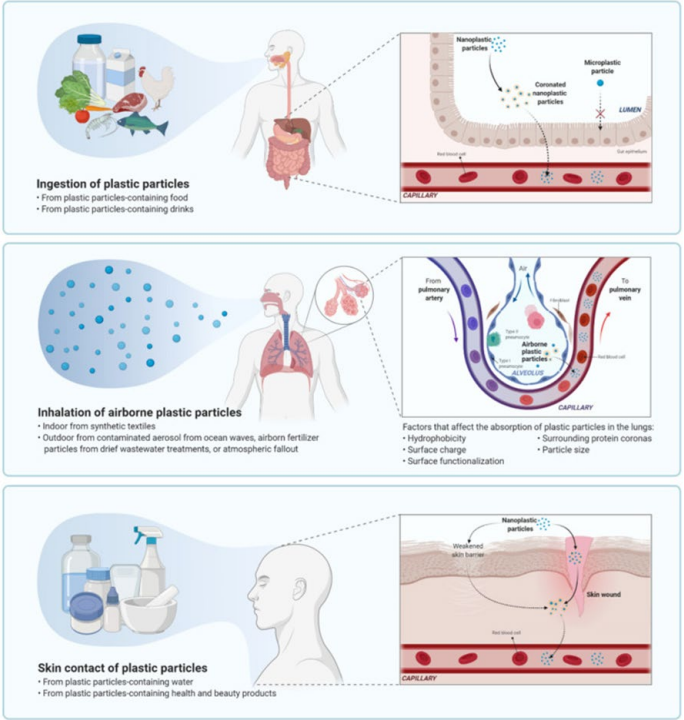
EU action against microplastics. Report 2023. https://data.europa.eu/doi/10.2779/917472

Routes of exposure to MNPs

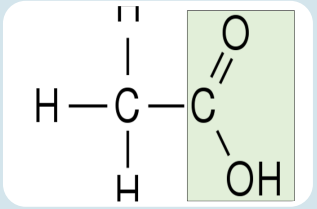
- **Ingestion**
- Inhalation
- (Dermal)

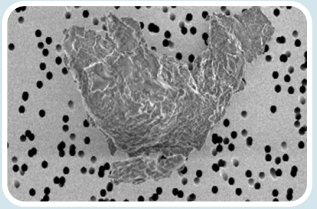
Evidence that small MNPs can translocate to the blood

After uptake in the body:
- Excretion via bile/faeces or urine
- Accumulation in the body
    Organs: spleen, liver
    Immune cells



Possible health effects of MNPs- Influenced by many variables





Size
- Macro
- Meso
- Micro
- Nano

Surface chemistry
- Charge
- Functional groups
- Protein corona
- Endotoxins

Shape*
- Fragments
- Fibers
- Various

Materials
- Polyetyleneterephthalate (PET)
- Polystyrene (PS)
- Polypropylene (PP)
- Polyvinylchloride (PVC)
- Rubber
- +++

Additives
- Plasticizers
- Flame retardants
- Pigments
- Non-intentionally added addivitives
- ++++

MNPs in human tissues

Environment International 163 (2022) 107199

Toxicological Sciences, 2024, 1–6
https://doi.org/10.1093/toxsci/kfae060
Advance Access Publication Date: May 15, 2024
Research Brief

Microplastic presence in dog and human testis and its potential association with sperm count and weights of testis and epididymis

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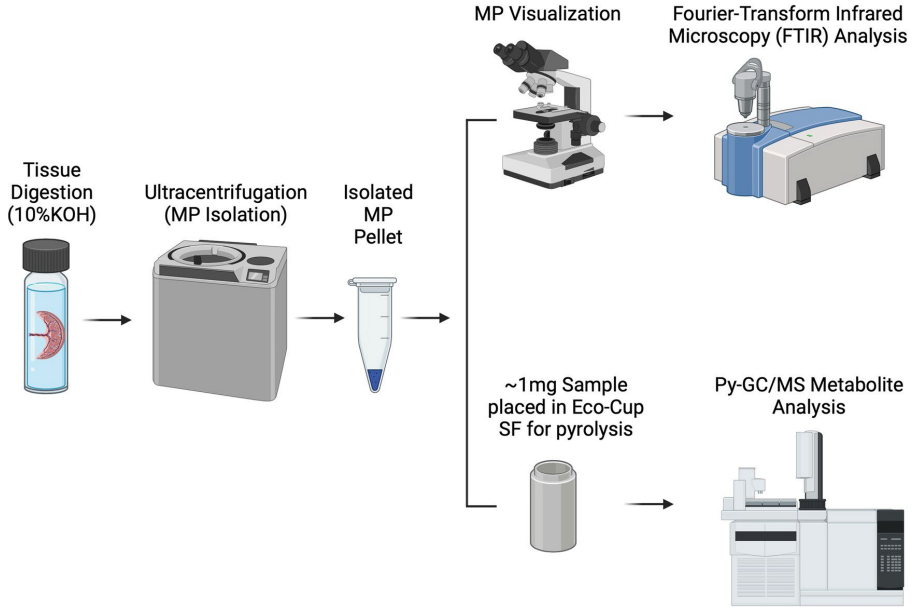
How are MNPs measured



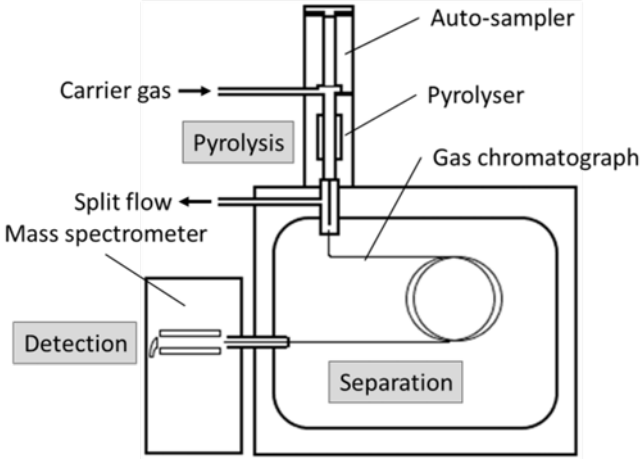
Pyrolysis GC-MS is mosten often used
- Gives information on the mass of polymers not on size of the particles

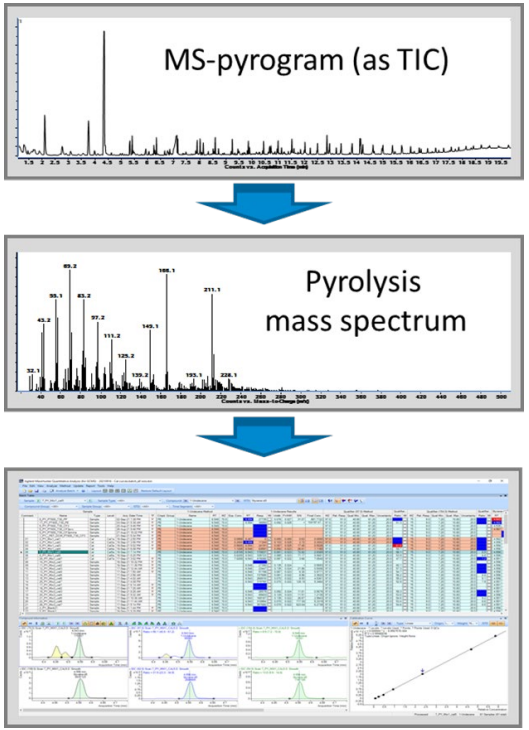
POLYRISK have also employed Scanning Electron Microscopy together with RAMAN spectroscopy

Contamination is a big problem
- Lot of lab disposables are made from plastics
- Use blanks

https://doi.org/10.1093/toxsci/kfae021

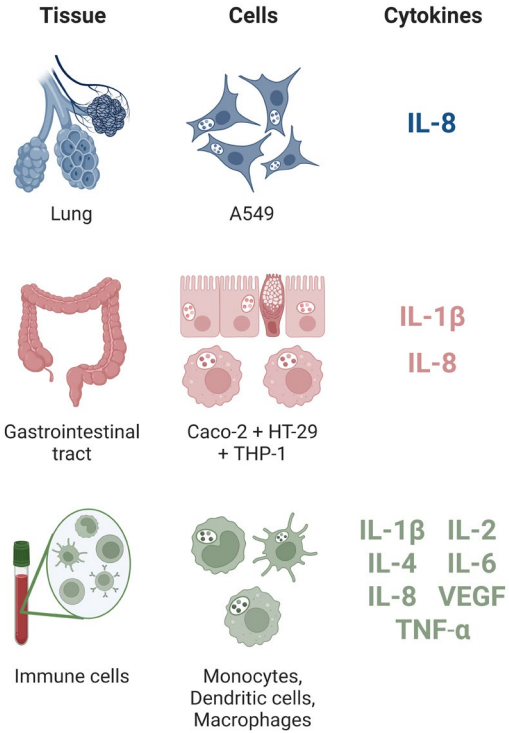
Pyrolysis GCMS





Picture from Lorenzo Scibetta VU Amsterdam

Cytokine release in human in-vitro models



Sources:
Brown DM et al. Toxicol Appl Pharmacol. 2001;175(3):191-199. doi:10.1006/taap.2001.9240
Busch M et al. Chemosphere. 2021;284:131345. doi:10.1016/j.chemosphere.2021.131345
Weber A et al. Environ Int. 2022;163:107173. doi:10.1016/j.envint.2022.107173
POLYRISK project

Assessing And Characterizing Of MNP Effects On Specific Immune Cells

Polyethylene (350nm, 82µg/ml)

Nanoplastics

Polypropylene (180nm, 41µg/ml)

Viability Assay 1

Presto Blue
(Metabolic activity measurement)

30K cells, 96 well flat bottom
LPS :50ng/ml for DCs
:100ng/ml for Monocytes

Polyethylene,350nm (82µg/ml)

Polypropylene,180nm (41µg/ml)

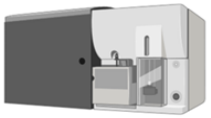
Cytokines (LUMINEX) 2

LUMINEX
13 Cytokines

IL-1β, IL-4, IL-6, TNF-α, GMCSF, IL-1α, IL-2, VEGF, IL-8, IFN-γ, IL-5, IL-10, IL-12

FACS (Flow Cytometry) 3

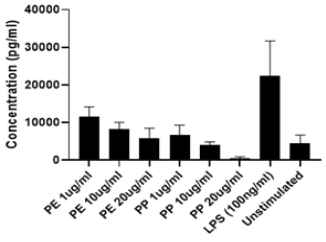
ONGOING



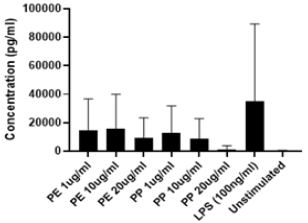
Monocytes: CD14, HLA-DR, CD86, CD80, CD11b, CD209, CD68

DCs: HLA-DR, CD11c, CD123, CD40, CD80, CD86, CCR7

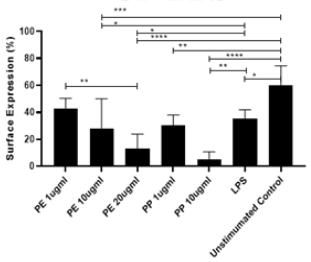
IL-8



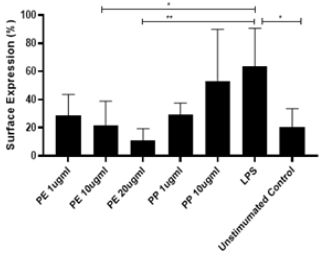
TNF-α



CD11b



CD209



Decline In Cell Viability After 48 Hrs

- Monocytes: No IFN-γ,IL-5, IL-10, and IL-12 Production
- IL-8, TNF-α, IL-6, IL-1β and many other cytokines were produced in response to PE and PP exposure after 48hrs by Monocytes

Immune Modulation by Monocytes

Various concentrations of PE and PP upregulated the expression of costimulatory molecules such as CD80 and CD86. The decreasing expression levels of CD11b with varying concentrations of PE and PP suggest an escalating inflammatory response.

POLYRISK

POLYRISK

POLYRISK:

- EU-project (2021 – 2025)
- Coordinated by Dr Raymond Pieters, University of Utrecht, the Netherlands
- Five human studies to study "real-life" exposure of MNPs

Objectives

Study human (external and internal) exposure to MNPs

Study biomarkers for effects in blood, urine and sputum

Funding acknowledgement: The POLYRISK project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 964766

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Five «real-life» studies

1. Traffic study

UU

Determine MNPs in outdoor air samples and in blood samples in volunteers that were for 4 hours along

- a busy road
- anurban parc
- a crossroad

Compare exposure to effects on immunecell profiling with spectra flow

2. Textile factory study

INCDP

Determine MNPs in indoor air samples and in blood samples from workers in a textile factory in Romania

Compare exposure to effects on immunecell profiling with spectra flow

3. Tyre refurbushment factory study

UU

Determine MNPs in indoor air samples and in blood samples from workers in a tyre refurbishment factory

Compare exposure to effects on immunecell profiling with spectral flow

4. Football study

NIPH

Determine MNPs in indoor air samples and in blood samples from volunteers playing a soccer match on artificial turf with and without rubbergranulates

Compare exposure to effects on immune cell profiling with CyTOF and with cytokine measurement (OLINK)

5. Bottled drinking water study

NIPH

Determine MNPs in 8 different brands of bottled drinking water that are for sale in Norway.

Measure MNPs in blood from volunteers that drink the water with low and high levels of MNPs, respectively and compare with immunecell profiling.

Football study

36 healthy volunteers (17-19 years) that played two football matches on artificial turf in indoor halls

Kamp 1:
Artificial turf without rubber granulates (Olive stones)

- Biological samples before the match
- Match 2*45 min
- Biological samples after the Match
- Biological samples 18h after the match

Two week between matches

Kamp 2:
Artificial turf with rubber granulates

- Biological samples before the match
- Match 2*45 min
- Biological samples after the match
- Biological samples 18h after the match

Analysis

Biological samples: blood, urine and saliva
Air samples during the match: MNP in air samples, Volatile Organic Compounds

Preliminary results of the studies in Norway

Low levels of MNP in bottled drinking water for sale in Norway

Human study terminated

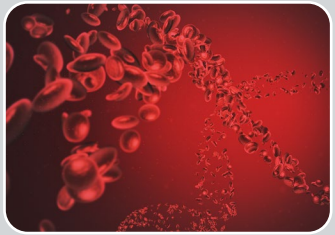
Low levels of rubber in air samples collected in the football halls

Determination of MNPs in airsamples

Ongoing

Cell profiling with CyTOF and cytokine analysis with OLINK

Ongoing



Determination of rubber and plastic levels in blood samples

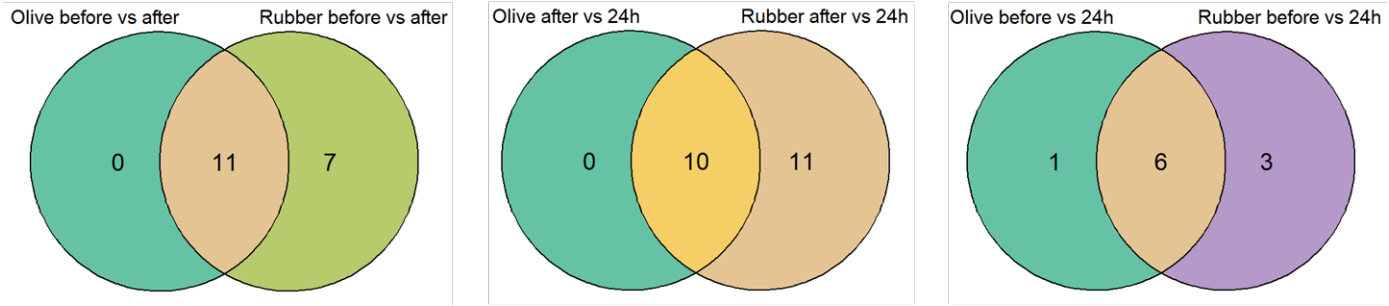
Ongoing

Conclusions football study

- Low levels of rubber detected in air samples in both halls
- MNP measurements in air samples and in blood samples are ongoing
- The levels of hydroxyphenanthrenes (metabolites of phenanthrene) in urine was higher after the match on rubber granulate infill compared to olive sand infill
- Minor changes in the immunological profiles of blood cells (CyTOF) detected
- Some significant changes in plasma cytokines detected in the rubber granulate hall
  - Possible confounders, need for additional analysis

Immunological effects – Cytokines in plasma

Total number of significant cytokines between 2 sampling points.



There's a significant correlation between multiple plasma cytokines and exposure to synthetic rubber granulate infill

MNP: Challenges and knowledge gaps

- Analytical chemical characterisation: risk of contamination
- We lack exposure data to perform a risk assessment
- We lack sensitive analytical methods for nanoplastics
- Throughput of analytical methods is quite low
- The particles that are studied in vitro are often less relevant for human hazard assessment
- Effects of chronic exposure are unknown

Wright, S., Cassee, F.R., Erdely, A. *et al.* Micro- and nanoplastics concepts for particle and fibre toxicologists. *Part Fibre Toxicol* **21**, 18 (2024). https://doi.org/10.1186/s12989-024-00581-x

Jun-Li Xu, Xiaohui Lin, Jing Jing Wang, Aoife A. Gowen (2022). A review of potential human health impacts of micro- and nanoplastics exposure, Science of The Total Environment, Volume 851, Part 1. https://doi.org/10.1016/j.scitotenv.2022.158111

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An opportunity: Partnership for the Assessment of Risks from Chemicals (PARC)

- Opportunity to perform an OECD guideline long term study in rats to study chronic effects of micro and nanoplastics
- But finding a representative, well-characterised testitem (nanoplastics) is a huge challenge.
- Preferably 100 nm in diameter, sufficient amounts, no endotoxins
- Suggestions are wellcome

PARC Partnership for the Assessment of Risks from Chemicals

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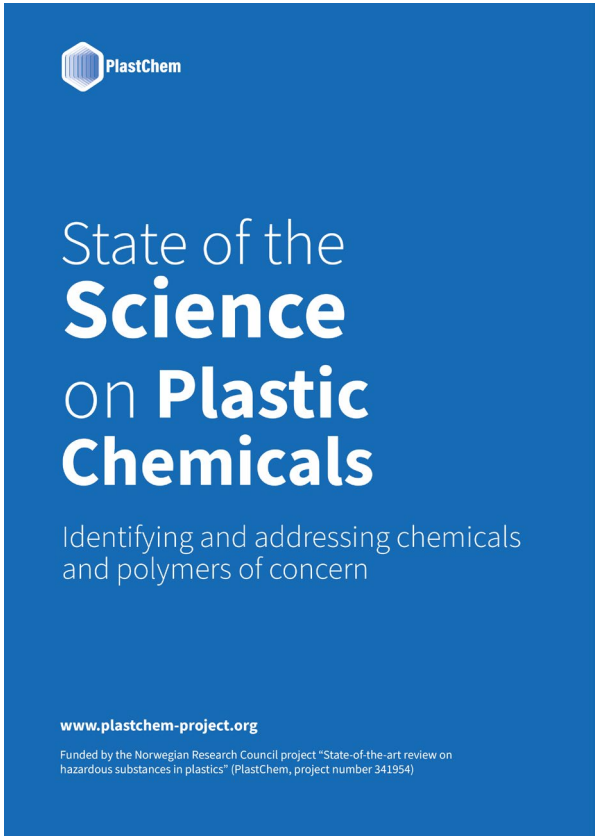

- 16 000 chemicals identified in plastics
- 6% are regulated internationally
- 4200 chemicals are PBT
  - (persistent, bioaccumation, toxic)
- No hazard data for 10 000 chemicals
- Mixture effects

The 15 priority groups of concern

- Aromatic amines
- Aralkyl aldehydes
- Alkylphenols
- Salicylate esters
- Aromatic ethers
- Bisphenols
- Phthalates
- Benzothiazoles
- Organometallics
- Parabens
- Azodyes
- Aceto/benzophenones
- Chlorinated paraffins
- Per- and polyfluoroalkyl substances (PFAS)

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Health effects of micro- and nanoplastics

NMPs meet the persistent and bioaccumulative criteria in the PBT
NMPs are mobile in the environment

Thanks

Berit Granum
Monica Andreassen
Neema Negi
Igor Snapkov
Dorte Hertze
Hege Hjertholm

Raymond Pieters
Gerard Hoek
Esther Jenssen
Emilia Visileranu

Lorenzo Scibetta
Marja Lamoree

Paul Miclea
Dirk Brossel

And many more

FHI

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

CUSP

Polyrisk is part of the European Cluster on
Health Impacts of Micro- and NanoPlastic, CUSP.

This project has received funding from the European Union's Horizon 2020
research and innovation programme under grant agreement No 964766.

polyrisk.science