

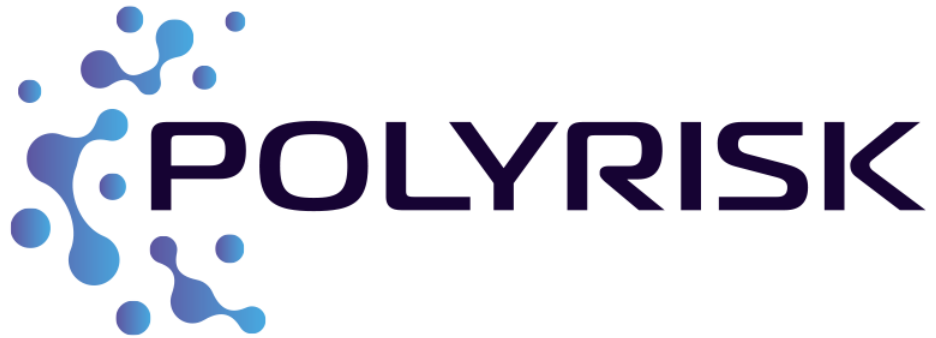
EU POLYRISK

Towards a Risk Assessment Framework for Micro- and Nanoplastic

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



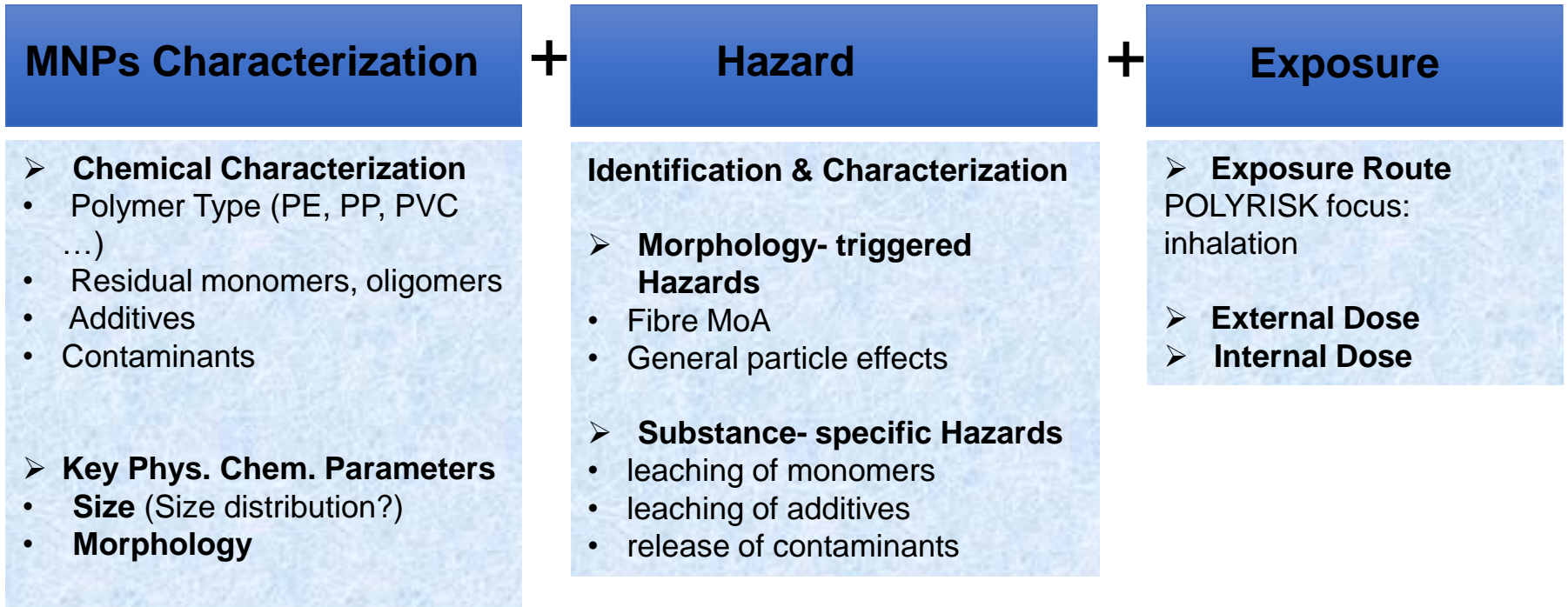
HORIZON 2020

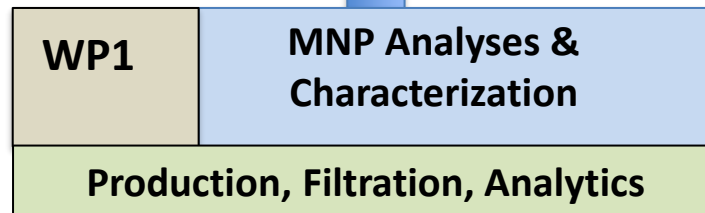
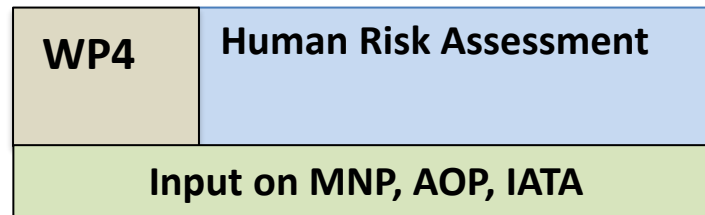
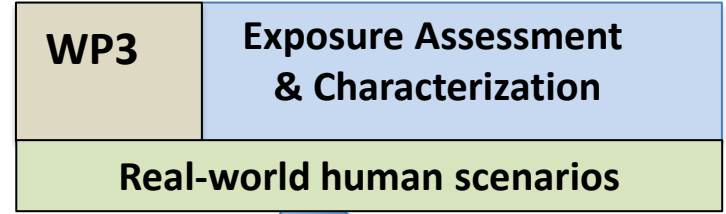
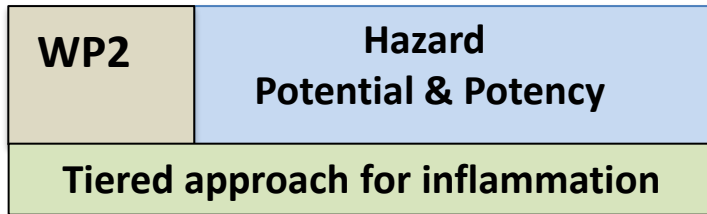
Overall Aim

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)**

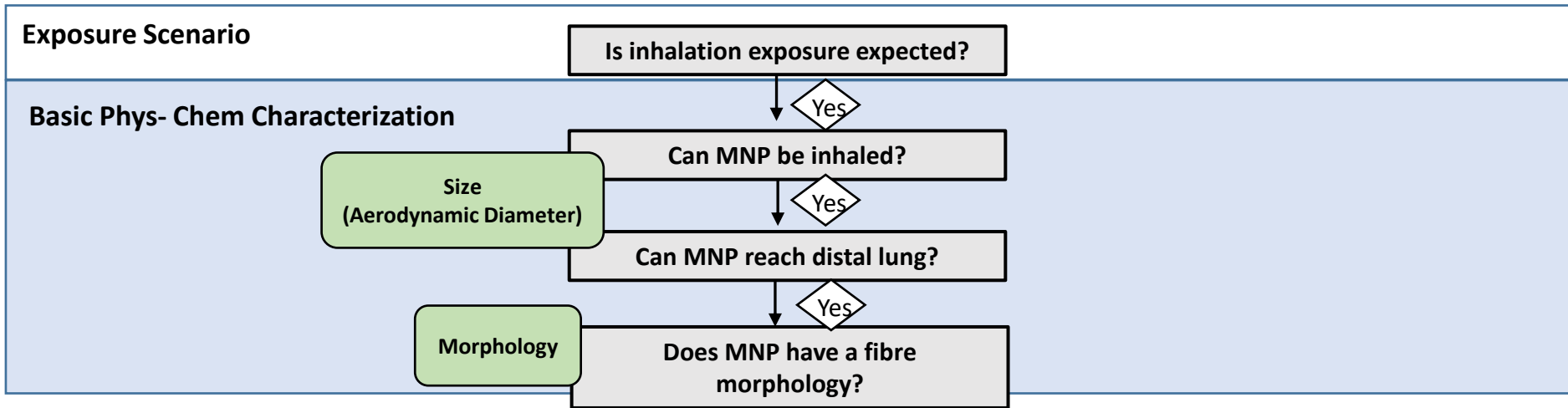
Risk assessment for Micro- and Nanoplastics (MNPs)



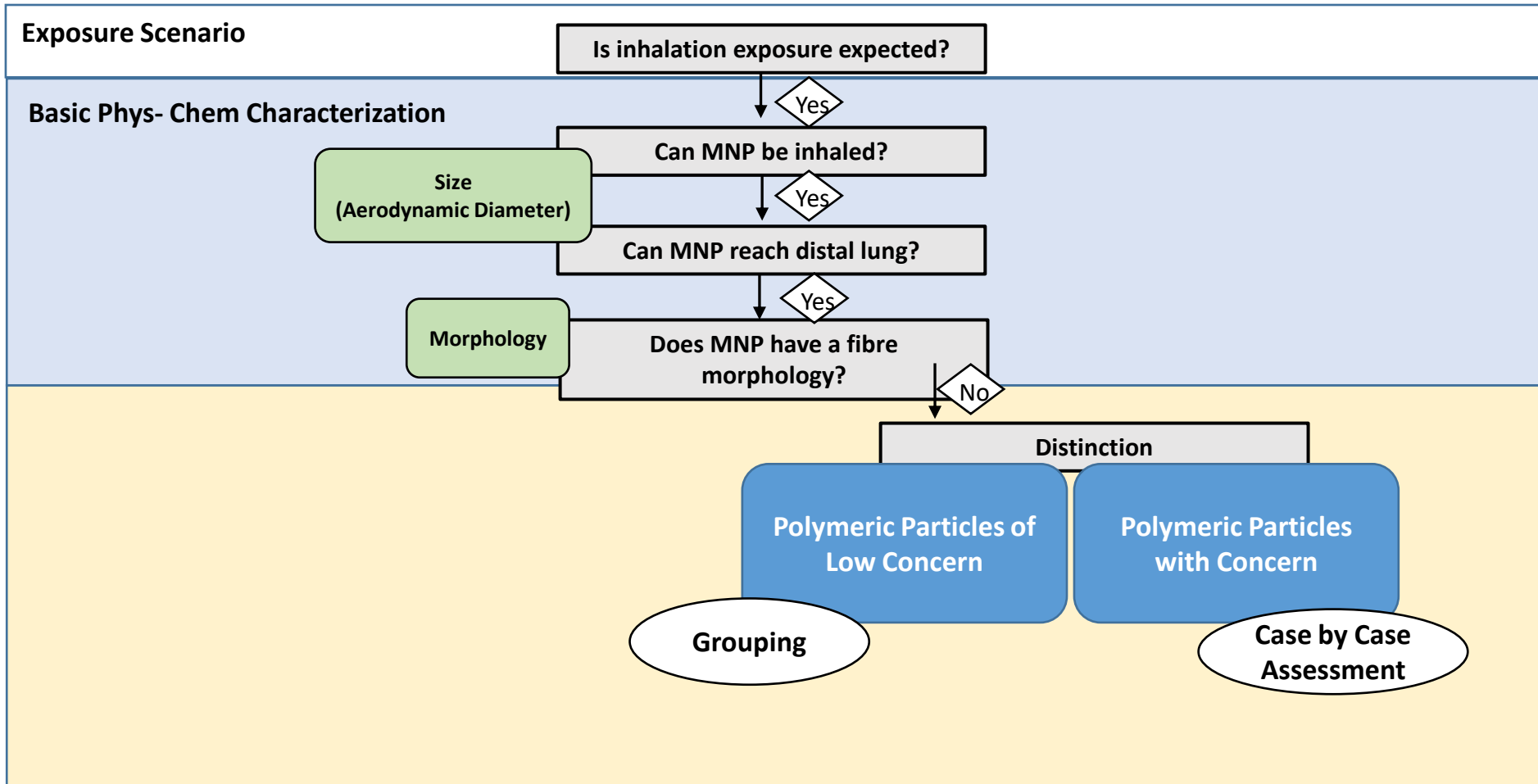


Dr Andrea Haasse, BfR, Germany

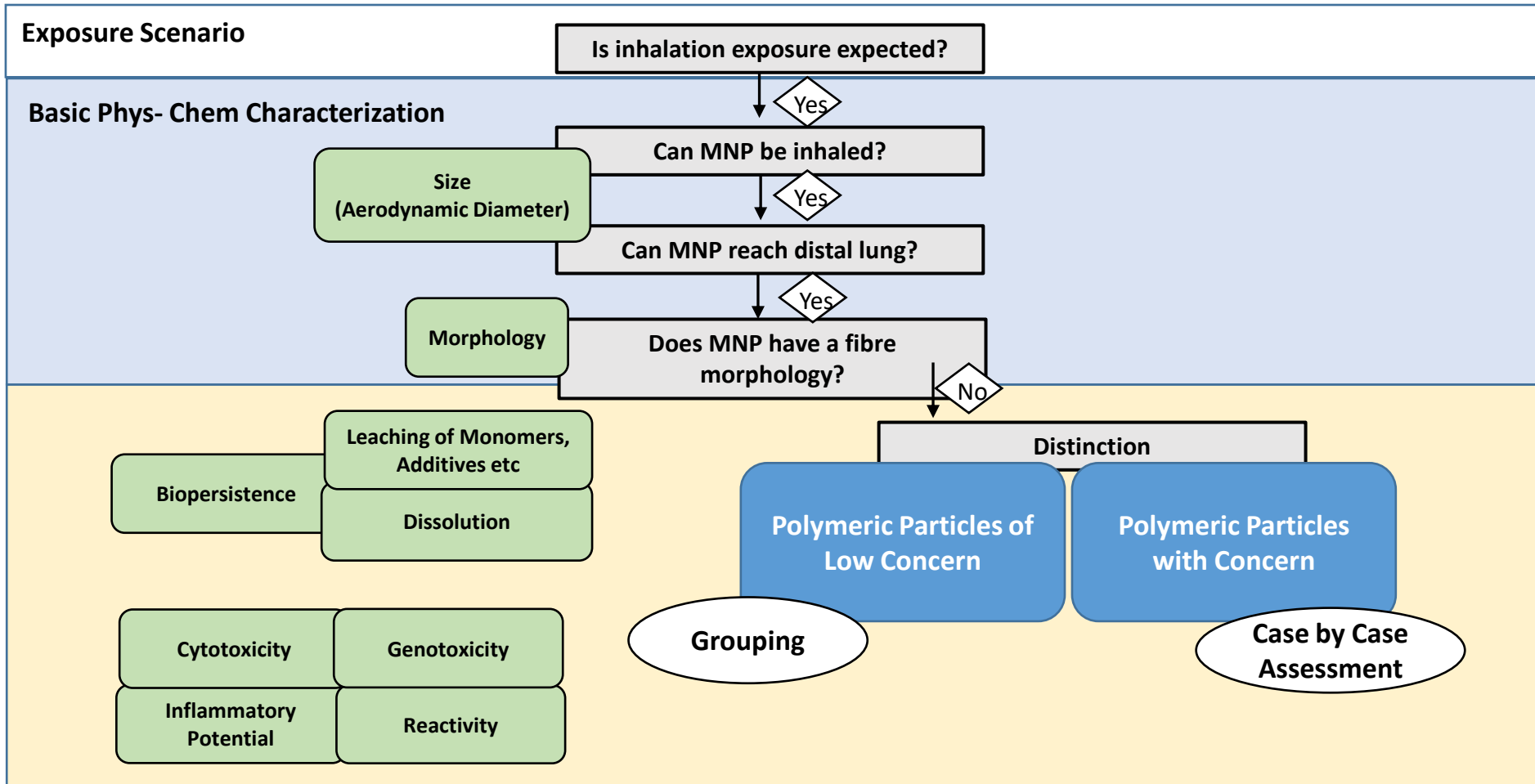
Towards a Risk Assessment Framework for MNPs



Towards a Risk Assessment Framework for MNPs



Towards a Risk Assessment Framework for MNPs



OECD Polymer of Low Concern (PLC)

OECD expert group classified polymers to simplify risk assessment (OECD, 2009):
Polymers of Low Concern (PLC) and Polymers of Potential Concern

PLC are deemed to have insignificant environmental and human health impacts.

➤ **Number-average molecular weight (M_n) ≥ 1000 Da**

➤ **Low molecular weight, oligomeric species (i.e., < 1000 Da and/or < 500 Da species)**

The higher the oligomer content, the more likely a polymer was to display concern. Most potential health concern polymers had $M_n < 10000$ Da and oligomer content values of $> 1\%$.

➤ **Low amount or no reactive functional groups**

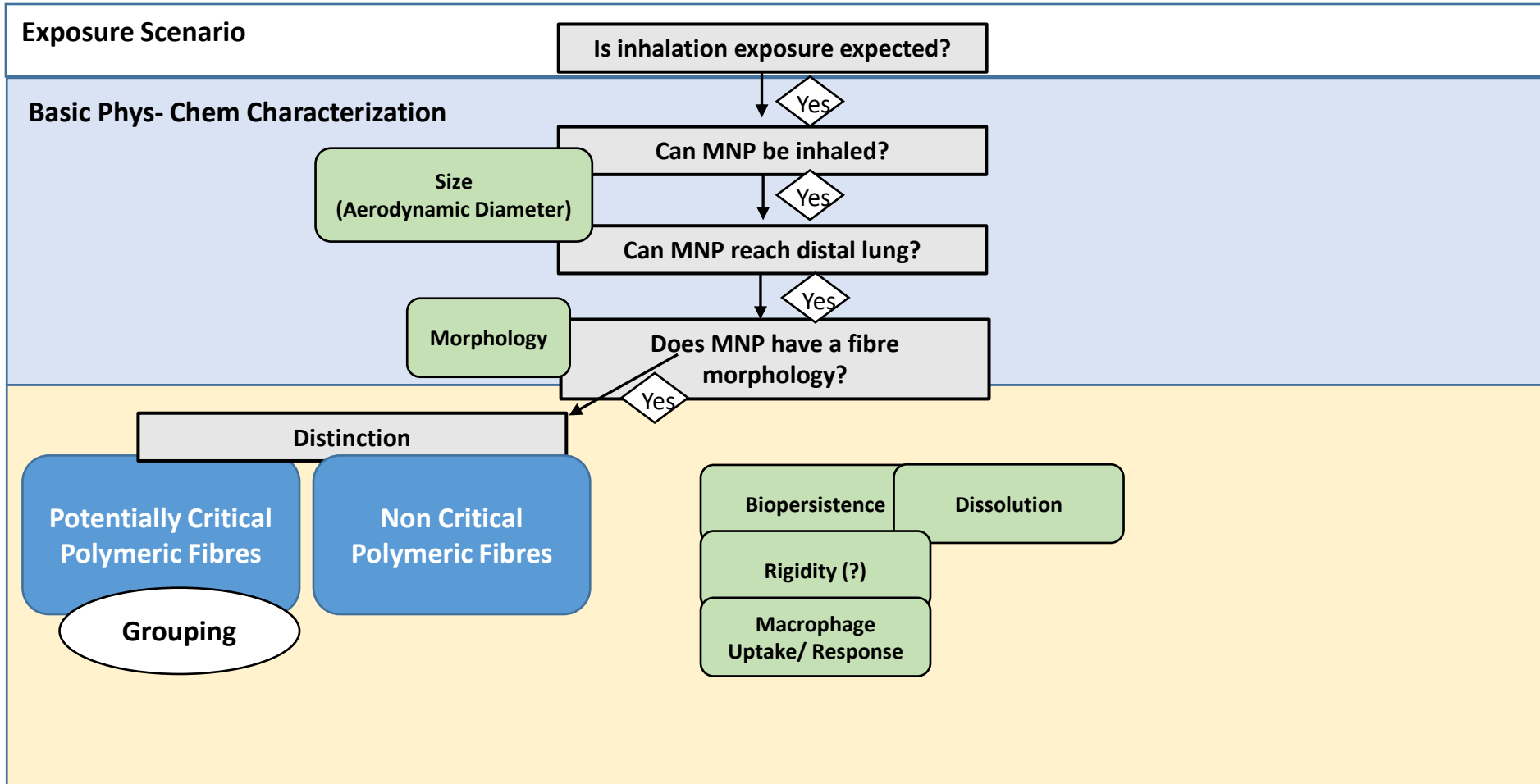
Functional groups that are known to be associated with toxicity of polymers

➤ **Water solubility**

Polymers with water solubilities < 10 mg/L showed generally low health concern

In addition, other useful criteria were discussed (e.g. **polymer's stability** or **residual monomer content**).

Towards a Risk Assessment Framework for MNPs

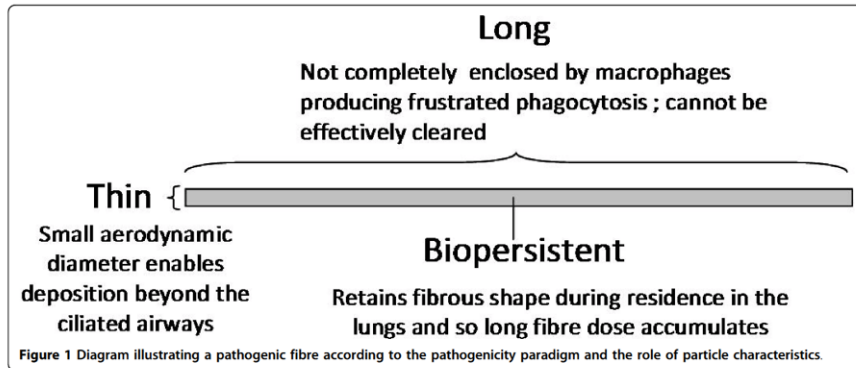


Fibre Toxicity

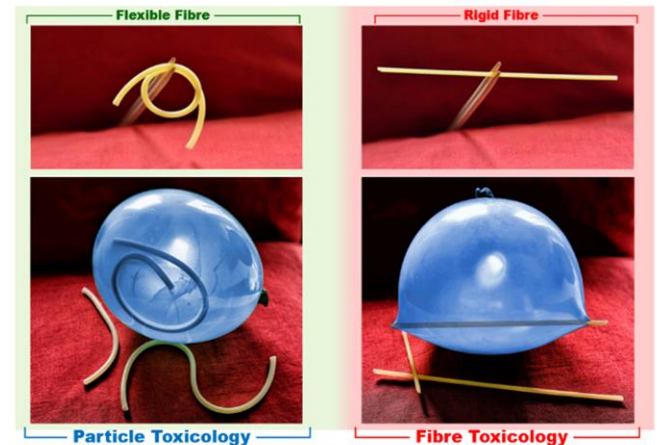
The Fibre Toxicity Paradigm is well established for inorganic fibres (in particular asbestos).

Classical Fibre Toxicity Paradigm: Respirable, long and biopersistent fibres are carcinogenic.

WHO Criteria: Length > 5 μm , Diameter < 3 μm , Aspect Ratio >3, Biopersistence



Donaldson et al 2010 PFT 2010, 7:5

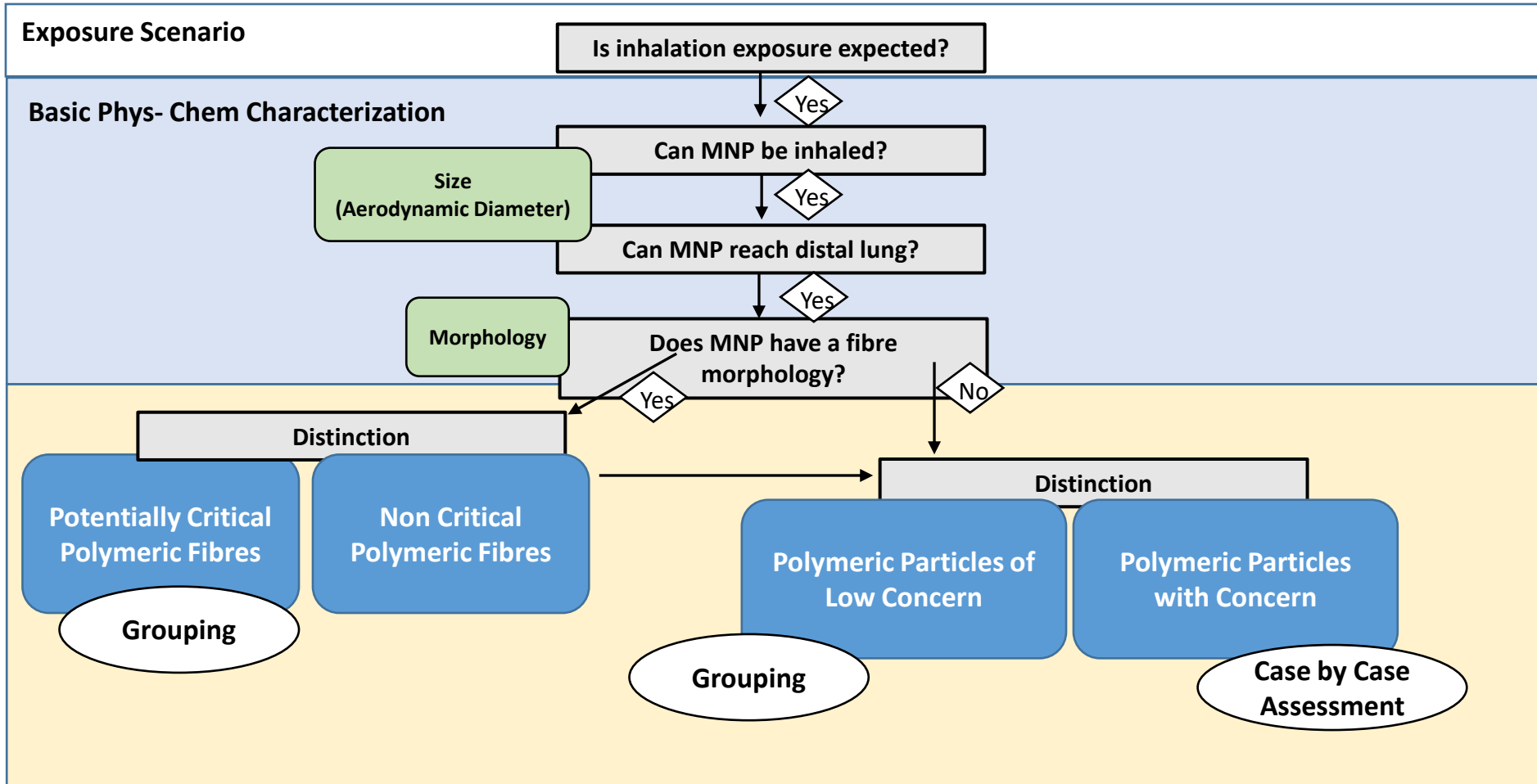


Macrophages perform the „Al-dente“-test
(Images by Asmus Meyer-Plath, BAuA)

Nanofibres challenge the classical fibre toxicity paradigm:

Rigidity hypothesis: Long, rigid fibres withstand bending during phagocytosis but flexible, thin fibres curl up.

Towards a Risk Assessment Framework for MNPs



POLYRISK's Real World Scenarios

External/internal exposure
Immune function effects



Air exposure at tire rubber refurbishing workplaces



Textile fibre workplace exposure



MNP in bottled drinking water



Utrecht University



Urban and rural outdoor air ambient MNP



Indoor Soccer Players exposure to rubber granulate-MNP

Sampling and analytical method development

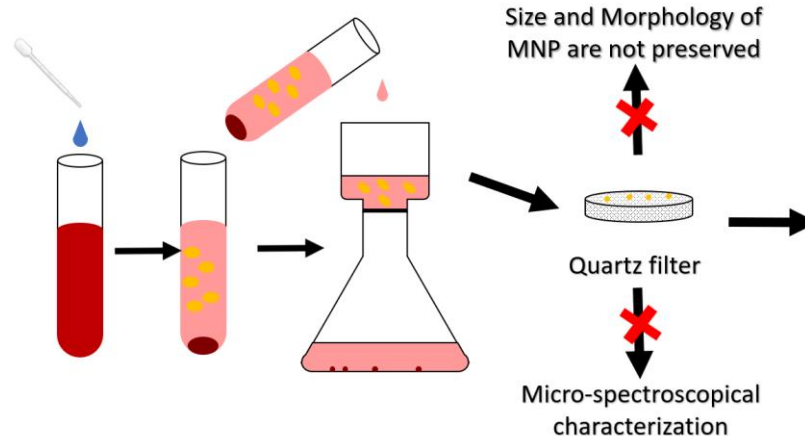
Protocols for:

- 1) blood analysis
- 2) analysis of air samples
- 3) liquid sample filtration
(using different types of filtration)



Figure: Digestion and filtration protocol for blood analysis.

Based on:
Leslie et al., *Environment International*, 163, 2022, 107199.



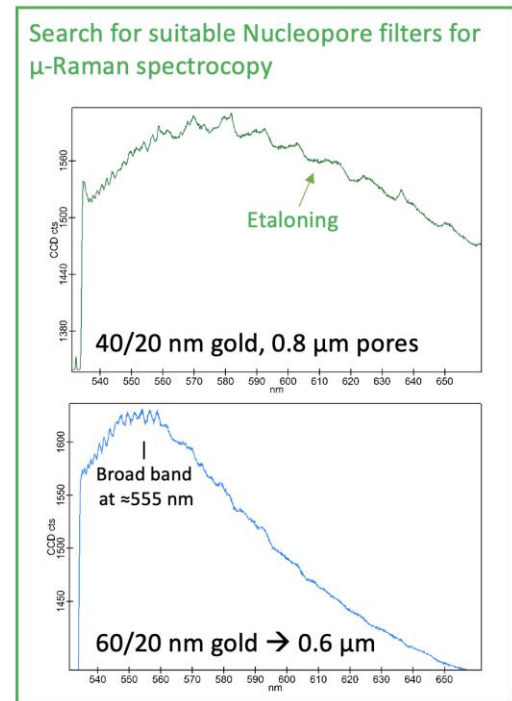
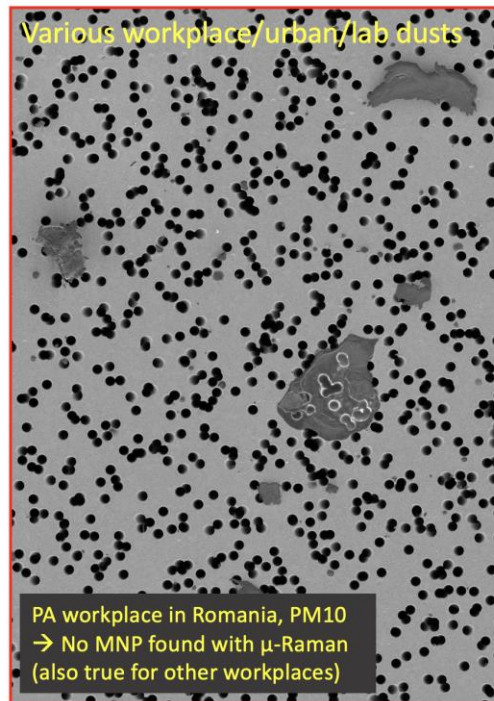
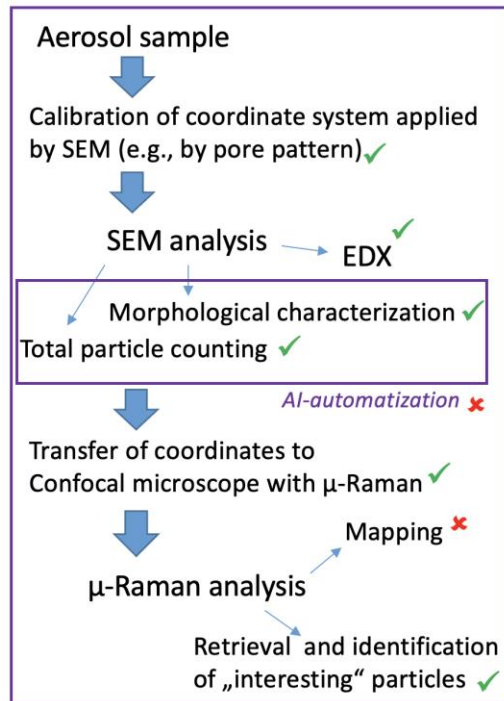
- Blood
- Digested blood
- MNP
- Organic residue



Py-GC/MS

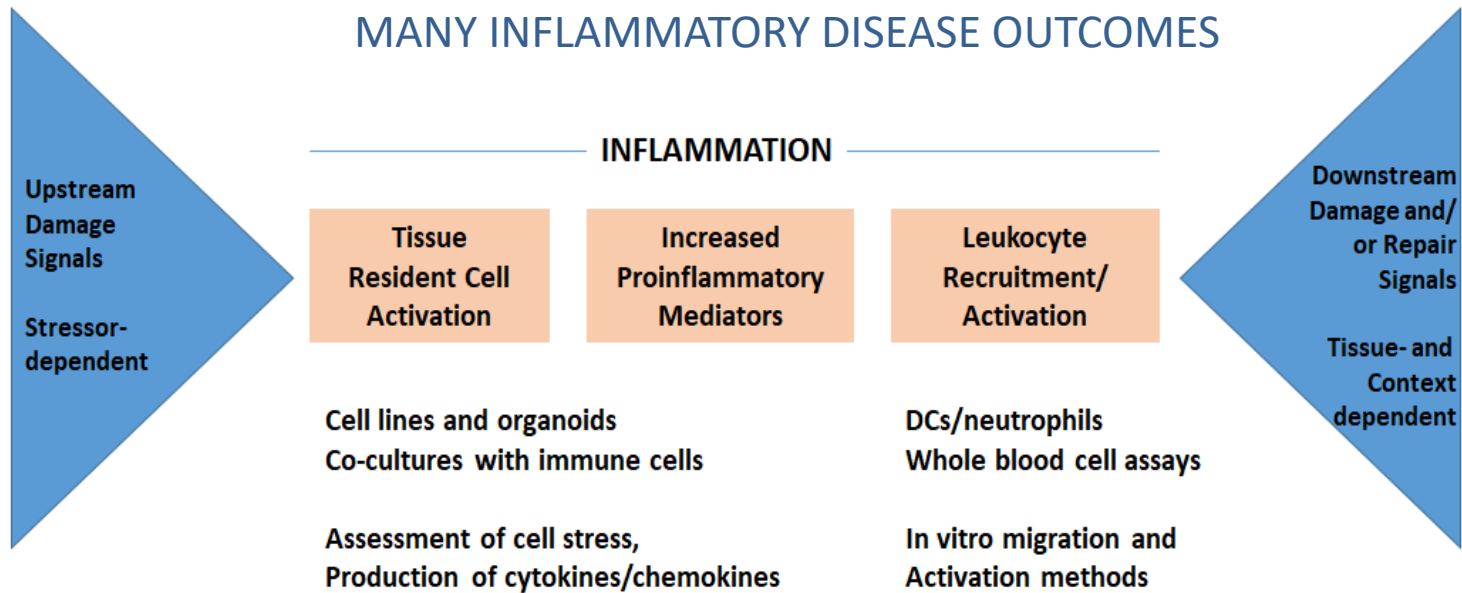
Sampling and analytical method development

Correlative microscopy, current status of Identification and Counting of MNP-Aerosols Correlative microscopy on Nucleopore filters



POLYRISK Hazard Characterization

KEY EVENTS CENTRAL TO MANY INFLAMMATORY DISEASE OUTCOMES



Inflammation

- 1) Cell Activation
(**macrophages**, epithelial cells, neutrophils, myeloid cells)
- 2) Inflammatory mediators release
- 3) Recruitment of e.g. neutrophils

Reactivity & Cellular ox. stress

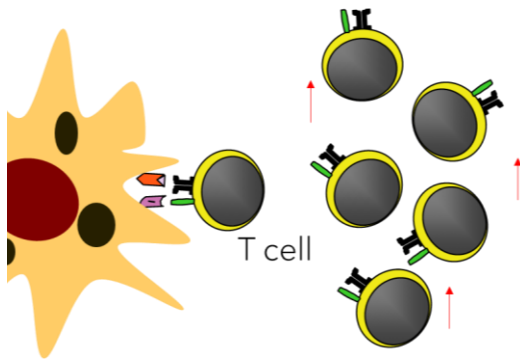
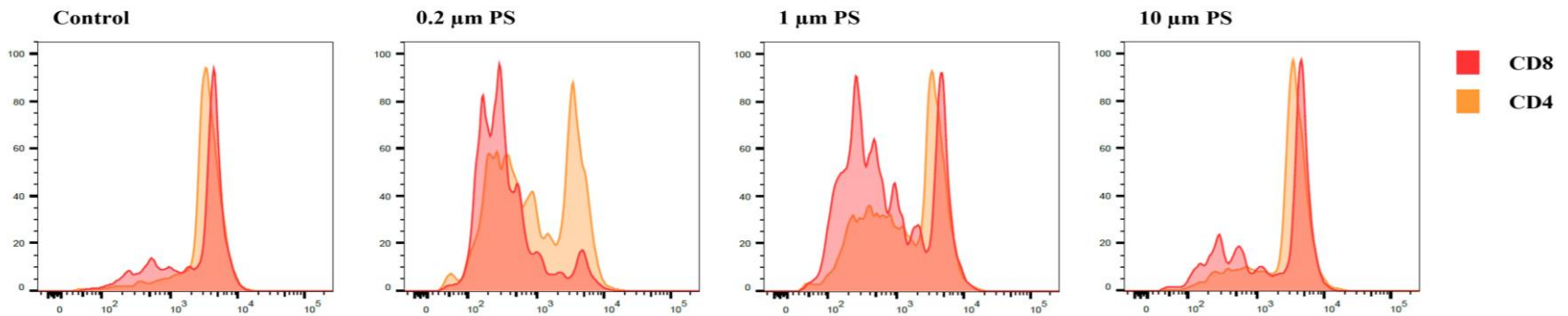
- 1) Acellular particle reactivity (e.g. FRAS, DCFDA assay)
- 2) Cellular oxidative stress (in vitro)
(various assays, **macrophages**, epithelial cells, neutrophils, myeloid cells)

Representing the Process of Inflammation as Key Events in Adverse Outcome Pathways

Daniel L. Villeneuve,^{*,†} Brigitte Landesmann,[†] Paola Allavena,[‡] Noah Ashley,[§] Anna Bal-Price,[†] Emanuela Corsini,[¶] Sabina Halappanavar,^{||} Tracy Hussell,^{||} Debra Laskin,^{|||} Toby Lawrence,[¶] David Nikolic-Paterson,^{**} Marc Pallardy,^{††} Alicia Paini,[†] Raymond Pieters,[¶] Robert Roth,[¶] and Florianne Tschudi-Monnet^c

Measuring functional DC maturation via mixed leukocyte reaction

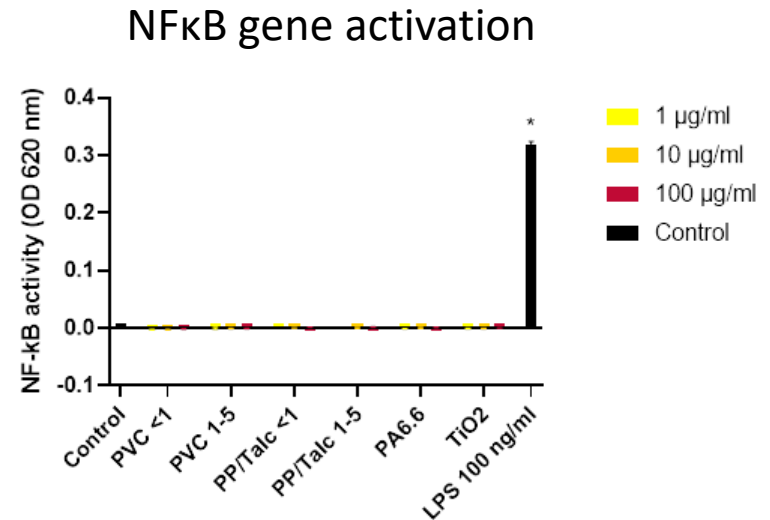
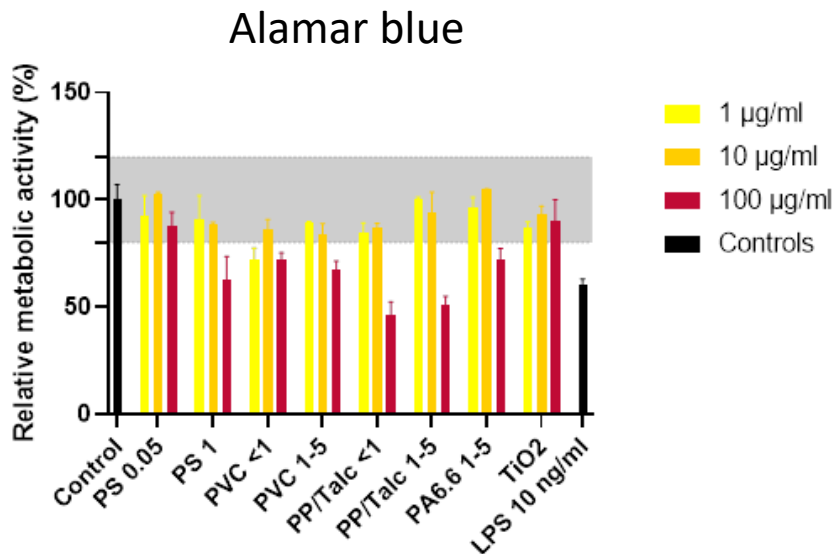
- In particular weathered 0.2 μm PS increase CD8 T-cell division



van den Berg AET, ...Pieters RHH. Environmentally weathered polystyrene particles induce phenotypical and functional maturation of human monocyte-derived dendritic cells. *J Immunotoxicol.* 2022 Dec;19(1):125-133. doi: 10.1080/1547691X.2022.2143968. PMID: 36422989.

PMA-differentiated THP1-blue macrophages after 24 hours of MNP exposure

Van den Berg et al, IRAS-UU



- Decrease in metabolic activity by some MNP, at 100 µg/ml
- No effect on NF-kB activity by any of the particles

Thank you for your attention.

