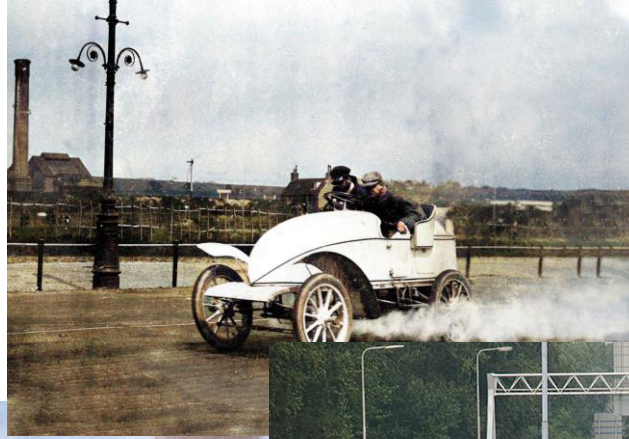
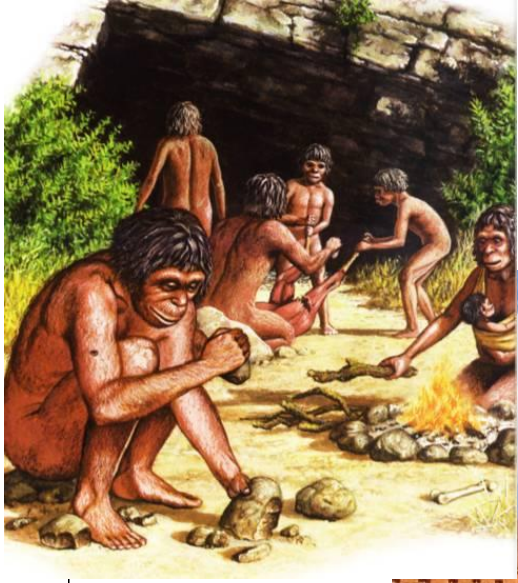


**THE NEED FOR REFERENCE MATERIALS IN MICROPLASTICS
STUDIES FROM A TOXICOLOGICAL PERSPECTIVE**

INGEBORG M. KOOTER

CHANGES



EXPOSURE



› PARTICLE EXPOSURE

Coal mine dust



PM2.5/PM10



Microplastics



["A Sprinkle of Dust" by Kelsey Hannah on Zealous](#)

- › Mixture of minerals
- › Occupational
- › 2-40 mg/m³ for 20 years
- › Lung function decrease, bronchitis
- › Complex mixture
- › Environmental
- › Up to 100 µg/m³
- › Increased mortality, lung cancer
- › Synthetic materials, additives
- › Omnipresent
- › Low levels
- › No general hazard identified

› MICROPLASTIC COMPLEX PARTICLE MIXTURES



NL

Source: TNO

› MICROPLASTIC

WHAT IF... WE DON'T DO ANYTHING? OR STOP WITH PLASTIC?



NL 2022
291 KT

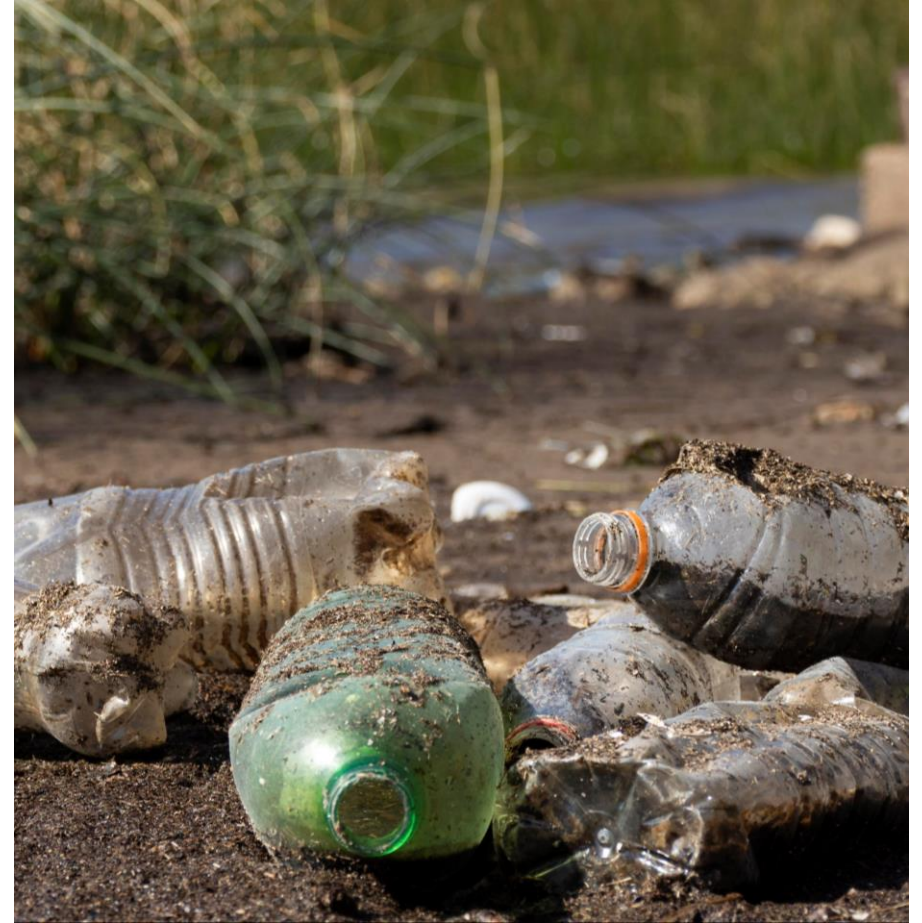


NL MAX 2050
1031 KT



NL STOP 2050
346 KT

Source: TNO



› MICROPLASTIC COMPLEX PARTICLE MIXTURES

› Polymer types and additives



 PET	 HDPE	 PVC	 LDPE	 PP	 PS	 OTHER
POLYETHYLENE TEREPHTHALATE	HIGH-DENSITY POLYETHYLENE	POLYVINYL CHLORIDE	LOW-DENSITY POLYETHYLENE	POLYPROPYLENE	POLYSTYRENE	OTHER
WATER BOTTLES; JARS; CAPS	SHAMPOO BOTTLES; GROCEY BAGS	CLEANING PRODUCTS; SHEETINGS	BREAD BAGS; PLASTIC FILMS	YOGURT CUPS; STRAWES; HANGERS	TAKE-AWAY AND HARD PACKAGING; TOYS	BABY BOTTLES; NYLON; CDS
						

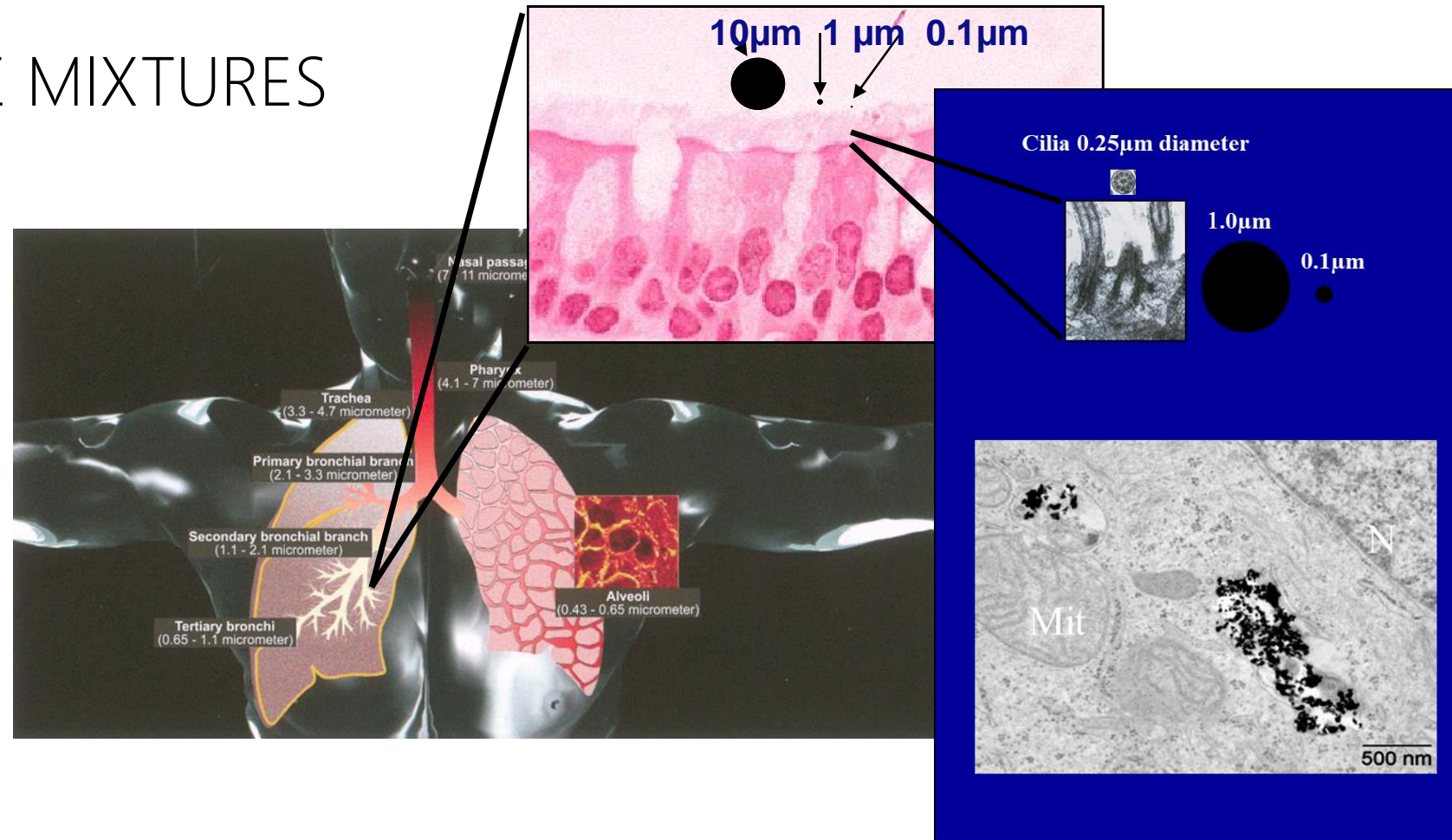
<https://www.plasticsforchange.org/blog/different-types-of-plastic>

› MICROPLASTIC COMPLEX PARTICLE MIXTURES

› Size

- › < 5 mm micro
- › < 0.1/1 μm nano

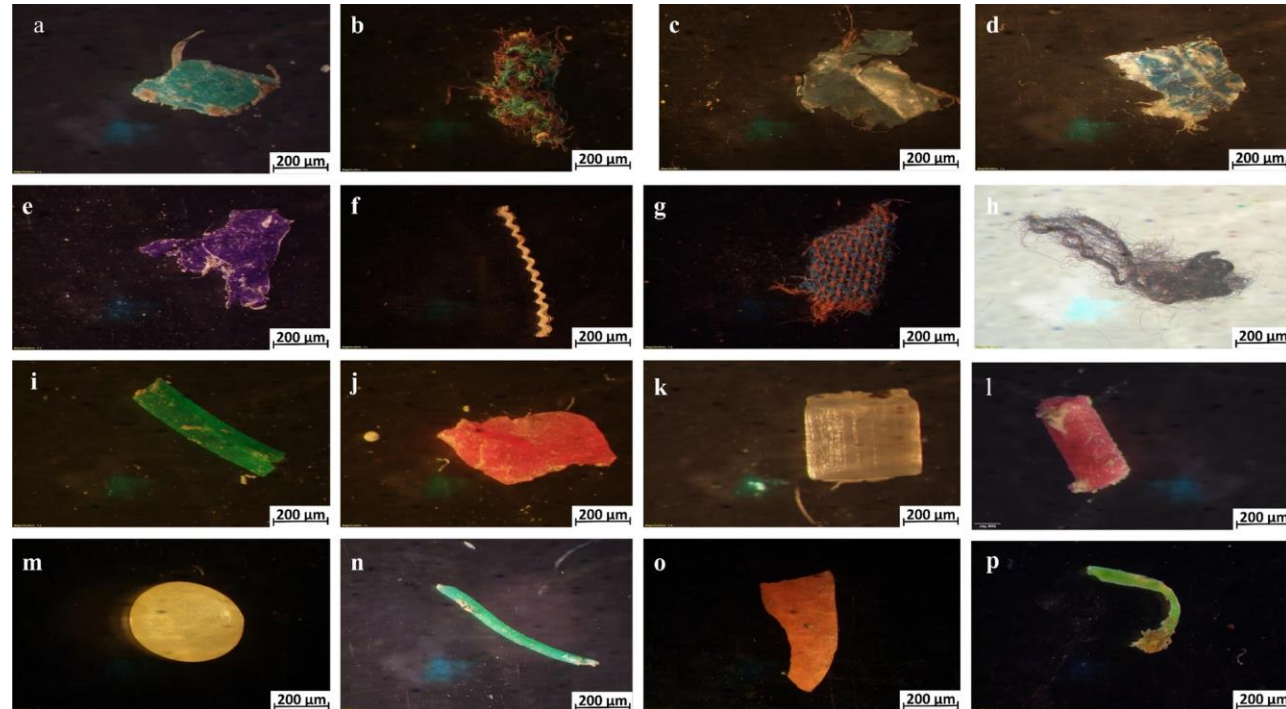
› Human cells



› MICROPLASTIC COMPLEX PARTICLE MIXTURES

› Shapes:

- › Sphere
- › Film
- › Fragment
- › Fiber



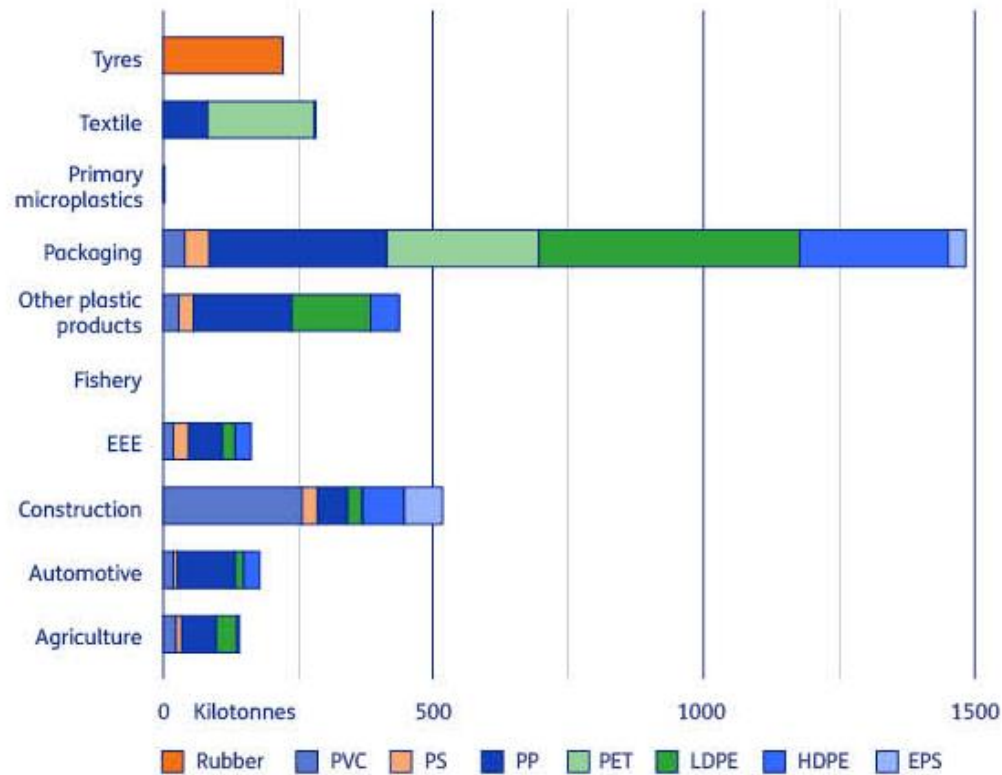
Rakib, M.R.J., et al. Sci Rep 12, 8581 (2022).
<https://doi.org/10.1038/s41598-022-12296-0>

› MICROPLASTIC PARTICLE MIXTURES

BIGGEST SOURCES: TYRES, PACKAGING AND AGRICULTURE

In The Netherlands

Plastics use per sector and polymer type (NL)



Microplastics formation per sector and polymer type (NL)



Source: TNO

› IS IT SAFE TO WHAT WE ARE EXPOSED TO?

› Risk = Exposure X Effect

› Exposure:

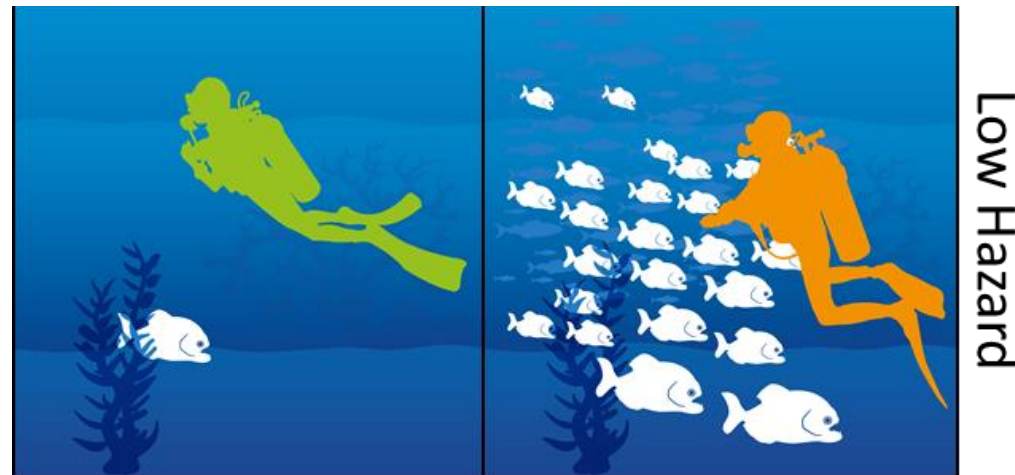
- › what is emitted?
- › concentration, chemical composition

› Effect:

- › what is the effect on humans?

toxicology

epidemiology



Low Exposure

High Exposure

› TOXICITY TESTING

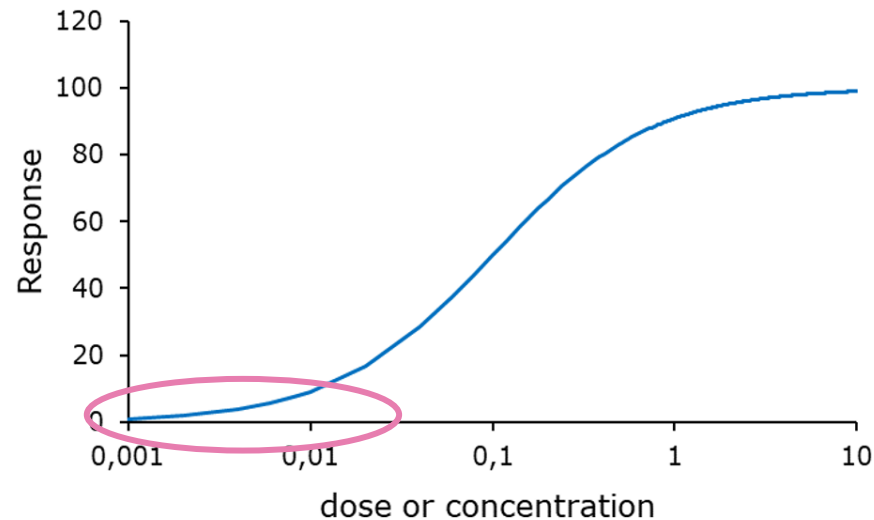
- › Toxicity testing aims:
 - › Hazard identification
 - › Establish relationship between the dose or concentration and the effect
- › Data needed for:
 - › Determine safe levels
 - › Predict the risks
 - › Prioritize chemicals



TOXICITY TESTING

DOSE DETERMINES THE EFFECT

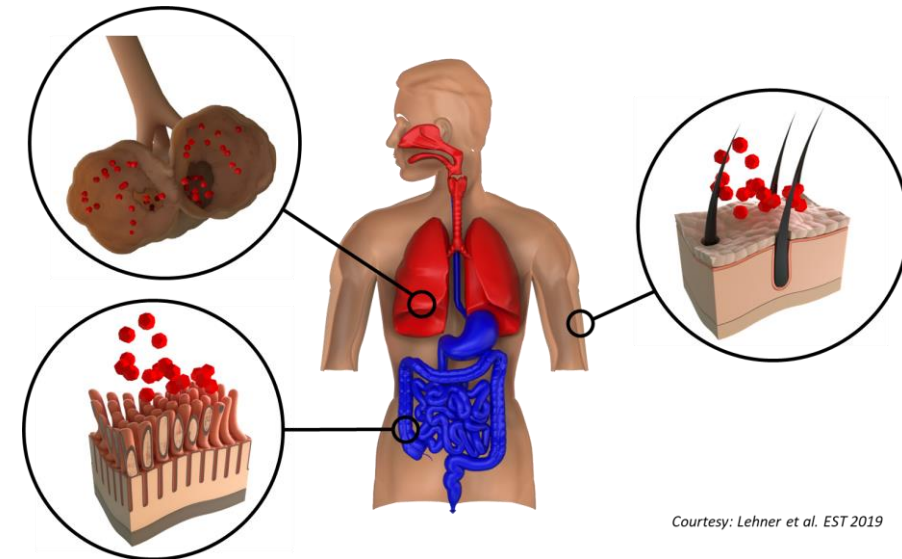
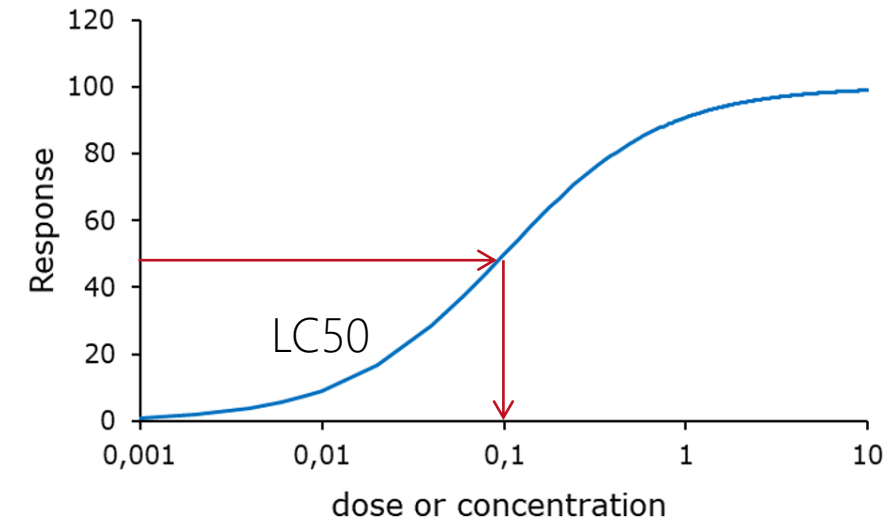
Paracelsus (1493-1541): 'any chemical is toxic, but that the dose determines the severity of the effect'



› TOXICITY TESTING

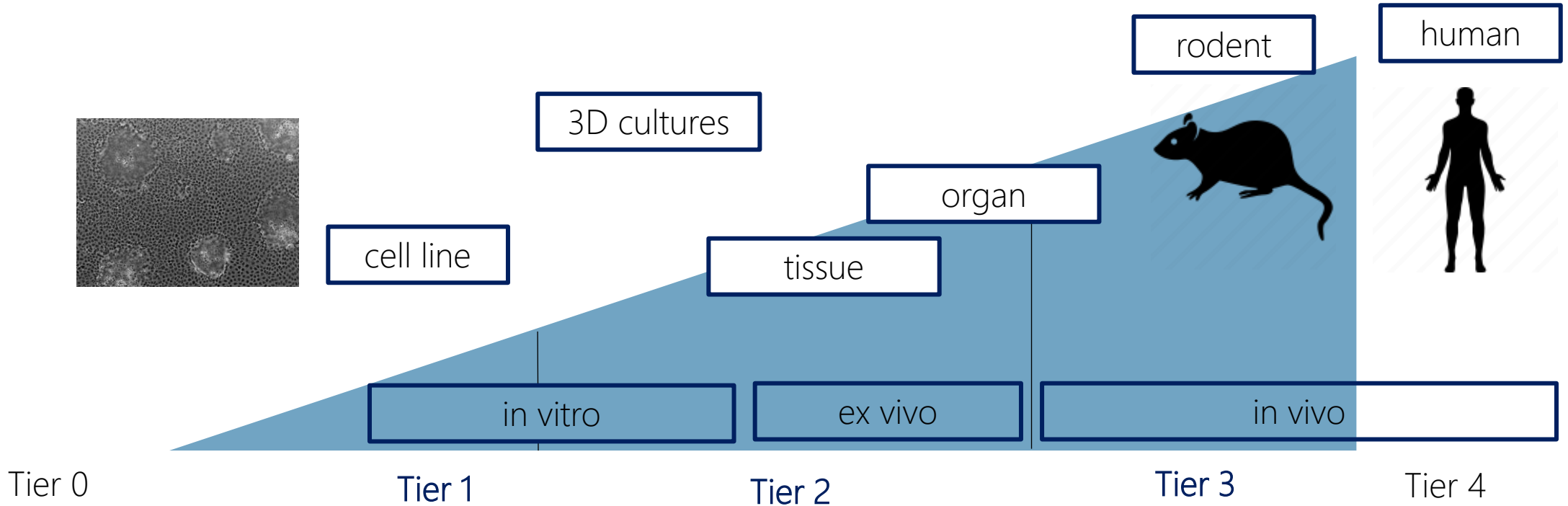
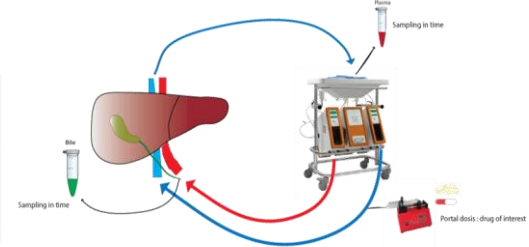
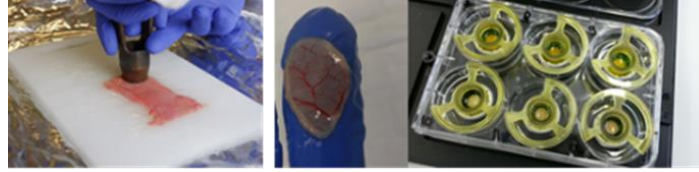
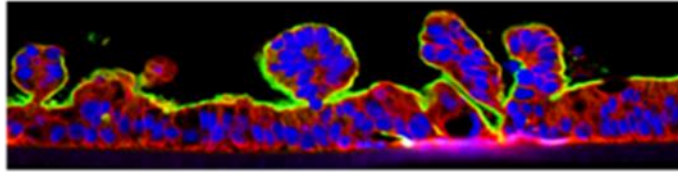
- › Toxicological test system (in vivo, in vitro)
- › Exposed to range of concentrations

- › Route of exposure
- › Time scale
- › Endpoints



Courtesy: Lehner et al. EST 2019

EXAMPLES OF TOXICOLOGICAL TEST SYSTEMS



› TOXICITY TESTING QUALITY CONTROL

› (biological) variation in outcomes

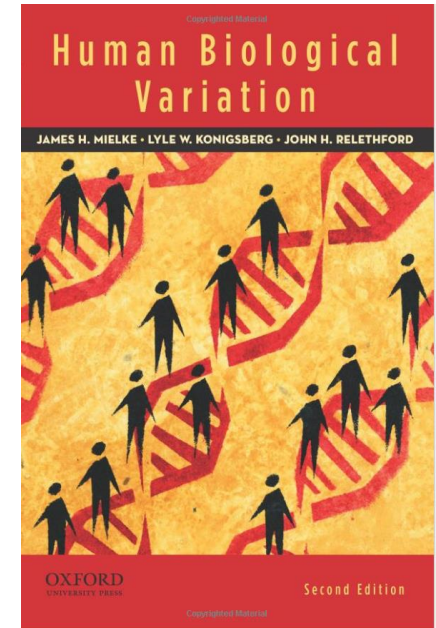
› Sufficient replication

› Careful test design

› Good choice of endpoints

› Negative control: Non-exposed control and solvent/vehicle control

› Positive control: a chemical with known toxicity



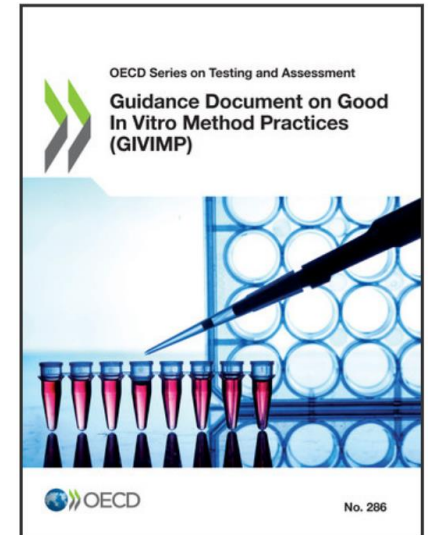
Mielke et al Human Biological Variation 2010

› TOXICITY TESTING

STANDARDISATION – STANDARD OPERATION PROTOCOLS

- › Standardization aims at reducing variation in test outcomes by carefully describing:
 - › methods for culturing and handling the test organisms
 - › the procedures for performing the test
 - › the properties and composition of test substance
 - › the exposure conditions
 - › analysis of the data

- › organized by international bodies:
 - › OECD, ISO, ASTM



› PARTICLE TOXICITY

WHAT WE DO KNOW

- › Surface
 - › Area
 - › Reactivity per area
 - › Availability
- › Dimension
 - › Length – diameter
- › Composition
 - › Volume
 - › Toxic material per volume
 - › Availability

Wright&Borm FrontPublHealth 2022

› TOXICITY TESTING

NEED FOR REFERENCE MATERIALS

› Efforts for RM are mainly on:

› Size

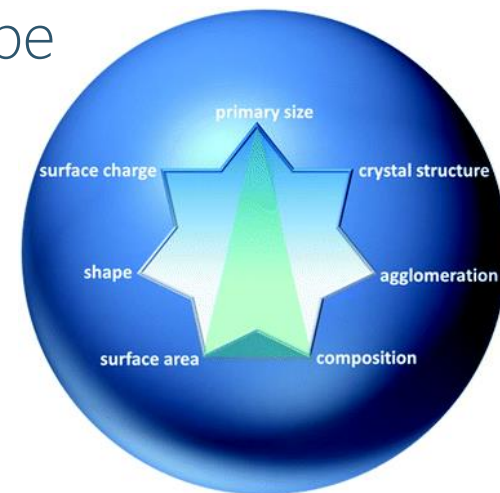
› Composition

› But agglomeration and formation of protein corona also needs to be addressed

› representative of existent materials

› present some toxicity

› be prepared in an adequate form to be used for toxicological studies



Orts-Gil et al. RSC Adv 2013

› CONCLUSIONS

THE NEED FOR REFERENCE MATERIAL IN MP TOXICITY TESTING

- › Micro and nanoparticles have always been present in nature
- › Introduction of man made plastic resulted in mainly secondary microplastic particles
- › Toxicological testing is needed to predict the risks and safe levels of microplastics
- › Full characterization of the test material is a crucial aspect in performing toxicological test
- › Toxicologists need reference materials in order to validate their toxicology testing methods for Risk Assessment and to deliver reliable results
- › Besides size, surface and composition, agglomeration and formation of protein corona also needs to be addressed
- › RM should be preferably 'ready to use' in toxicological tests



› **THANK YOU FOR
YOUR TIME**

TNO innovation
for life