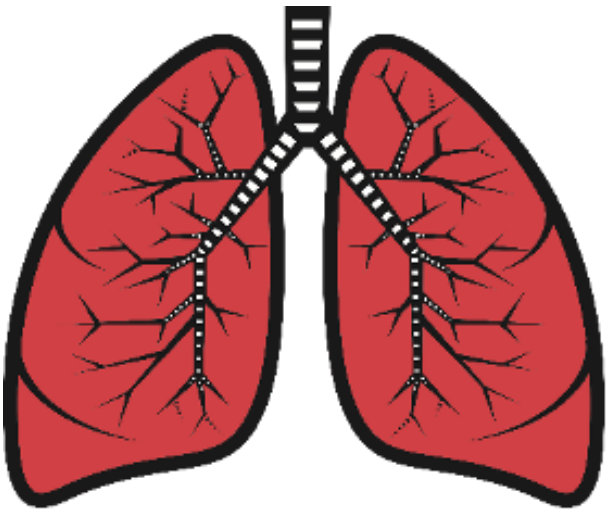
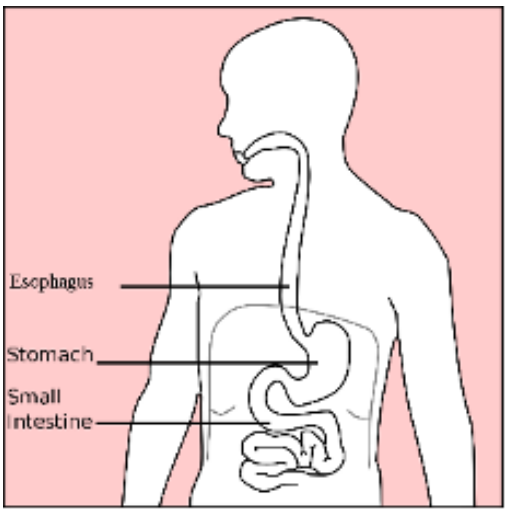
Distribution of engineered nanomaterials in the body

Background

Engineered nanomaterials (ENMs) may, after inhalation and oral intake, translocate from the site of intake to the blood and reach the secondary organs due to their small size. This may lead to accumulation of ENMs in secondary tissues over time. There is concern that after exposure of longer duration even to small amounts, these accumulated nanomaterials may pose a human health risk. To accommodate the need for safety assessment of different types of nanomaterials, non-animal models are being developed in PATROLS.





Non-animals models need data

Cellular models of the lung, liver and gastrointestinal tract (GIT) are being developed to assess the hazard of nanomaterials. In order to use the information obtained in cellular models in human risk assessment, extrapolation from *in vitro* to expected hazard *in vivo* is required. For this, a comparable measure of the dose *in vitro* and *in vivo* needs to be established. Physiologically-based Kinetic (PBK) models that describe the distribution of the dose in the body can be used here. These models include the quantity as well as the time frame in which the dose is delivered.

To be able to develop these non-animal models, high quality *in vivo* data is required. A review of existing literature at the start of the project identified data gaps.

This project has received €12.7M in funding from the European Union's Horizon 2020 research and innovation programme under grant agreement 760813

PATROLS
Advanced Tools for NanoSafety Testing

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Data generation using existing tissues as well as new studies

- Existing tissue samples from previously conducted inhalation and oral studies were reanalyzed using microscopic techniques.
- This revealed the specific place in the organs where nanomaterials accumulate and with which cell types the nanomaterials interact.
- Data gaps in distribution of nanomaterials were filled with a few dedicated rat .
- The amount of accumulated nanomaterials in several tissues and in some cases also blood and excretions were determined after inhalation and oral intake.

Lessons learned

- The *in vivo* studies have confirmed that the lung, liver and gastrointestinal tract are indeed highly important for hazard assessment and provided data regarding expected levels of tissue accumulation.
- The results on cellular localization have improved our understanding of the interaction between ENMs and specific cell types. This knowledge can improve the development of cellular models.
- From an animal welfare point of view, the repeated dosing of nanomaterial in a snack was less stressful to rats and provided effective and controlled administration of dose.

Achievements

- Distribution data will become available to others according to the FAIR principle.
- The distribution results are used to improve physiologically based kinetic models.
- The results contribute to a scientific basis for the OECD Test guideline development on toxicokinetics for nanomaterials in the Malta initiative.

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