

# PATROLS

Advanced Tools for NanoSafety Testing

## **PATROLS: Physiologically Anchored Tools for Realistic nanomaterial hazard assessment**

*Alternatives to Animal Testing*

# Current position... what's next?

- **Inadequacy** of current existing *in vitro* and *in silico* hazard assessment test systems.
- High priority to **develop and adopt advanced and physiologically relevant *in vitro* tests** with potential to substantially improve the relevance of *in vitro* approaches and provide **suitable alternatives to *in vivo* animal testing**.
- Improve regulatory guidelines to develop a **battery of standardised, versatile *in vitro* test systems** that can be utilised for **high-throughput ENM hazard assessment**.

## PATROLS H2020 Vision:



Establish and standardise a battery of next generation hazard assessment tools to predict adverse effects caused by long-term, low dose ENM exposure to humans & the environment, supporting regulatory risk decision making.



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# PATROLS Concept

## ITS for ENM Hazard Assessment



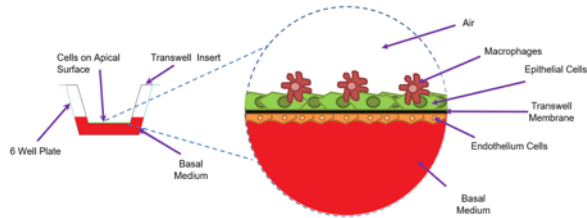
# Lung Models

## Stage 1:

*3D lung epithelial cell monocultures taken to the air-liquid interface*

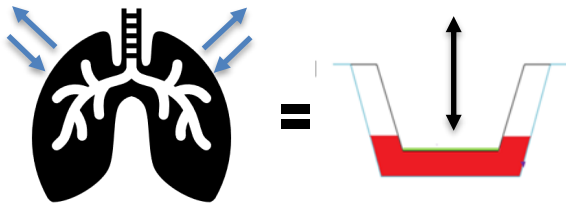
## Stage 2:

*+ monocyte derived macrophages*



## Stage 3:

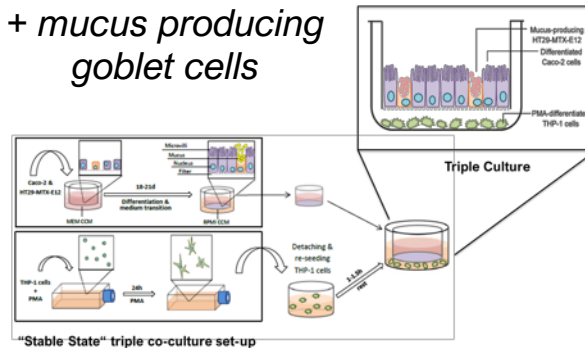
*+ mechanical flexing  
+ fluid flow system*



# GI Tract Models

*GIT epithelial cell 3D co-cultures with enterocytes and macrophages*

*+ mucus producing goblet cells*

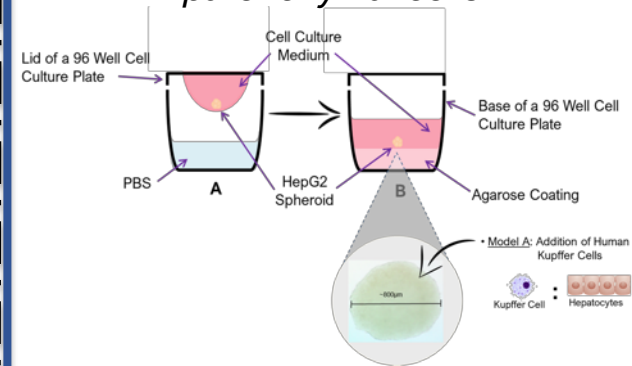


*+ ENM pre-treatment with simulated digestive fluids  
+ fluid flow system*

# Liver Models

*Both primary human hepatocyte and cell line derived 3D liver monoculture spheroids*

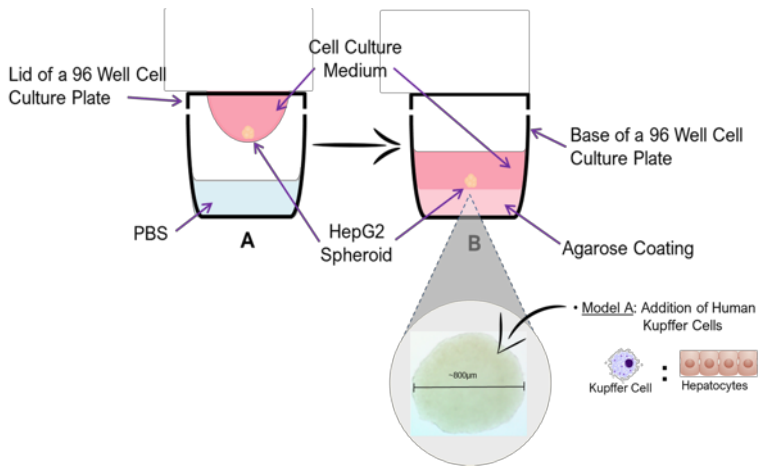
*+ primary liver macrophages or non-parenchymal cells*



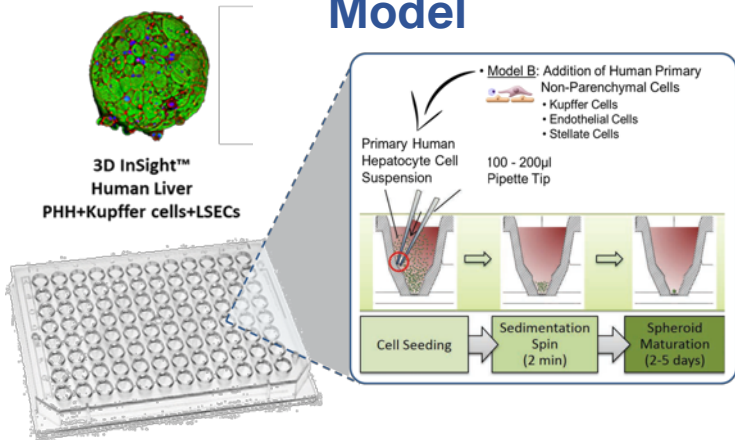
*+ ENM pre-treatment with either simulated lung or digestive fluids followed by blood plasma  
+ fluid flow system*

# Liver Models

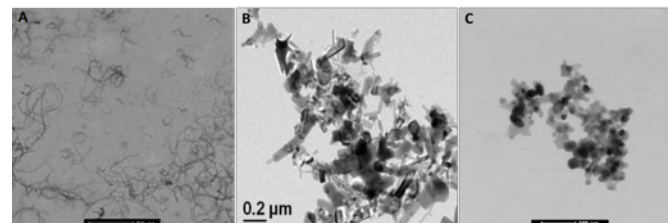
## Immortalised Cell Line Model



## Primary Human Hepatocyte Model



## ENM Exposure Scenarios



**Figure 1.** TEM images of (A) Multi-Walled Carbon Nanotubes (MWCNT), (B) Zinc Oxide (ZnO) and (C) Titanium Oxide (TiO<sub>2</sub>) ENMs from the European Commission's Joint Research Centre (JRC). <https://ec.europa.eu/jrc/en>

## Adverse Outcome Pathways

*In Vitro-In Vivo*  
Extrapolation

Improved  
Predictive  
Capability

*In Silico*  
Computational  
Simulation



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# End-User Benefits

1. Innovative and physiologically relevant *in silico* and 3D *in vitro* models of the lung, liver and GI tract.
2. Reduces uncertainty in ENM associated risk assessment promoting critical investment and consumer acceptance.
3. Enables early modification of ENMs and nano-enabled products at the beginning of innovation pathways.
4. SOPs generated in line with regulatory test guidelines.



# Thank you & questions!



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[www.patrols-h2020.eu](http://www.patrols-h2020.eu)