A tiered-testing strategy for nanomaterial hazard assessment

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INTRODUCTION

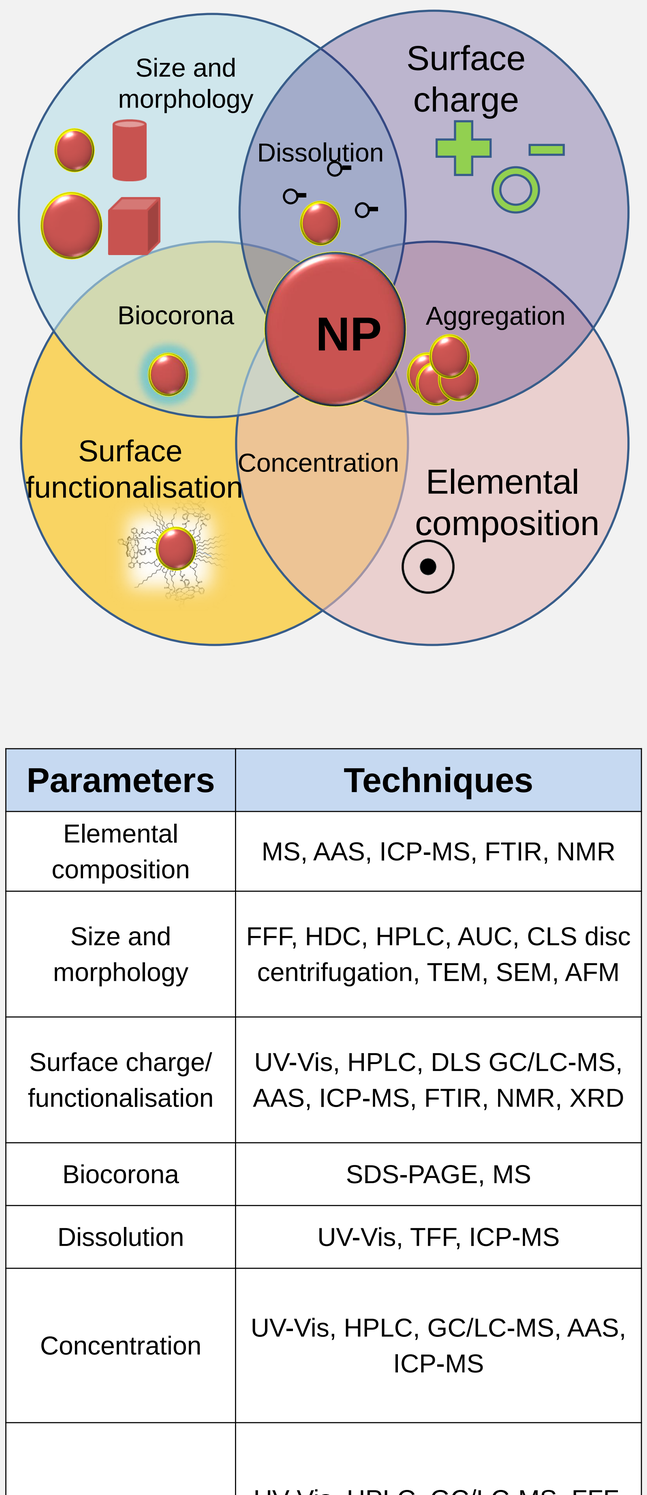
A step-wise testing strategy can be used to accurately, rapidly, and cost-effectively assess nanomaterials (NMs) for toxicity. One recommended approach based on the available literature includes the following:

- generation and thorough characterisation of standard reference NMs in their pristine form, as intended for use, and as present in the final biological system
- assessment using multiple *in silico* and *in vitro* model systems, including high-throughput screening (HTS) assays and 3D systems
- data sharing among researchers from government, academia, and industry through web-based tools such as the Nanomaterial Registry or NanoHUB
- organisation of available data into adverse outcome pathways (AOPs)
- risk assessment and management

The proposed strategy is consistent with the 2007 report from the US National Academy of Sciences, "Toxicity Testing in the 21st Century: A Vision and a Strategy", which recommends the use of *in vitro* methods involving human cells and cell lines for mechanistic pathway-based toxicity studies.

Implementation of the proposed strategy will generate meaningful information on NM properties and their interaction with biological systems, which is cost-effective, reduces animal use, and can be applied for assessing risk and making intelligent regulatory decisions regarding the use and disposal of NMs.

Characterisation

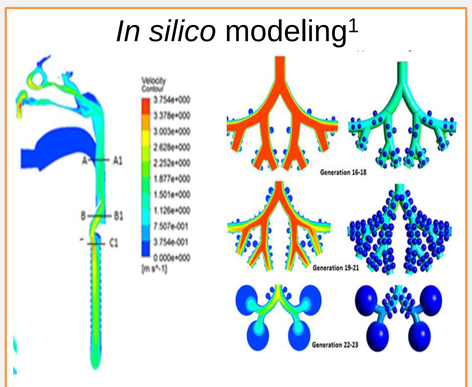


Parameters	Techniques
Elemental composition	MS, AAS, ICP-MS, FTIR, NMR
Size and morphology	FFF, HDC, HPLC, AUC, CLS disc centrifugation, TEM, SEM, AFM
Surface charge/ functionalisation	UV-Vis, HPLC, DLS GC/LC-MS, AAS, ICP-MS, FTIR, NMR, XRD
Biocorona	SDS-PAGE, MS
Dissolution	UV-Vis, TFF, ICP-MS
Concentration	UV-Vis, HPLC, GC/LC-MS, AAS, ICP-MS
Aggregation	UV-Vis, HPLC, GC/LC-MS, FFF, disc/gradient centrifugation

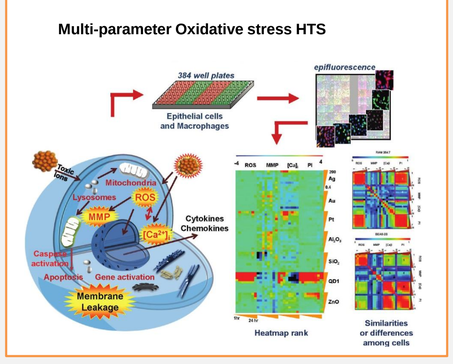
Nanotoxicology

Grouping → *In silico* → HTS → Acellular → Cell-based → Complex 3D tissue/organ systems

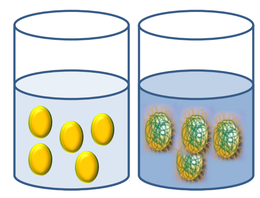
In silico modeling[1]



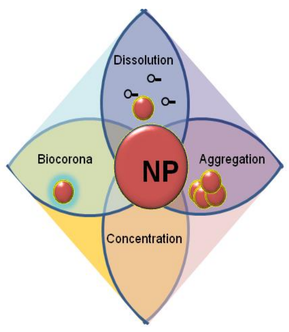
High-throughput screening[2]



Acellular assays[3,4] (stimulant or artificial fluids)

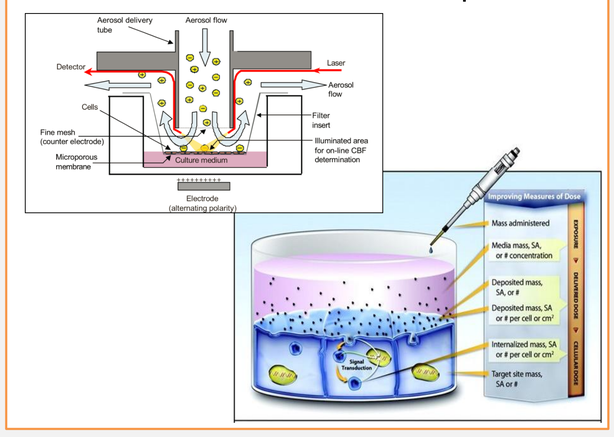


Characterisation and grouping

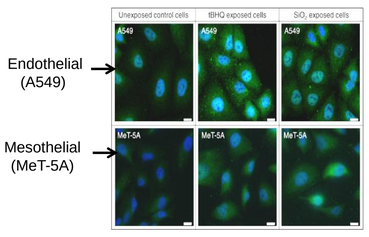


Grouping based on parameters such as NM type, physico-chemical property, bioeffects

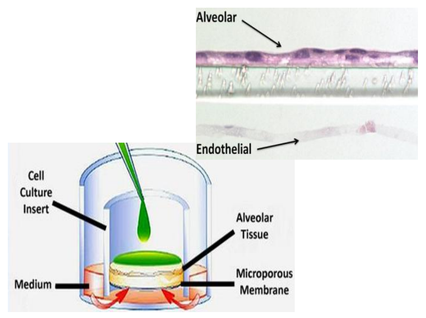
Relevant mode and dose of exposure[5]



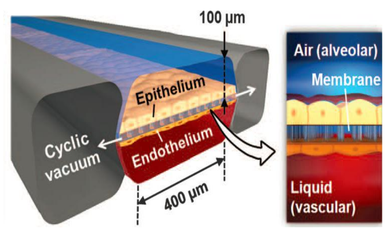
Cell-based assays[6]



EpiAlveolar™ tissue model (MatTek)



Lung-on-a-chip[7]



Risk

- Prioritisation of NMs for toxicity analysis
- Regulatory decision making
- Development of standard testing protocols
- Harmonisation in data reporting
- Recognition of novel materials

Outcome

- Well-structured nanotoxicity assessment paradigm
- Reduced duplicative testing
- Reduced animal use
- Accurate predictions of human health effects
- Increased transparency between researchers and regulators

Information Sharing and Organisation

Nanomaterial Registry | NanoHUB | AOPWiki | NanoWiki | Nano Journals | Webinars/Conferences

Abbreviations

AAS - atomic absorption spectroscopy
AFM - atomic force microscopy
AOP-Adverse outcome pathway
BET - Brunauer Emmett Teller
DLS - dynamic light scattering
FFF - field flow fractionation
FTIR - Fourier transform infrared spectroscopy
GC-MS - gas chromatography mass spectrometry
HPLC - high performance liquid chromatography
ICP-MS - inductively coupled plasma mass spectrometry
LC-MS - liquid chromatography mass spectrometry
MS - mass spectrometry
NMR - nuclear magnetic resonance
SEM - scanning electron microscopy
TEM - transmission electron microscopy
UV-Vis - ultraviolet-visible
XRD - x-ray diffraction

Groups that produce standards, guidance documents, and recommendations

- Organisation for Economic Cooperation and Development (OECD)
- The European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM)
- Scientific Committee on Consumer Safety (SCCS)
- International Organisation for Standardisation (ISO) Technical Committee 229
- ASTM Technical Committee E56

References

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