

Murphy et al.:

How to Formulate Hypotheses and IATA to Support Grouping and Read-Across of Nanofoms

Supplementary Data

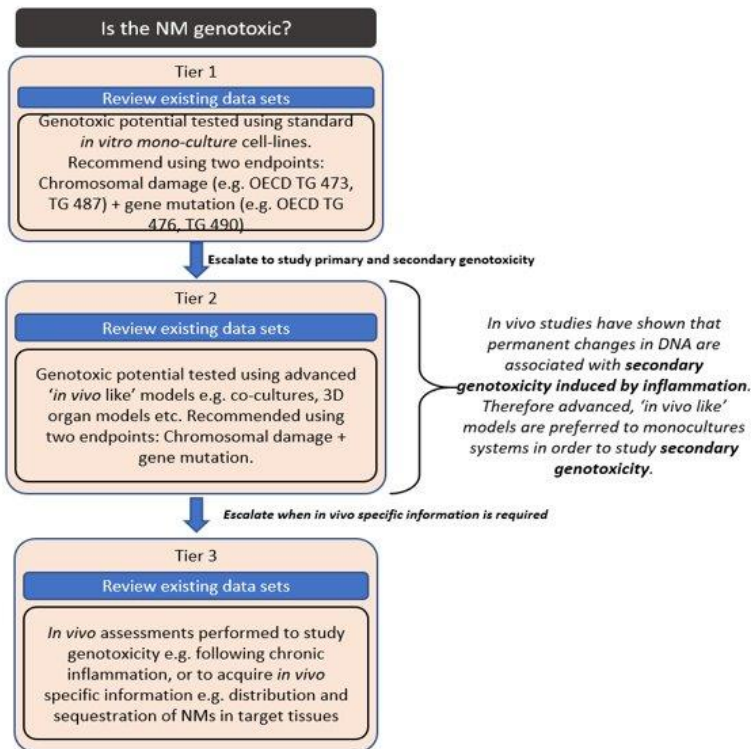


Fig. S1: Tiered testing strategy for genotoxicity
Adapted from Verdon et al. (2022).

Tab. S1: Example of a blank simplified data matrix for IATA H-I-1

Decision node	Tier	Study	NF1	NF2	NF3 ...
Basic information		Carbon %			
		Length			
		Diameter			
		Shape aspect ratio			
		Specific surface area			
DN1	1	Mean diameter			
		Density			
	2	MMAD			
DN2	3	Quantification of lung burden			
	1	Dissolution rate in lung lining fluid			
DN3	2	Dissolution rate in intracellular environment			
	1	Dissolution rate in lysosomal fluid			
DN4	2	Dissolution rate in intracellular environment			
		Average fiber length			
	1	Fiber length distribution			
DN5	2	Fiber length distribution in airborne dispersion			
		Fiber width distribution			
	1	Agglomeration state			
DN6	2	Fiber width dispersion in airborne dispersion			
		IL-1 β release			
		Cathepsin B activity/release			
		Qualitative assessment of protrusion/piercing cell membrane			
	1	Qualitative assessment of lysosomal disruption			
DN7	3	Development of 3D macrophage granulomas			
		<i>In vivo</i> hazard response			
	1	<i>In vitro</i> testing using cell lines			
		Cytotoxicity			
		Cytokine release			
		Oxidative stress			
		DNA damage			
	2	Cytokine release			
		DNA damage			
		Granuloma formation			
		Cell transformation			
	3	<i>In vivo</i> hazard response			

Reference

Verdon, R., Stone, V., Murphy, F. et al. (2022). The application of existing genotoxicity methodologies for grouping of nanomaterials: Towards an integrated approach to testing and assessment. *Part Fibre Toxicol* 19, 32. doi:10.1186/s12989-022-00476-9