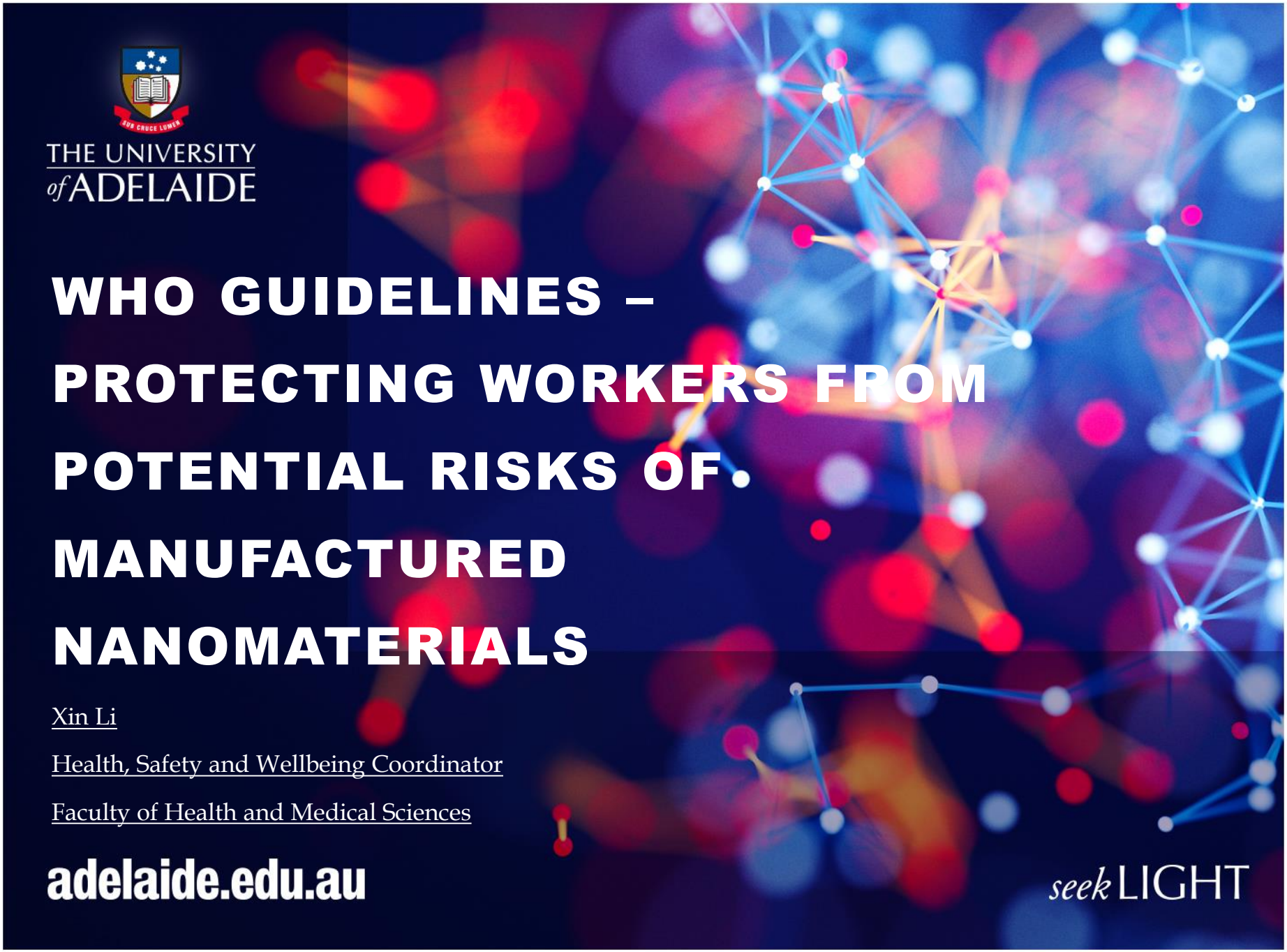

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WHO GUIDELINES – PROTECTING WORKERS FROM POTENTIAL RISKS OF MANUFACTURED NANOMATERIALS

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seek LIGHT

Manufactured Nanomaterials (MNMs)

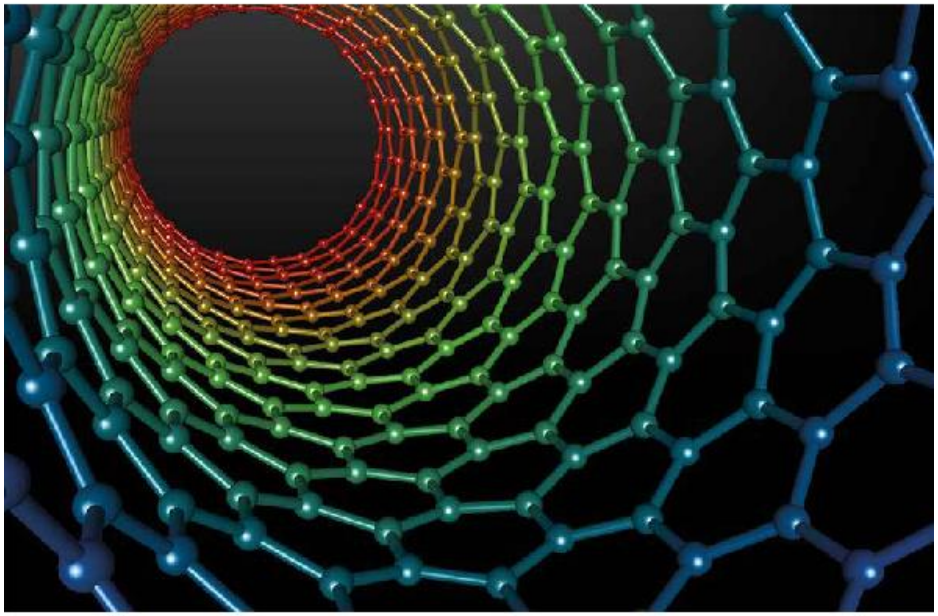
Size < 100 nm, size of a virus particle

Shape Fibrous; granular biopersistent

Toxicity of ENMs

- Uncertain – mainly oxidative stress at the moment, NO human study
- Specific toxicity dependent on physicochemical properties
  - Size — The smaller the size, potentially more hazardous
  - Shape — Fibre may be more hazardous than granular
  - Composition
  - Surface Composition — Higher the surface area, higher the reactivity
  - Charge — Positive surface charge is worse than negative
  - Rate of dissolution — Higher the rate, easier release the metal ions and hence potentially more hazardous
  - Fate inside human body

WHO GUIDELINES ON PROTECTING WORKERS FROM POTENTIAL RISKS OF MANUFACTURED NANOMATERIALS



World Health Organization

Relevent Sections

Guiding Principles

Precautionary Approach

Toxicity VS Exposure 

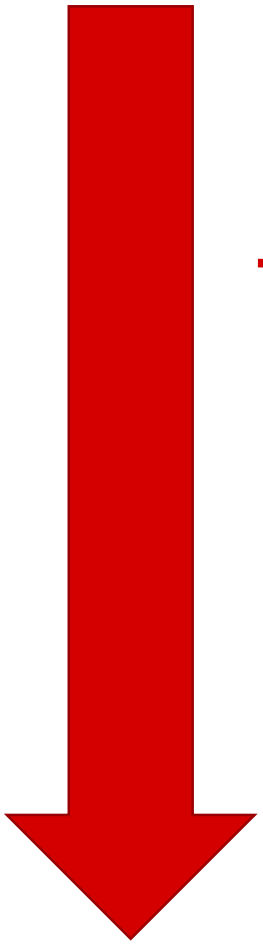
Why?

~~Risk = Likelihood x Consequences~~ ????

Risk = Exposure x Possibility x Severity

Guiding Principles

Hierarchy of Control



Elimination

~~Substitution~~ **Process Change** – no ENM release into air

Engineering

Administration

PPE

Best Practice

1. Classification of MNMS

The GDG considers it best practice to class MNMs into the following three groups: those with specific toxicity, those that are respirable fibres and those that are granular biopersistent particles.

Specific Toxicity

Respirable Fibres

Granular Biopersistent Particles (GBP)

Best Practice (Continued...)

2. Worker Involvement

The GDG considers it best practice that workers should be involved in health and safety issues and that this will lead to more optimal control of health and safety risks.

Worker Participation

Best Practice (Continued…)

3. Additional Training and Education of Workers

The GDG considers it best practice that workers potentially exposed to MNMs should be educated on the risks of MNMs and trained in how they can best protect themselves.

Some points recommended include

- Workers are aware of the risk of the bulk material
- Hazards specific to MNMs that is different to bulky material
- SDS do not always provide reliable information on MNMs
- Hazard class assigned to the MNMs
- Route of exposure
- Which routes of exposures are measured
- Which tasks put workers most at risk
- MNM specific control (different from bulky material)

- **OELs**
- **Control banding**

Best Practice (Continued…)

3. Additional Training and Education of Workers

The GDG considers it best practice that workers potentially exposed to MNMs should be educated on the risks of MNMs and trained in how they can best protect themselves.

https://tools.niehs.nih.gov//wetp/public/hasl_get_blob.cfm?ID=9094

Specific Recommendations

1. Assess health hazards of MNMs

Recommendation 1: The GDG recommends assigning hazard classes to all MNMs according to the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals for use in safety data sheets. For a limited number of MNMs this information is made available in these guidelines

Most common classifications

- ❑ Specific target organ toxicity after repeated exposure
- ❑ Carcinogenicity
- ❑ Germ cell mutagenicity
- ❑ Serious eye damage
- ❑ Respiratory or skin sensitization.

Serious eye damage / eye irritation	Category 1	 GHS05	Danger	H318	Causes serious eye damage
	Category 2A	 GHS07	Warning	H319	Causes serious eye irritation

Germ cell mutagenicity	Category 1A	 GHS08	Danger	H340	May cause genetic defects [5]
	Category 1B				
	Category 2		Warning	H341	Suspected of causing genetic defects [5]
Carcinogenicity	Category 1A		Danger	H350	May cause cancer [5]
	Category 1B				
	Category 2		Warning	H351	Suspected of causing cancer [5]
	(5) = State route of exposure if it is conclusively proven that no other routes of exposure cause the hazard.				

Reproductive toxicity	Category 1A	 GHS08	Danger	H360 [6]	May damage fertility or the unborn child.
				H360F [7]	May damage fertility.
				H360D [7]	May damage the unborn child
				H360FD [7]	May damage fertility. May damage the unborn child.
	Category 1B			H360Fd [7]	May damage fertility. Suspected of damaging the unborn child.
				H360Df [7]	May damage the unborn child. Suspected of damaging fertility.
	Category 2		Warning	H361 [6]	Suspected of damaging fertility or the unborn child.
				H361f [7]	Suspected of damaging fertility.
				H361d [7]	Suspected of damaging the unborn child.
				H361fd [7]	Suspected of damaging fertility. Suspected of damaging the unborn child.
	Additional category for effects on or via lactation	No Pictogram	No Signal Word	H362	May cause harm to breast-fed children.
	(6) = (state specific effect if known)(state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard). (7) F = Fertility, D= Development (lowercase f, d = suspected effect).				

Specific target organ toxicity (repeated exposure)	Category 1	 GHS08	Danger	H372	Causes damage to organs [8] through prolonged or repeated exposure [9]
	Category 2		Warning	H373	May cause damage to organs [8] through prolonged or repeated exposure [9]
	(8) = (state all organs affected, if known). (9) = (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard).				

Specific Recommendations

Recommendation 2: The GDG recommends updating safety data sheets with MNM-specific hazard information, or indicating which toxicological end-points did not have adequate testing available (**STRONG, moderate-quality evidence**).

Recommendation 3: For the respirable fibres and granular biopersistent particles' groups, the GDG suggests using the available classification of MNMs given in **Table 2** for provisional classification of nanomaterials of the same group (**CONDITIONAL, low-quality evidence**).

TABLE 2. CLASSIFICATION OF HAZARDOUS PROPERTIES OF NANOMATERIALS (MNMS) THAT HAVE AN EXISTING OECD DOSSIER

MNM	Acute toxicity	Skin corrosion/ irritation	Serious eye damage/eye irritation	Respiratory or skin sensitization	Germ cell mutagenicity	Carcinogenicity	Reproductive toxicity	Specific target organ toxicity (single exposure)	Specific target organ toxicity (repeated exposure)
Fullerene (C_{60})	No[a]	No	No	No	No	No data[b]	No data	No data	No
SWCNT	No	No	No	No	Cat 2B[c] (L)[d]	No data IARC[e] 3	No data	No data	Cat 1 (L)
MWCNT	No	No	Cat 2A (H)[f]	No	Cat 2 (H)	MWCNT-7: Cat 2 (M)[f], IARC 2B Other MWCNTs: IARC 3	No	No data	Cat 1 (M)
AgNP	No	No	No	Cat 1B (M)	No	No data	No	No data	Cat 1 Inhalation (H) Cat 2 oral (H)
AuNP	No data	No data	No data	No data	No data	No data	No data	No data	Cat 1 Inhalation (H)
SiO_2	No	No	No	No	No	No data	No	No data	Cat 2 Inhalation (H)
TiO_2	No	No	No	No	No	No data; IARC 2B	Cat 2 (L)	No data	Cat 1 Inhalation (H)
CeO_2	No	No data	No data	No data	No data	No data	No data	No data	Cat 1 Inhalation (M)
Dendrimer	No data	No data	No data	No data	No data	No data	No data	No data	No data
Nanoclay	No data	No data	No data	No data	No data	No data	No data	No data	No data
ZnO	No	No	No	No data	No	No data	No	No data	Cat 1 Inhalation (M)

AgNP: silver nanoparticles; AuNP: gold nanoparticles; CeO_2: cerium dioxide; MWCNT: multi-walled carbon nanotubes; SiO_2: silicon dioxide; SWCNT: single-walled carbon nanotubes; TiO_2: titanium dioxide; ZnO: zinc oxide.

[a] No: no hazard class assigned based on data.

[b] No data: no studies available in OECD dossier.

[c] GHS categories: Cat 1 usually implies serious and/or irreversible damage; Cat 2 milder or reversible damage. Within a category A implies more serious and B milder damage.

[d] L: low level of evidence.

[e] IARC refers to the International Agency for Research on Cancer categories of confidence in carcinogenicity: IARC Cat 2B = possibly carcinogenic; IARC Cat 3 = not enough evidence to draw conclusion.

[f] M: moderate level of evidence.

[g] H: high level of evidence.

Specific Recommendations (Continued…)

2. Assess Exposure to MNMs

Recommendation 4: The GDG suggests assessing workers' exposure in workplaces with methods similar to those used for the proposed specific OEL value of the MNM (**CONDITIONAL, low-quality evidence**).

- Using the same method as the proposed OELs (Annex 1)
- Tiered approach when no proposed OELs
  - Qualitative assessment of exposure (absence and presence)
  - Quantative assessment of exposure concentration
  - Comprehensive assessment – size distribution, morphology, chemical composition

Specific Recommendations (Continued…)

2. Assess Exposure to MNMs

Recommendation 5: Because there are no specific regulatory OEL values for MNMs in workplaces, the GDG suggests assessing if workplace exposure exceeds a proposed OEL value for the MNM. A list of proposed OEL values is provided in Annex 1 of these guidelines. The chosen OEL should be at least as protective as a legally mandated OEL for the bulk form of the material (**CONDITIONAL, low-quality evidence**).

- Choose a proposed OEL as low as possible
- Choose a proposed OEL at least as protective as a legally mandated OEL for the bulk material

Category	Study reference	Nanomaterials and specifications	OEL name	Mass concentration µg/m³	Particle concentration (particle/ml, fibres/cm²)	Surface concentration (nm²/cm²)	Derivation approach
Inhalation exposure: general MNM approach							
MNM	Guldotti 2010	Fine particulate matter ≤2500 nm	BOEL	30	ND	ND	Environmental
MNM	McGarry 2013	Airborne particles from nanotechnology processes	PCVs	ND	3 times LBPC for more than 30 minutes	ND	Environmental
Inhalation exposure: categorical MNM approach							
CMAR	BSI 2007	CMAR nanomaterials, NM	BEL	0.1 × bulk WEL	ND	ND	Bridging
Fibres	AGS 2013	Non-entangled fibrous NM	Acceptance level (default), respirable fraction	ND	0.01	ND	Bridging/ grouping
Fibres	BSI 2007	Fibrous NM	BEL	ND	0.01	ND	Bridging/ grouping
Fibres	Stockmann-Juvala 2014	Carbon nanofibres, CNFs	OEL	ND	0.01	ND	Bridging/ grouping
Fibres	van Broekhuizen 2012	Carbon nanotubes, CNTs, insoluble NM with high aspect ratio >3:1	NRV	ND	0.01	ND	Bridging/ grouping

Benchmark Exposure Limits – Australia (2010)

Nanoparticle characteristic as per the BSI Guide grouping	Suggested Benchmark Exposure Level (BEL)	Some types of engineered nanomaterials in each group
Fibrous nanomaterials	0.01 fibres/ml	Carbon nanotubes, nanowires
CMAR nanomaterials	0.1x *WEL bulk material	Ni nanoparticles
Insoluble nanomaterials	0.066 x *WEL bulk material	Nanocrystals, quantum dots, ceramic oxides, metals
Soluble nanomaterials	0.5 x * WEL	Lipid-type nanoemulsions, dendrimer-type drug delivery systems

*WEL bulk material: Workplace Exposure Limit (i.e. Exposure Standard) for the bulk form of the chemical

Specific Recommendations (Continued...)

2. Assess Exposure to MNMs

Recommendation 6: If specific OELs for MNMs are not available in workplaces, the GDG suggests a stepwise approach for inhalation exposure with, first an assessment of the potential for exposure; second, conducting a basic exposure assessment and third, conducting a comprehensive exposure assessment such as proposed by OECD or CEN (**CONDITIONAL, moderate-quality evidence**). For dermal exposure assessment, there was insufficient evidence to recommend one method of dermal exposure assessment over another.

Specific Recommendations (Continued...)

2. Assess Exposure to MNMs

- The initial assessment provides information on the likelihood of MNMs being released during an activity or process, and usually does not comprise any measurements.
- The basic assessment, using hand-held or personal devices or samplers, measures exposure as particle number concentration(s) or as respirable mass, or both, in the breathing zone or the workstation air and in the background air. These measurements are supported by laboratory analysis of the samples to characterize the MNM(s) either by chemical composition or morphology.
- In addition to the basic assessment, the comprehensive assessment provides a characterization of the aerosols in the breathing zone that enables, for example, estimation of the dose of MNMs that is deposited in the gas-exchange region of the lung.

Specific Recommendations (Continued...)

3. Control exposure to MNMs

Recommendation 7: Based on a precautionary approach, the GDG recommends focusing control of exposure on preventing inhalation exposure with the aim of reducing it as much as possible (**STRONG, moderate-quality evidence**).

Recommendation 8: The GDG recommends reduction of exposures to a range of MNMs that have been consistently measured in workplaces especially during cleaning and maintenance, collecting material from reaction vessels and feeding MNMs into the production process. In the absence of toxicological information, the GDG recommends implementing the highest level of controls to prevent any exposure of workers. When more information is available, the GDG recommends taking a more tailored approach (**STRONG, moderate-quality evidence**).

Specific Recommendations (Continued...)

3. Control exposure to MNMs

- Assess and control the task exposure – not the MNM
  - Scale of use matters
  - Inhalation and dermal exposures are unlikely when enclosed
  - If not fully enclosed, inhalation can occur as well as dermal exposure
  - In suspension/liquid form, dermal and ingestion can still occur without inhalation
    - CNTs and CNFs, inhalation does not occur in synthesis and handling/transfer liquids. Dermal does not occur in synthesis
    - Si-based, metal oxides and other MNMs – inhalation and dermal does not occur in reaction synthesis

Specific Recommendations (Continued...)

3. Control exposure to MNMs

Recommendation 9: The GDG recommends taking control measures based on the principle of hierarchy of controls, meaning that the first control measure should be to eliminate the source of exposure before implementing control measures that are more dependent on worker involvement, with PPE being used only as a last resort. According to this principle, engineering controls should be used when there is a high level of inhalation exposure or when there is no, or very little, toxicological information available. In the absence of appropriate engineering controls PPE should be used, especially respiratory protection, as part of a respiratory protection programme that includes fit-testing (**STRONG, moderate-quality evidence**).

Specific Recommendations (Continued…)

3. Control exposure to MNMs

Recommendation 10: The GDG suggests preventing dermal exposure by occupational hygiene measures such as surface cleaning and the use of appropriate gloves (**CONDITIONAL, low-quality evidence**).

Specific Recommendations (Continued...)

3. Control exposure to MNMs

Effects of Exposure

- Enclosure – most effective (PF>100)
- Ventilation – may/may not be effective (0.12<PF<55)
- Fume cupboards – vary depending on inward airflow velocity when sash is open and worker movement
- N95 masks (P2 equivalent) – 10<PF<11
- P100 respirators – very effective PF =100
- Cloth mask – very ineffective (1.1 <PF <1.35)
- Air purifying respirator – extremely effective (PF>1.1 million)

Specific Recommendations (Continued...)

3. Control exposure to MNMs

Recommendation 11: When assessment and measurement by a workplace safety expert is not available, the GDG suggests using control banding for nanomaterials to select exposure control measures in the workplace. Owing to a lack of studies, the GDG cannot recommend one method of control banding over another (**CONDITIONAL, very low-quality evidence**).

Control Banding

Hazard Band

Exposure Band

Resulting Band to determine the risk fall into

Control Banding

Table 1. Key differences of currently available control banding tools.

Control Banding Tools	Purpose/Main Targets	Hazard Band					Exposure Band				Overall Score	Controls and Exposure Route	Reference
		Total Bands	No. of parameters				Total Bands	No. of parameters					
			Parent Material	Nano specific physicochemical properties	Nanotoxicology	Life Cycle of ENMs		Frequency & Quantity	Inhalable Dust Level	No. of Workers Exposed			
CB NanoTool & CB NanoTool 2.0	Research Laboratory, Researchers and WHS Professionals	4	6	4	5	0	4	3	1 but only qualitatively dustiness	1	4 Risk Levels - RL 1 - 4	Engineering Control on inhalation only	Paik et al. 2008; Zalk, Paik & Swuste 2009
GRIDELET OHB Approach	Industrial workplaces and workers	5	0	1 but used to determine exposure NOT hazard	10	0	5	1	3 but only estimates the possibility of emission	0	4 Coloured Risk Levels - Blue, Green, Yellow & Red	No controls recommended. Included whether actions need to be against each band.	Gridelet et al. 2015
Precautionary Matrix	Workers, consumers and environmental release, synthesised ENMs, SMOs	unspecified	0	3	0	4	unspecified	7	0	0	2 Classes – Class A (low risk) & Class B (higher risk)	No controls recommended. Included the need for classification under Class B	Höck et al. 2008;
NanoSafer 1.1	SMOs, down-stream use powder only	4	1	5	0	0	5	10	1	0	5 Risk Levels – RL 1-5	Standard guidance on risk management and advice on risk assessment via online media	Jensen et al. 2014
FRENCH ANSES	Workers in small to large enterprises	5	1	2	0	0	4	0	0	0	5 Risk Control Bands 1-5	Engineering control (ventilation) on inhalation only	Reidiker et al. 2012
Stoffenmanager Nano 1.0	Both workers and employers	2	0	2	0	0	4	8	0	0	3 Risk Ranking 1-3	Risk priority ranking only. Priorities of tasks for organisations to action.	Van Duuren-Stuurman et al. 2012
Guidance IVAM	Both workers and employers	3	0	3	0	0	3	3	0	0	3 Classes, A, B and C	Engineering control (ventilation) & Occupational Hygiene Strategy	Cornelissen et al. 2011

Specific Recommendations (Continued...)

4. Health Survillence

The GDG cannot make a recommendation for targeted MNM-specific health surveillance programmes over existing health surveillance programmes that are already in use, due to the lack of evidence.

Specific Recommendations (Continued...)

5. Method of training

The GDG considers training of workers and worker involvement in health and safety issues to be best practice, but cannot recommend one form of training of workers over another, or one form of worker involvement over another, owing to the lack of studies available.

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