Risk Assessment of Nanomaterials

Safe Nanotechnology – Exposure Assessment, Risk Assessment and Regulatory Challenges

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Contents

• Risk assessment for chemicals: An introduction
• Why are nanomaterials difficult?
• Approaches to risk assessment for nanomaterials.
• Proving compliance with regulatory risk assessments
Risk vs Hazard

High Hazard
Low Exposure

Low Hazard (?)
High Exposure
How is risk calculated?

Risk = Exposure x Hazard

• Quantitative risk assessment requires knowledge of both exposure AND risk.
• Qualitative risk assessment is possible if these values are not available.
Risk Assessment for Chemicals (REACH)

**Exposure Assessment**
- Define uses
- Worker exposure
- General Population exposure
- Environmental Exposure

**Hazard Assessment**
- Physical
- Toxicological
- Ecotoxicological

**Risk Characterisation**
- Substance in PBT, vPvB or dangerous (as described by 67/548/EEC)

**Risk Controlled?**
- Yes
- No

**Document in CSR**

**Communicate using eSDS**
Risk mitigation

• Hazard is intrinsic to a chemical
• Reduced Exposure = Reduced Risk
• Reducing Exposure in workers
  • Operating protocols, technical measures, personal protective equipment
• Reducing exposure to environment
  • Reduce amount released, onsite trapping technology
• Reducing risk to general population
  • Direct exposure: reduce quantities, reduce amount released from products
  • Indirect exposure (via environment): see above
Identification of Exposure Scenarios

Substance Lifecycle
(Manufacture, formulation, industrial, professional and consumer use)

- Synthesis
- Distribution
- Formulation
- Use as a coating (professional)
Exposure Assessment for chemicals
Interconvertibility of nanoforms

Original primary particles

Coated (deliberate or environmental) particles

Agglomerate

Smaller primary particles
Exposure assessment for nanomaterials

NanoFORM 1
Primary particles

NanoFORM 2
Agglomerates

NanoFORM 3
Synthetic coating

NanoFORM 4
Natural coating

Synthesis

Workers
Consumers
Environment

Degradation

Workers
Consumers
Environment

Consumers
Environment
Risk Assessment of nanomaterials

• Interconvertibility of nanoforms = greater complexity of risk assessment.

• Hazard not intrinsic to all forms.
  • Risk can be reduced by reducing hazard

• Safe by Design
  • Control of nanoforms in synthesis
    • Size
    • Form
    • Coating
Risk assessment of nanomaterials: Difficulties

• Lack of information
  • Complete hazard information of all nanoforms?
  • How do nanoforms behave in environment?

• Absence of tools
  • Nanomaterials do not behave like simple organic substances
  • Most established tools based on exposure modelling of organic substances

• Setting of boundaries of assessment
  • Should an assessment only look at nanoforms?
Risk assessment of nanomaterials: New approaches

• Why are you doing a risk assessment?
  • Safe working practice
  • Regulatory obligations
  • Development decisions

• What answer are you looking for?
  • Quantitative versus qualitative
Risk assessment of nanomaterials: Workers

• MARINA FP7 project
• 2-stage approach
• Identify potential exposure scenarios
  • Where might risk occur?
• Evaluate relevant exposure scenarios
  • What is the risk and how can it be managed.
  • Where are there data-gaps?

Risk assessment of nanomaterials: Workers

• Which route of exposure is most relevant
  • Most nanomaterials are powders or suspensions
  • Inhalation most likely route
  • Transfer of particles across skin is difficult

• Which nanoform is the worker exposed too?
• Which nanoform do you have data for?
• Need to simplify
• Use grouping for hazard and exposure (and hence risk)
• Can nanomaterials be treated as a mixture?
Risk assessment of nanomaterials: Environment

- Another MARINA FP7 paper
- Similar structure to worker risk assessment.
  - 2-stage assessment
  - Identify key exposure scenarios for assessment.

Scott-Fordsmand et al. (in press). Int. J. Environ. Res. Public Health
Risk assessment of nanomaterials: Environment

• Environmental RES can be identified by (P)MFA (Probabilistic Material Flow Analysis) – A top down model
  • Many models do not account for transformation of nanoforms
  • Expert judgement needed
  • Time-dependent aspects are included in latest versions

• Exposure estimated by modelling
  • Traditional modelling tools are not appropriate to nanomaterials

• Exposure modelling validated by monitoring
  • NanoMonitor tool
Risk assessment of nanomaterials: Environment

• Potentially very complex due to transformation of nanoforms

• Fate of NM governed by kinetics not thermodynamics
  • Different tools needed
  • Temporal consideration needed

• Can it be simplified?
  • Identify key environmental compartments
  • Nanomaterials tend to get coated, agglomerate and/or adsorb to env. particles and accumulated in sediment/sludge/soil
  • Use grouping for hazard AND exposure (and hence risk)

• Can nanomaterials be treated as a mixture?
Use of Grouping in Chemical Risk Assessment (Hazard)

• Categorisation
  • Look for a trend in toxicity across a group of similar forms. Predict toxicity of new member of the group.
    • (Q)SAR

• Grouping
  • Identify group of similar forms with the same toxicological profile
  • Apply one toxicological endpoint value to all members

• Read-across
  • Apply toxicological of an existing form to a new form
  • Needs very good scientific justification (mechanistic, structural, toxicokinetics)
Use of Grouping in Chemical Risk Assessment (Exposure)

- Widely used in regulatory exposure assessment.
- “Use Descriptor” concept
  - PROC (worker activities), ERC (environmental release), PC or AC (consumers)
- Often regarded as very conservative
- Can be further refined for sector specific activities
  - SpERCs, SWEDs, SCEDs
- Commonly used risk management measures can form part of the grouping.
Use of Grouping in Nanomaterial Risk Assessment (Hazard)

• Hazards of every nanoform may be uncertain

• Recent evaluations by ECHA have requested information on all identified nanoforms.
  • 1000 grades of silica identified
  • Testing for reproductive toxicity on each grade might cost € 350,000,000 and sacrifice 80,000 animals!

• There is extensive guidance to using alternative to animal testing
  • In vitro, in silico, grouping, read-across, (Q)SAR
  • Can they be applied to nanomaterials?
Use of Grouping in Nanomaterial Risk Assessment (Hazard)

• Look for groups of forms that display similar or predictable effects.
• The boundaries of the group can be defined by different parameters
  • Chemical composition
  • Size and shape of primary particle and/or agglomerate
  • Coating
  • Toxic mechanism
  • Toxicokinetics
  • Behaviour in environment
• Through a life-cycle the nanomaterial might move in and out of groups.
Use of Grouping in Nanomaterial Risk Assessment

Material properties
- Chemistry
- Size/shape

Release
- Powder
- Solid matrix

Exposure
- Worker inhalation
- Sediment organisms

Uptake/ Biodistribution
- Poor elimination from lungs

Apical toxic effect
- Cancer formation
- Reproduction rate inhibition

Cellular effect
- Inflammation
- Cytotoxicity

Bio-physical Interaction
- Release of ions
- Biological corona

Arts et. al. (2014). Regulatory toxicology and pharmacology, 70, 492 - 506
Example of the Use of Grouping

• DF4nanoGrouping
  • Landsiedel et al. (2015). A decision-making framework for the grouping and testing of nanomaterials (DFnanoGrouping). Regulatory toxicology and pharmacology, 71, S1-S27
  • Landsiedel et al. (2016). Case studies putting the decision-making framework for the grouping and testing of nanomaterials (DF4nanoGrouping) into practice

• Identified 4 groups
  • Soluble NMs
  • Biopersistent High Aspect Ratio NMs
  • Passive NMs
  • Active NMs
Conclusion on the use of grouping for NM Risk Assessment

• Essential to simplify very complex assessments
• Particle characterisation across lifecycle essential
• Processes will improve overtime and with better understanding of biological, chemical and physical processes
• An open mind on defining group parameters is important.
• Is grouping for NM risk assessment appropriate? Should it be grouping for particle risk assessment instead?
Tools for NM Risk Assessment

• Many tools have been developed BUT
  • Are they freely available and validated?
  • Are they qualitative?
  • How are they viewed by regulators?


• Some are intended to be user friendly for industry wide use.
  • Guidenano
  • NanoSafer
  • SimpleBox4Nano
NM Risk Assessment tools - NanoSafer

- www.nanosafer.org
- Control Banding approach
- Occupational health tool
- Can be applied for specific situations.
- Output is a risk level with which advice on appropriate risk management measures is given.
NM Risk Assessment tools - GuideNano

- [http://www.guidenano.eu/](http://www.guidenano.eu/)
- Control banding approach
- Supported by experimental data
- Assesses workplace, consumer and environmental risk
- Gives advice on suitable risk management measures
NM Risk Assessment tools – SimpleBox4nano

- Environmental exposure modelling programme
- Multimedia mass balance model
- Applies kinetic principles to calculations
Conclusions

• Risk assessment is potentially very complex

• Simplify as much as possible
  • Grouping can help with this but it is a developing area of research
  • Define what you want out of the assessment. Will a qualitative assessment suffice?

• Detailed knowledge of your substance is vital
  • Good characterisation through lifecycle

• Don’t treat nanomaterials in isolation from other particles
Thank you

Any questions?