Risk Assessment of Nanomaterials

Safe Nanotechnology – Exposure Assessment, Risk Assessment and Regulatory Challenges

Lancaster (UK), 24 October 2017

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NanoMONITOR is partly funded by the European Commission Life+ with grant agreement LIFE14 ENV/ES/000662

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

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Risk vs Hazard

High Hazard

Low Exposure

Low Hazard (?)

High Exposure

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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.

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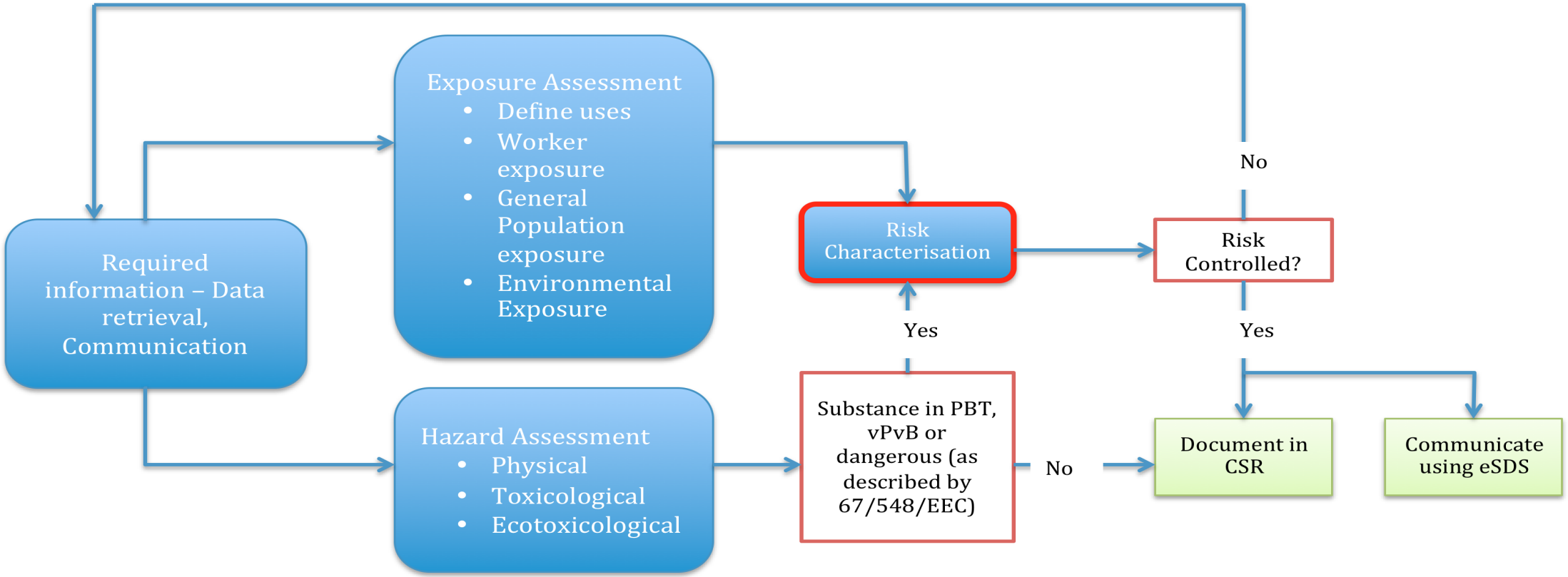
Risk Assessment for Chemicals (REACH)



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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

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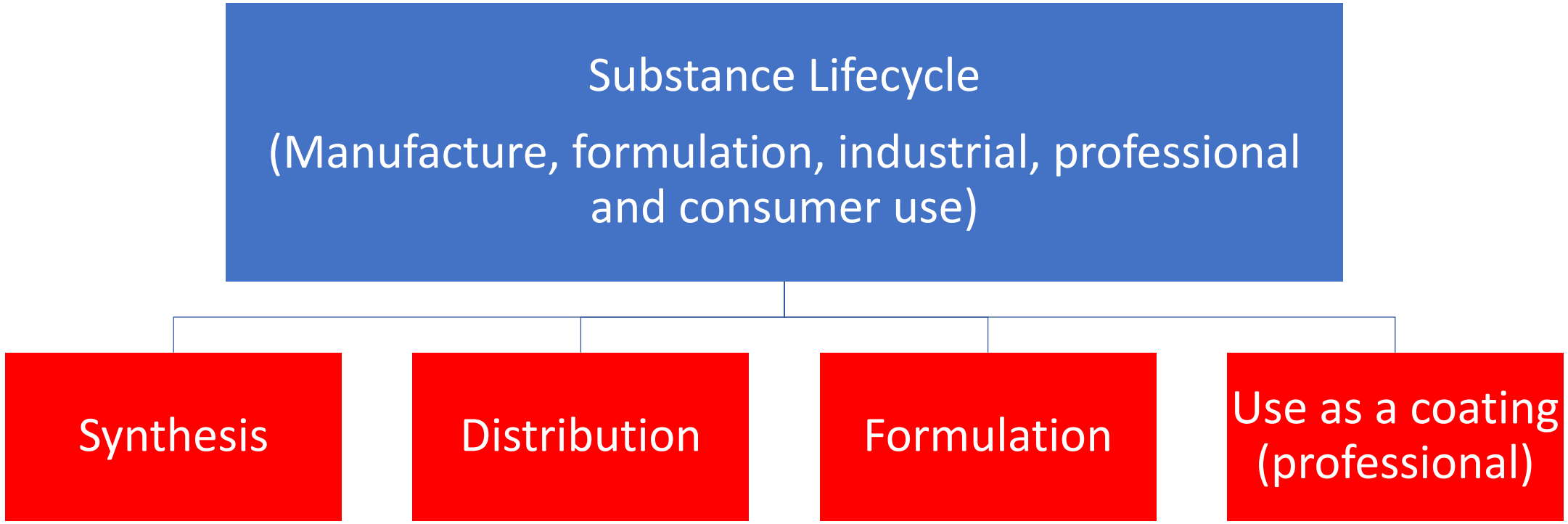
Identification of Exposure Scenarios



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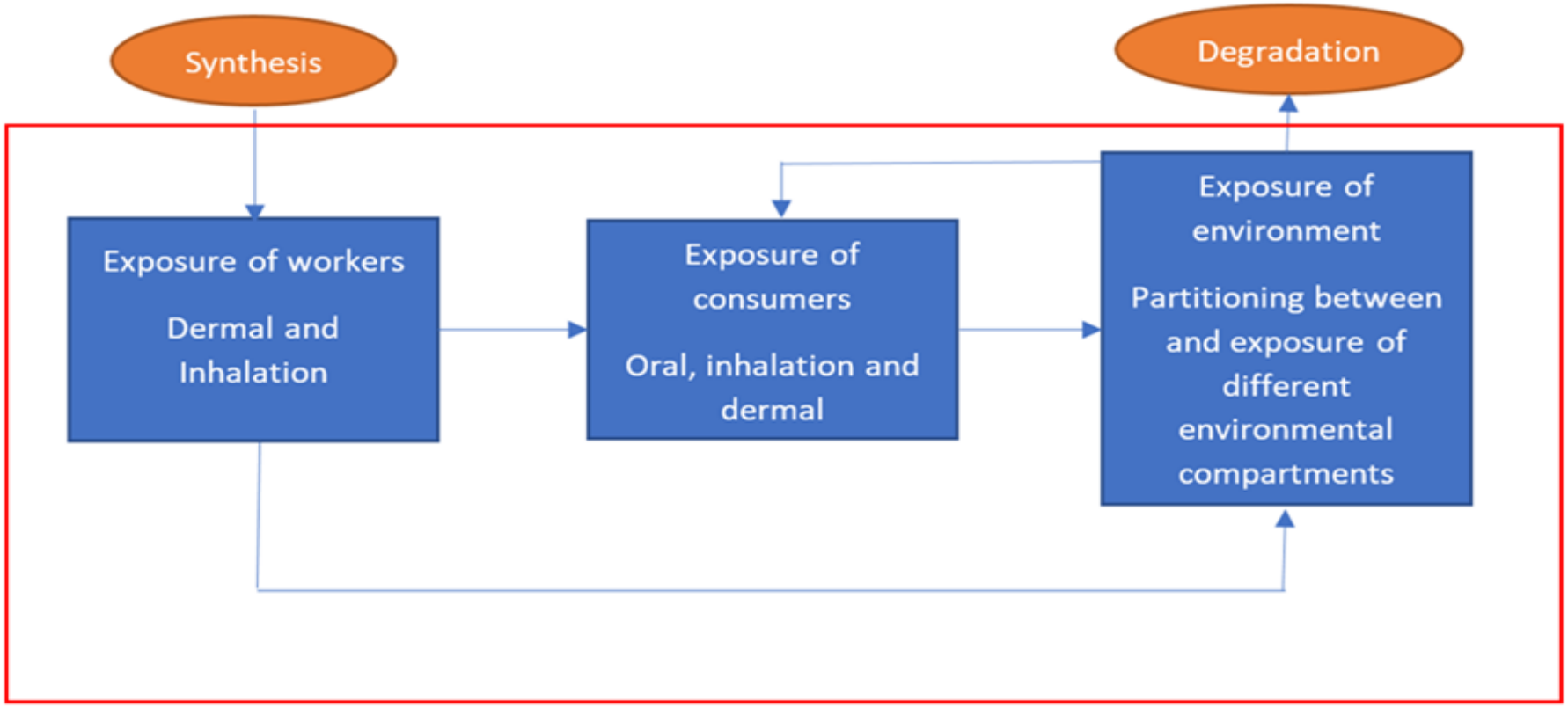
Exposure Assessment for chemicals



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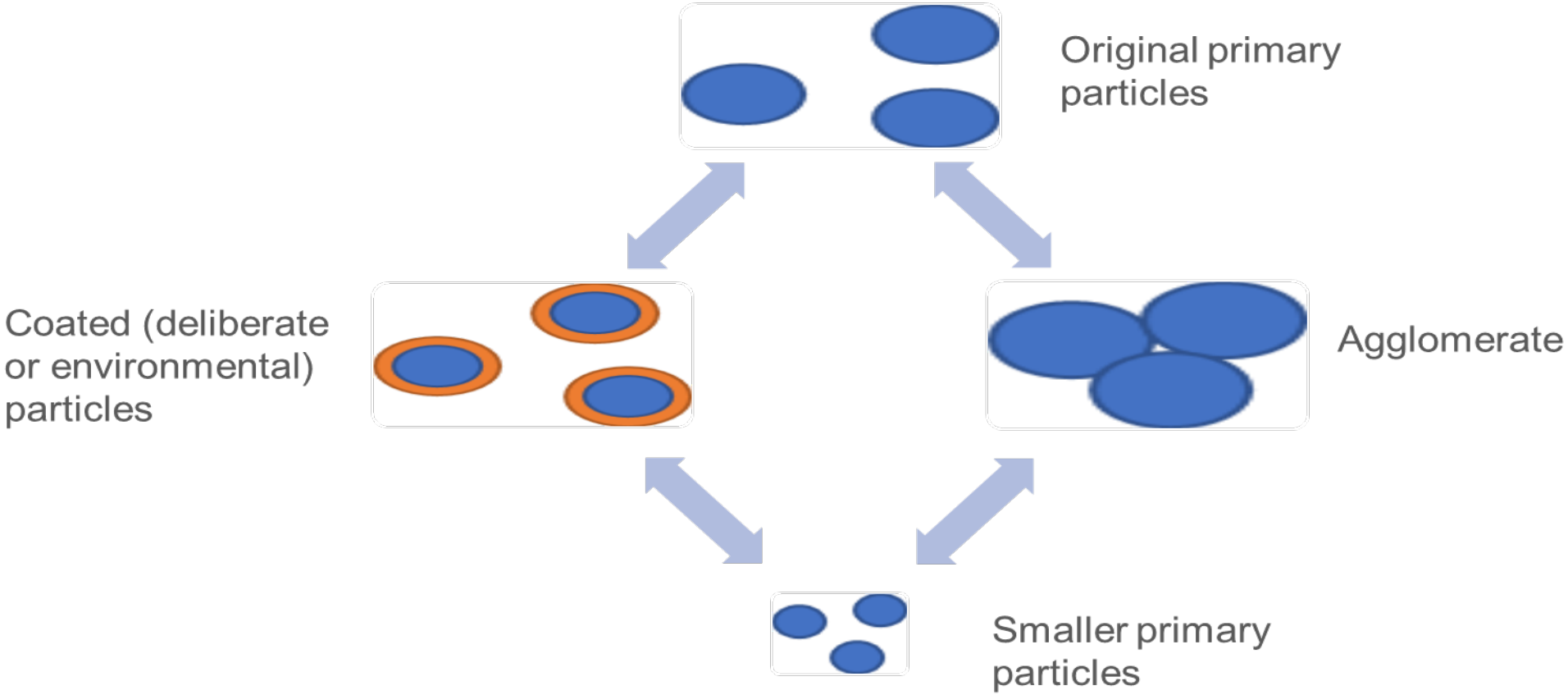
Interconvertibility of nanoforms



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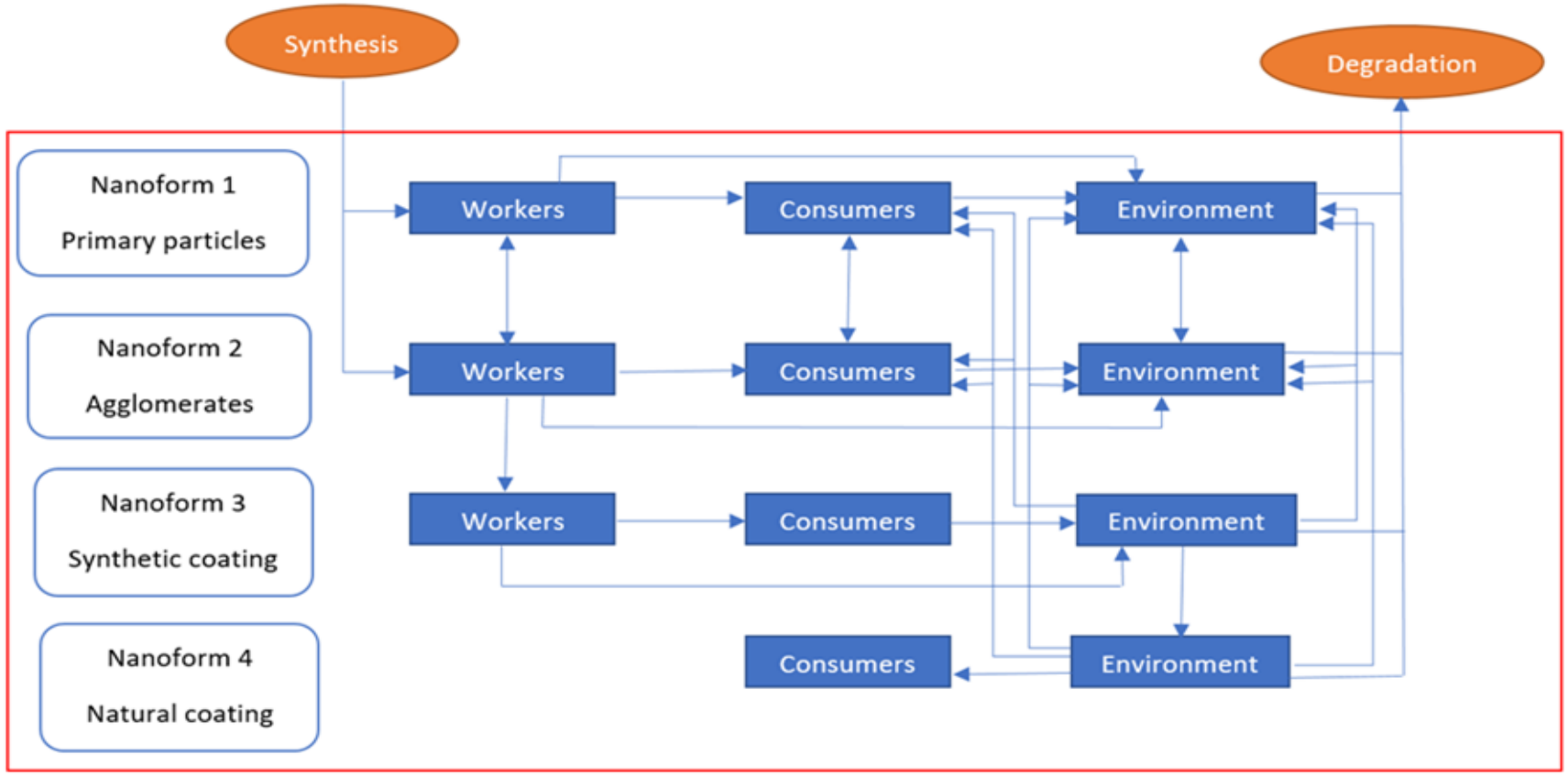
Exposure assessment for nanomaterials



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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

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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?

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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

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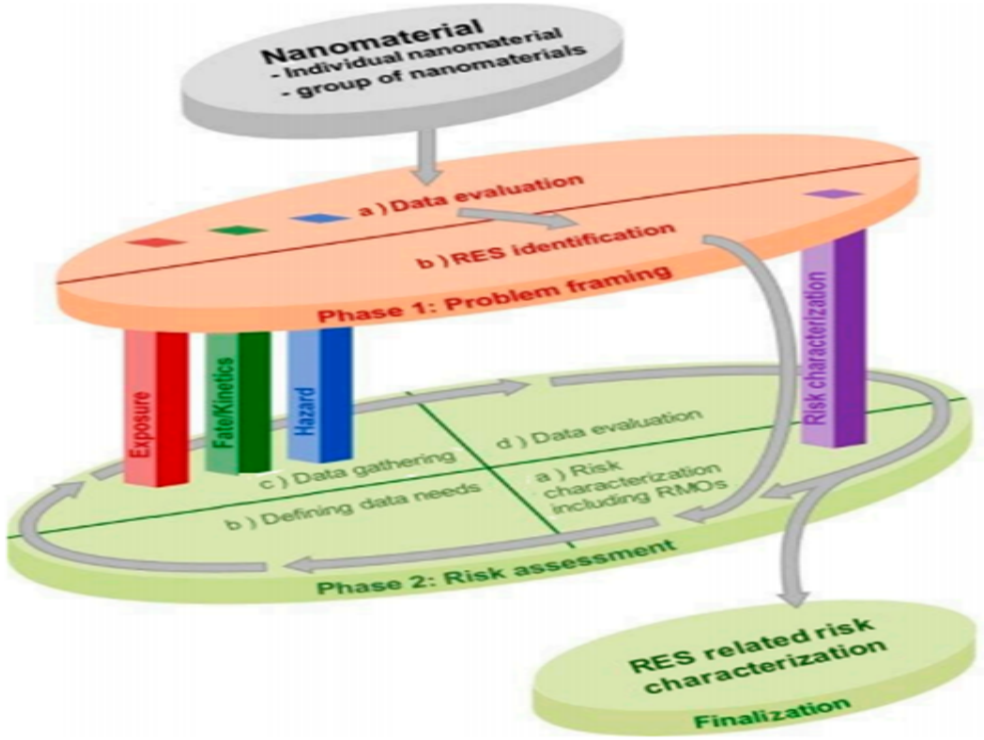
Risk assessment of nanomaterials: Workers

- 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?



Bos et. al. (2015). Int. J. Environ. Res Public Health, 12, 15007 - 150021

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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?

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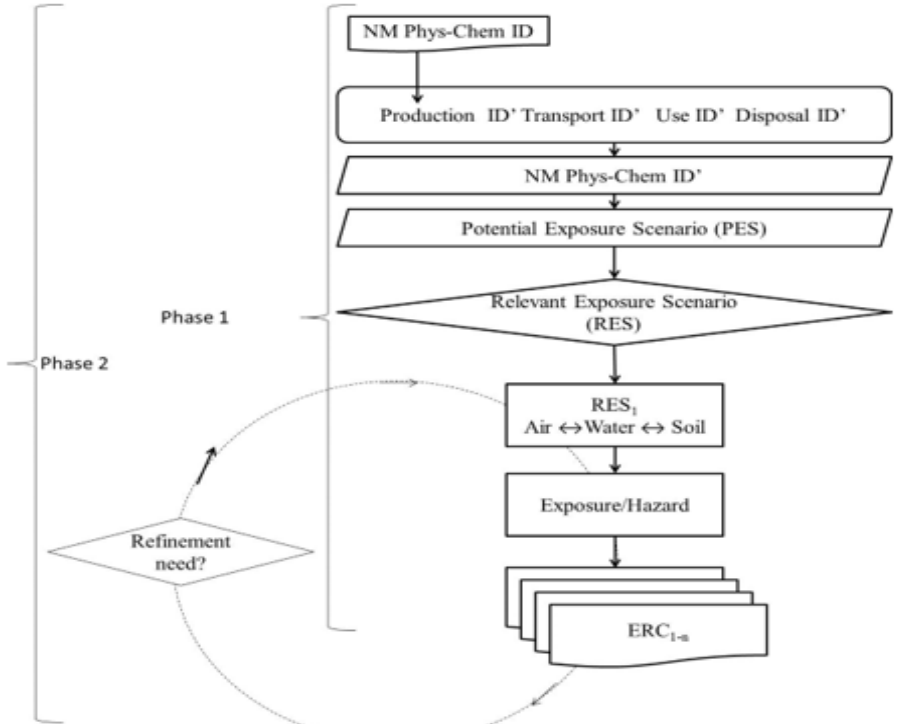
Risk assessment of nanomaterials: Environment

- 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

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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

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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?

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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)

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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.

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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?

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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.

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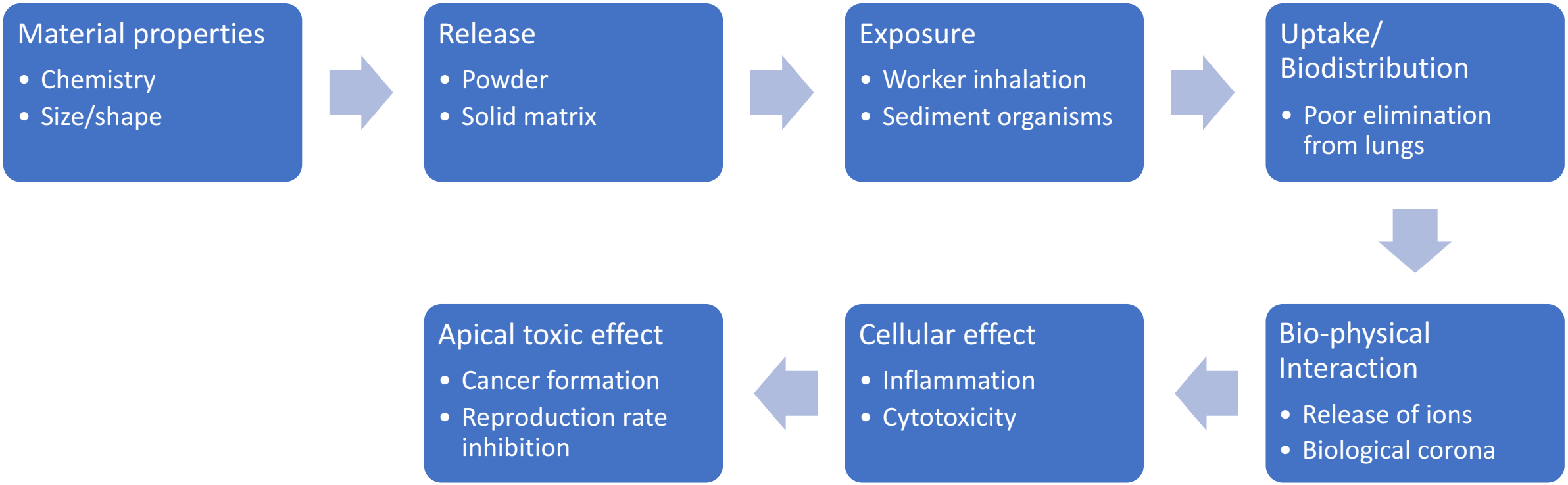
Use of Grouping in Nanomaterial Risk Assessment



Arts *et. al.* (2014). Regulatory toxicology and pharmacology, 70, 492 - 506

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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

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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?

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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?
- For a compilation and review see Hristosov *et al.* (2016). Frameworks and tools for risk assessment of manufactured nanomaterials. Environment International, 95, 36 – 53.
- Some are intended to be user friendly for industry wide use.
  - Guidenano
  - NanoSafer
  - SimpleBox4Nano

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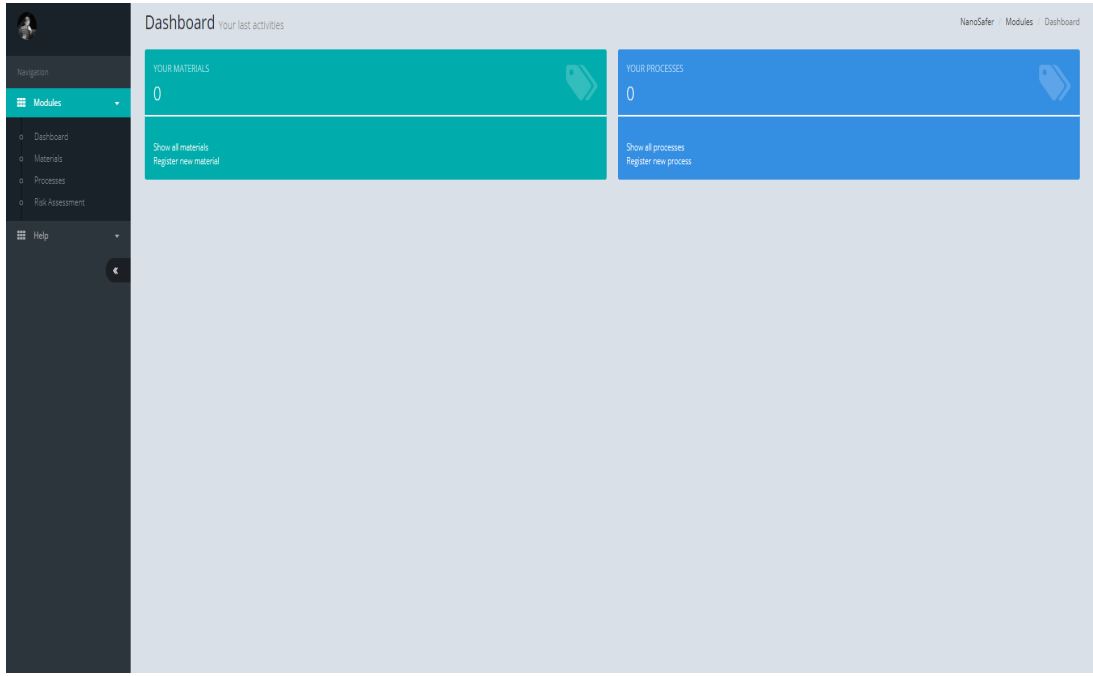
NM Risk Assessment tools - NanoSafer

- 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.



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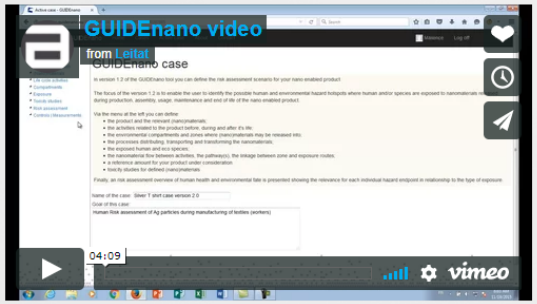
NM Risk Assessment tools - GuideNano

- http://www.guidenano.eu/
- Control banding approach
- Supported by experimental data
- Assesses workplace, consumer and environmental risk
- Gives advice on suitable risk management measures



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NM Risk Assessment tools – SimpleBox4nano

- Environmental exposure modelling programme
- Multimedia mass balance model
- Applies kinetic principles to calculations
- http://www.rivm.nl/en/Topics/S/Soil_and_water/SimpleBox4nano
- Meesters *et al.* (2014). Multimedia modelling of engineered nanoparticles with SimpleBox4nano: Model definition and evaluation. Environ. Sci. Technol., 48, 5726 – 5736.

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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

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Thank you

Any questions?

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