# Current best practice for human health and environmental exposure assessment and risk characterisation for NMs

## Outcome of the Third GAARN meeting

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# Outline

1. Objectives of Third GAARN meeting
2. Setting of GAARN events
3. Best practice
4. Conclusions

# 1. Objectives of Third GAARN meeting

- Best practice and recommendations on how to fill potential information gaps.
- Assessing the safety of nanomaterials under the REACH Regulation
  - Human and environmental exposure assessment and risk characterisation for nanomaterials
- Increase confidence and mutual understanding among stakeholders

# Three GAARN meetings held

1. Physicochemical properties and substance identity information
2. Human health and environmental hazards
3. Exposure assessment and risk characterisation

# 2. Setting

- Three registration dossiers identifying nanoforms or nanomaterials selected
- Exchange of questions between ECHA and lead registrants prior to the meeting
- Experts participating:
  - Member States
  - European Commission
  - ECHA
  - Two industry organisations
  - Three lead registrants

# 3. Best practice

3.1. General considerations

- Best practice based on the Third GAARN meeting published on ECHA nanomaterials web page:

  http://echa.europa.eu/chemicals-in-our-life/nanomaterials

# 3.1.1. Exposure assessment (1)

Identified hazards that may trigger and exposure to ensure the safe use of the substance (sections 1-4, Annex I):

1. Hazards for which there are **classification criteria** and there is information to establish that the **substance meets the criteria** and is therefore classified;

# 3.1.1. Exposure assessment (2)

2. hazards for which there are **classification criteria** and there is information on these properties of the substance showing that it does have these properties, but the severity of the **effects is lower than the threshold criteria** for classification;
3. hazards not yet classified but for which there is information to show that the substance has **specific hazardous properties**.

# 3.1.1. Exposure assessment (3)

- Focus on endpoints for which classification is not derived but **available data show hazardous effects**
- Not to overlook potential hazard due to (technical) difficulties
- Include **specific exposure scenarios for NMs** (or other forms) in registration dossiers if they differ from the bulk materials
- Exposure scenarios shall describe:
  - **a) How the substance is produced**
  - **b) Its uses through the whole life-cycle**
  - **c) How human and environmental exposure is controlled**
  - **d) SPERCs for NMs**

# 3.1.2. Risk characterisation

- The classical risk assessment framework for chemicals includes four main steps:
  1. Hazard identification;
  2. hazard characterisation including dose-response assessment;
  3. exposure assessment; and
  4. risk characterisation.

Specific considerations needed when applied to NMs

# 3.1.3. Updating IUCLID with relevant and new information

- **Update** the registration dossier when **new information** becomes available (Article 22 of REACH)
  - Identified uses and/or new uses advised against (Section 3.4, Annex VI)
  - New knowledge available on the hazard/exposure/risk of the substance to human health and/or the environment
  - Update or an amendment of the chemical safety report or on the Guidance on safe use (Section 5 of Ann VI)
- **Report** any potentially **on-going studies** in the IUCLID dossier

# 3.1.4. Life-cycle considerations for the exposure assessment and risk characterisation (1)

- Characterise NMs during the entire product life-cycle
- Consider potential release of nanoforms during manufacture, use and disposal
  - **Provide analytical or/and experimental data to demonstrate and support any "no release" statement**
  - **Provide supportive data when aggregates and agglomerates, formed during specific life-cycle stages, are claimed not to be relevant for the risk assessment of the substance**

# 3.1.4. Life-cycle considerations for the exposure assessment and risk characterisation (2)

- According to the EU recommendation:
  - "*Agglomerated or aggregated particles **may exhibit the same properties as the unbound particles**. Moreover, there can be cases during the life-cycle of a nanomaterial where the particles are released from the agglomerates or aggregates. The definition in this Recommendation **should therefore also include particles in agglomerates or aggregates whenever the constituent particles are in the size range 1 nm-100 nm***."
  - The aggregates are not the "constituent particles" – the primary particle in the aggregate is the constituent particle.

i.e. the aggregate **is not** considered as bulk

# 3.2. Specific considerations

# 3.2.1. Metrics (1)

- The most appropriate metrics are those that **correlate better** with the effects observed
- For fibres the **number** concentration seems the most adequate metric
- For insoluble (or poorly soluble) particles the **surface area** or **number** might be more relevant
- As most information is currently available in the mass metric – the uncertainty associated with this situation should be addressed by the registrant. In line with RIP-oN2 and 3, the results should also preferably be presented in **several metrics**, **always including the mass metric**.

# 3.2.1. Metrics (2)

However, in practice the selection of the best metric is based on:

- Available data
- Feasibility of the toxicity test using alternative metric
- Possibility of measuring those levels/ metrics with available techniques

# 3.2.2. Exposure models

- Lack of validated modelling tools
- Field **measurements** are preferred for risk characterisation.

# 3.2.3. Measuring exposure concentrations (1) - occupational

- Technical measurement difficulties related to background nano-aerosols. Several strategies can be applied:
  - Measure when the activity with the NM is not being performed
  - Measure in a location not affected by the release of NMs, but one that is considered to have a similar background concentration.
  - Combine with sampling and analysis to confirm that the NM is present.
- Report background measurements and state whether the measurement of the exposure from the activity is corrected with the background or not.

# 3.2.3. Measuring exposure concentrations (2) - occupational

- Complex task: no single approach can currently be used nor recommended
- The most appropriate choice depends on the substance-specific information and the measuring techniques available
- When intending to perform a risk assessment for nanomaterials, it is clear that the units of the exposure and the DNEL must be the same.

# 3.2.3. Measuring exposure concentrations (3) - occupational

- Currently, most of reference values available are **mass based**. However, the analysis tools might not be sensitive enough to achieve very low mass concentrations.
- A general recommendation is to follow a **multi-metric** approach if possible, and use mass as one of the metrics in the overall assessment (table R14-4.1 in Appendix 14-4)

# 3.2.3. Measuring exposure concentrations (4) - Environmental

- Challenging to detect and quantify NMs from porous media, particularly for NMs made of chemical constituents that are highly abundant in the natural environment
- Technical and analytical challenges with measuring NMs in the environment include:
  - ambient concentrations below the detection limit of most analytical methods;
  - potential co-existence of natural and manufactured NMs; etc.

# 3.2.3. Measuring exposure concentrations (5) - Environmental

- The total count concentration could be considered to be a worst case (RIPoN 3) if it is not possible to segregate background concentration
- Added risk approach: only the concentration added to natural background is considered in the exposure and effects assessment

The relevance of the chosen approach for NMs always needs to be demonstrated

# 3.2.4. PNEC derivation and indirect effects

- Consider the relevance of potential indirect effects at environmentally relevant concentrations or at concentrations which are considered to be safe for the environment
- When relevant for the risk characterisation, the indirect effects should be considered in the PNEC derivation (e.g., local PEC/PNEC scenarios)
- If indirect effects are not considered in the PNEC derivation, the approach chosen should be justified

# 3.2.5. Risk management measures

- Conventional risk management methodologies and hierarchy of controls are adequate for NMs
- Publications support the effectiveness of RMMs to reduce the concentration of nanoparticles
- The control technologies used to handle dusty materials are applicable to NMs and provide good control.
- The performance and efficiency of the RMMs should be verified, as it is affected by several factors e.g. particle size, maintenance and (in)adequate use

# 3.2.6. Improving justifications for safe use claims

- Provide explicit and transparent documentation of the scientific assumptions made during hazard, exposure and risk characterisation
- Consider a worst case approach and address the remaining uncertainty though experimental and scientific data in a transparent manner
- Lack of (hazard) data does not automatically mean there is a lack of specific hazards or risks for a substance or NM

# 4. Conclusions (1)

The existing risk assessment paradigm developed for traditional chemicals should also be applied to NMs

- Due to the lack of validated modelling tools for nanomaterial exposure, field measurement data are currently preferred to support the risk assessment
- The risk assessment should follow a multi-metric approach if possible
- The use of qualitative approaches is allowed to support measured or estimated exposure data
- For RMM, the conventional control technologies to handle dusty materials are applicable to NMs and provide good control if implemented and maintained correctly

# 4. Conclusions (2)

- Lack of specific hazard data complicates the risk assessment
- The applicability of conventional exposure assessment models is limited
- Collect information on environmental release when possible
- Legal obligation that registration dossiers need to be updated with new nano-specific studies as scientific knowledge is progressing
- Lack of (hazard) data does not automatically mean there is a lack of specific hazards or risks for a substance

# 5. References

- Report from Third GAARN - Best practice for REACH registrants:
  http://echa.europa.eu/documents/10162/5399565/best_practices_human_health_environment_nano_3rd_en.pdf
- ECHA nanomaterials web page:
  http://echa.europa.eu/chemicals-in-our-life/nanomaterials

- Specific Advice on Fulfilling Information Requirements for Nanomaterials under REACH (RIP-oN 2):
  http://ec.europa.eu/environment/chemicals/nanotech/pdf/report_ripon2.pdf

- Specific Advice on Exposure Assessment and Hazard/Risk Characterisation for Nanomaterials under REACH (RIP-oN 3):
  http://ec.europa.eu/environment/chemicals/nanotech/pdf/report_ripon3.pdf

# Thank you!

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