Supporting Risk Assessment of Nanomaterials with quality-Approved Information DaNa Literature Criteria Checklist

Dr. Clarissa Marquardt - Institute of Applied Computer Sciences (IAI)
Applications?

Image source: fotolia.com
Nanotechnology......

Effects on......

Worker

SAFETY ?

Environment

Image source: fotolia.com
Effects on……

SAFETY ?

Reliable Source of information?

Image source: fotolia.com
Literature on Nanotoxicology

- Drastic increase in Number of Publications increases drastically


Oberdörster 2005 “Nanotoxicology: An Emerging Discipline Evolving from Studies of Ultrafine Particles”
Quality & Usability of Publications

Literature Review on 3 major uptake pathways &
comparison Instillation vs Inhalation

- Majority of studies was poorly conducted
- Characterisation of NM was insufficient
- Applied dosage in most cases under overload conditions

- Results NOT applicable for risk assessment!!!

„When things are large, they are what they are. When they are small, it’s a different game: they are what our measurements make them.”

(George M. Whitesides, No Small Matter. Science on the Nanoscale)
Characterisation…..

„When things are large, they are what the are. When they are small, it’s a different game: they are what our measurements make them.”

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Key challenge for nanosafety assessment & safe-by-design approaches is to

- Understand which phys.-chem. properties are driving the nanomaterials’ toxicity
- Standardised testing methods & materials
- Dose & dosimetry in Nanotoxicology
- Naming & categorizing nanomaterials

Requirements…

- Quality standards for (nano)toxicological studies
- Physico-chemical characterisation fit-for-purpose & relevant for addressed purpose
- Validated standard methods & reference materials
- Relevant models & concentrations
Key Tasks of the DaNa - Knowledge Base Nanomaterials
(DaNa = Database Nanomaterials)

- Communication of current nanotechnology safety research
  - Scientific Literature Review & Quality Management
    - Collecting – Evaluating & Processing of Nanosafety Information for Website
    - for Interested Laymen, Stakeholders, Scientists
  - Website www.nanoobjects.info

- Support for German Nanosafety Research projects
  - NanoCare, NanoNature, ERA-Net SIINN

Supported by
- Federal Office for the Environment FOEN
- Federal Office of Public Health FOPH
- FKZ 03X0131
Core Team

- DECHHEMA
- KIT (Karlsruher Institut für Technologie)
- Empa (Materials Science and Technology)
- Helmholtz Zentrum für Umweltforschung UFZ

External Experts

- Goethe Universität Frankfurt am Main
- Baua: Bundesanstalt für Arbeitsschutz und Arbeitsmedizin
- Universität Salzburg
- Technical University of Denmark
- DTU
- University of Exeter
Literature Quality Management

- Evaluation of peer-reviewed literature with publicly available quality criteria
  
- Topics Human- & Eco-Toxicology
  
- Sorting of approved & rejected literature using the DaNa Literature Criteria Checklist

- > 800 quality-approved literature citations on the website
DaNa Literature Criteria Checklist

→ Mandatory & Optional Criteria

<table>
<thead>
<tr>
<th>Assessment Criteria</th>
<th>must</th>
<th>might</th>
<th>fulfilled</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Physico-chemical NM properties (powders or suspensions as prepared or delivered)</td>
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<tr>
<td>Name of substance (or code), form of delivery (powder, suspension)</td>
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<tr>
<td>Chemical composition: Form(s), contaminations (e.g. elements, element concentrations, anions)</td>
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<tr>
<td>Particle size, size distribution in suspensions (incl. dispersion medium)</td>
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<td>Specific surface area of powders (e.g. BET surface)</td>
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<td>Surface chemistry (functionalisation, hydrophobic, hydrophilic, ...) / coatings / modifications</td>
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<tr>
<td>Morphology (shape)</td>
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<td>Crystallinity (crystalline or amorphous phase; phase analysis (pure or mixed))</td>
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<td>Surface reactivity (surface charge (zeta potential), specific polar)</td>
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<tr>
<td>Formation of radicals (photo-chemical activity)</td>
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<tr>
<td>Hygroscopity, defect density, magnetic properties</td>
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<tr>
<td>2. Sample preparation (dispersed as prepared or delivered NM in media used for biological experiments)</td>
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<tr>
<td>Dispersion procedure described in detail (type of medium used, preparation of stock solution or direct dosing, way of dispersing, energy input, nominal concentration)</td>
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<tr>
<td>Extent of agglomeration / aggregation, particle size distribution under experimental conditions (e.g. culture medium, culture solutions w/ proteins)</td>
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<tr>
<td>Water solubility (discriminate between soluble, metastable and persistent particles; metastable: soluble within days or weeks)</td>
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<tr>
<td>3. Testing parameters:</td>
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<tr>
<td>Controls (positive and negative controls), check for interferences</td>
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<tr>
<td>Concentration administered in μg/ml, μg/µl, n (particle/cell) or µg/cell</td>
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<td>Decide used classified clearly to be “non-overload” or “overload conditions”</td>
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<tr>
<td>Method 1 for biological endpoints</td>
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<tr>
<td>Additional 2nd method for biological endpoints</td>
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<tr>
<td>Use of reference material</td>
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<tr>
<td>4. General aspects:</td>
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<tr>
<td>Data evaluation / TOXICITY</td>
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<td>Criteria of standardisation (e.g. OECD, ISO, CECC guidelines)</td>
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<td>Final evaluation:</td>
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</tbody>
</table>

Legend: fulfilled = x; not fulfilled = n; not assessable = - or 0

DaNa Literature Criteria Checklist

Mandatory & Optional Criteria

- Physico-Chemical characterisation

DaNa Literature Criteria Checklist

Mandatory & Optional Criteria

- Physico-Chemical characterisation
- Sample Preparation

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### Assessment Criteria

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Mandatory & Optional Criteria

- Physico-Chemical characterisation
- Sample Preparation
- Testing Parameters
  - Biological assays
  - dose & dosage
  - controls,…
- General Aspects
  - Evaluation / Statistics
  - SOPs, Guidelines,…

Standard Operating Procedures (SOPs)

- DaNa SOP Template
- Validated SOPs & Lab-Protocols from German NanoSafety Research Projects
- Protocols from other projects (NANOMMUNE, V.I.G.O,...)

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**Standard Operating Procedures of the NanoCare and NanoNature projects**

All SOPs listed here were created by projects from the funding initiatives NanoCare and NanoNature. The projects or the listed authors are solely responsible for the content.

**Title** | **Document**  
---|---
Nanokin (2012) “Detection and semi-Quantification of Endotoxin Contaminations in Nanoparticle Suspensions” | Nanokin SOP 2.2.2 (pdf. 34KB)
Fe-NANOSIST (2014) “Dispersion of Zeolite Suspensions for Ecotoxicological Tests” | Fe-NANOSIST DispZeolite 2.0 (pdf. 79KB)
Nanogem (2011) “Preparing suspensions of nanomaterials in serum-containing medium” | Nanogem SOP PrepSusp 2.1 (pdf. 54KB)
Nanogem (2012) “Short-Term In vitro Study in Rats for Testing of Nanomaterials” | Nanogem SOP ShortTermInst 1.1 (pdf. 41KB)
Nanogem (2012) “Assessing exposure to nanomaterials, following a tiered approach” | Nanogem SOP TestTierApp 1.1 (pdf. 74KB)

Laboratory protocols, “recipes for the lab” - not validated

Here you will find experimental documentations with respect to Nanotoxicology Assessment from individual laboratories that have not been validated by second. The authors of the protocols are solely responsible for the content.

**Title** | **Document**  
---|---
Nanokin-Stavalla (2011) “Profiling of the nanomaterial/protein corona” | Nanokin SOP Proteomics (pdf. 34KB)

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**Dispersion of Carbo-Iron® Suspensions for Ecotoxicological Testing**

1. PURPOSE

This SOP describes the preparation and application of Carbo-Iron suspensions to be used in subsequent ecotoxicological tests. Dispersion is considered a crucial step in toxicity testing, hence, the preparation of a nanomaterial stock suspension has to follow a reproducible procedure in order to ensure e.g. stability of the dispersion over the anticipated test duration.

2. OBJECTIVE

Standardized ecotoxicological testing of suspended nanomaterials involves the preparation of stock suspensions from nanomaterial powder in a reproducible manner. Carbo-Iron is a nanocomposite composite material made of zero-valent iron and activated carbon. It is applied in powdered or as a granulated material by injecting a carboxymethyl cellulose (CMC) stabilized Carbo-Iron suspension into the buffer. Based on this technical approach, Carbo-Iron stock suspensions are standardized with CMC before transfer into the test media. CMC is increasing the colloidal stability of the particles and prevents their aggregation. Due to the need of removing the suspension in an ecotoxicological test, the stability of the suspension is of utmost importance while dispersing. Ecotoxicological studies are therefore carried out on aged material. Suspension preparation prior to ecotoxicological testing is based on a two-step approach. First, dispersion of Carbo-Iron is conducted by ultrasonication in order to achieve a homogenized stock suspension. Second, serial dilutions are prepared from the stock suspension by adding a CMC-water suspension. These dilutions are added to the respective test media in a fixed ratio.

3. REGULATORY BASIS, REFERENCE DOCUMENTS

Standardized guidelines and norms that serve as basis for the SOP

- ISO 14308-2:2011 Particle size analysis - Dynamic light scattering (XL,5)
- ISO 13328-2:2011 Particle size analysis - Laser diffraction methods
- Description of calometric method to determine delivered acoustic energy and specific energy | energy density
- Toxicol J. 1982;6(4): 269-279
- Ultrasound dispersion of nanoparticles for environmental, health and safety assessment – issues and recommendations. Nanotoxicology
- Multi-step dispersion methods for the testing of nanomaterials
Welcome to DaNa².0 (Data and knowledge on Nanomaterials)

What exactly are nanoparticles? What is meant by “exposure”? When do toxicologists speak of a risk? This and many more questions regarding research on safety aspects of nanomaterials are answered here.

Knowledge Base

Carbon black in tires, quantum dots in LEDs or titanium nitride in PET bottles...

Our knowledge base provides information on products and applications of nanomaterials, illuminates health and environmental aspects.

More
Conclusions

- DaNa Literature Checklist – A tool for quality management of publications
- Increasing SOP collection
- DaNa Knowledge base – Reliable & objective information source
- Knowledge communication essential for any technology development
Thank you for your Attention!

Dr. Clarissa Marquardt
+ 49 721 608-25729
clarissa.marquardt@kit.edu

www.nanoobjects.info

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@nano_info