RISK MANAGEMENT OF NANOMATERIALS

PRESENTATION OF SPECIFIC PROJECT ACTIVITY ON THE RISK MANAGEMENT MEASURES FOR NANOMATERIALS

With thanks to

VILLUM FONDEN

OVERVIEW

I. Elements of Risk Management

II. Risk Identification

III. Risk Assessment

IV. Approaches for Risk Assessment

V. Hazard Control

VI. Regulatory approaches on Risk Management

VII. Final Remark

I. ELEMENTS OF RISK MANAGEMENT

- Risk identification of nanomaterials (NM)
- **Risk Assessment of NM**
- Hazard control of NM
- Risk communication on NM

II. RISK IDENTIFICATION

- Known unknowns (within a range of known possiblities)
  - Uncertainties in production, use, fate and behaviour of free insoluble nanoparticles give rise to concerns over possible human health and environmental risks.
  - No generally applicable paradigm for NM hazard identification.
  - A case by case approach to assess NM is necessary.
- Unknown unkowns (completely unexpected results)
  - Risk assessment for nanomaterials should not neglect unexpected results.

III. RISK ASSESSMENT OF NM (1)

Gaps / Challenges for Risk Assessment of NM:

- Gaps in nanoparticle characterisation, detection and measurement.
- Gaps in the fate and persistence of NP in humans and environment.
- Gaps in aspects of (eco)toxicology (interaction at subcellular and molecular levels).
- No full understanding of how the material properties may cause adverse health/environment outcomes.

III. RISK ASSESSMENT OF NM (2)

Gaps / Challenges for Risk Assessment of NM:

- **Result:** Conventional approach to derive limit values (agreed toxicity test systems & safety factors) is hampered due to ‘new’ properties of NM, incomplete information about their hazards, varying size distribution, heterogeneous composition.
- Conducting full testing for every variant of NM will lead to enormous amount of data that may be not necessary for risk assessment.
- Applicability of alternative test methods to avoid animal tests.

III. RISK ASSESSMENT OF NM (3)

Guiding „principles“ for Risk Assessment of NM:

- Existing risk assessment paradigm for traditional chemicals can be applied to nanomaterials. But research necessary to determine what characteristics of NM may pose unique hazards (OECD).
- The hypothesis that smaller means more reactive and thus more toxic cannot be substantiated by the published data (OECD).
- Generally accepted to apply the precautionary principle if risks are unkown but likely.

IV. APPROACHES FOR RISK ASSESSMENT (1)

Grouping / categorization:

- A group of substances whose properties are likely to be similar/ follow a regular pattern.
- Possible grouping of NM (ECETOC 2014):
  - production, use and release (throughout the life cycle);
  - physico-chemical characteristics of a NM, which can be different in different life cycle stages;
  - uptake, biodistribution & -persistence (biokinetics) of a NM in an organism and the physico-chemical characteristics of a NM inside the organism at different target sites;
  - early and apical biological effects.
- At present broad general groups based on phys-chem properties are used (e.g. Carbon based nanomaterials , Metals and metaloxides, Nano-tubes / nano-wires).

IV. APPROACHES FOR RISK ASSESSMENT (2)

Problems with grouping NM (1):

- No unified global grouping concept.
- Different purpose of grouping:
  - focus on (priorization) for testing strategy (= select low-toxic potential materials and high-toxic potential ones. The latter requires more information & more complete risk assessment) or
  - to fill in data gaps for risk-assessment (read across).
- **Known characteristics** of NM (like release of toxic ions, surface, impurities, coatings, shape, ability to cross biolgical barriers) is **not enough for grouping**.

IV. APPROACHES FOR RISK ASSESSMENT (3)

Problems with grouping NM (2):

- Many nanomaterial properties are interdependent, e.g. changing nanomaterial shape/length may cause surface defects or change the surface chemistry.
- Nanomaterials age and are transformed throughout their life-cycle.

(Lynch et al., 2014).

IV. APPROACHES FOR RISK ASSESSMENT (4)

Examples of grouping approaches for decision:

- Read-across,
- Control banding approach,
- Nano reference values (NRV) and
- Multi-perspective approach.

IV. APPROACHES FOR RISK ASSESSMENT (5)

Read-across approach:

- Technique to predict information on an endpoint for a target chemical by using data from the same endpoint from a source chemical(s) (either qualitatively or quantitatively).
- Pre-requesite: both chemicals are similar, e.g. on the basis of structural similarity and similar properties and/or activities (bulk to all nano-forms, bulk to spec. nano-form, nano-form to nano-form)
- In **quantitative read-across** known value(s) of a property for one or more source chemicals is used to estimate the unknown value of the same property for the target chemical, thus obtaining for example a dose-response relationship.
- **Qualitative read-across** gives only “yes” or “no” answers.

IV. APPROACHES FOR RISK ASSESSMENT (6)

Control-banding approach (for occupational health):

- Technique that determines a **control measure** (e.g. dilution ventilation, engineering controls, containment, etc.) based on a **"band" of hazards** (such as skin/eye irritant, very toxic, carcinogenic, etc) and **exposures** (small, medium, large exposure).
- Gains growing acceptance among risk assessors.
- Different control-banding tools are available. All use two-dimensional matrix, combining a **qualitative assessment of hazardous properties** of NM with an estimate of the **likeliness of inhalatory exposure**.

IV. APPROACHES FOR RISK ASSESSMENT (7)

NRV approach (for occupational health):

- Using particle number concentration (particle/fibre per cm^3) instead of the conventional quantative approach (g/m^3).
- Background: Surface of nanoparticles seems to be important trigger for toxic effect, not mass.
- NRV is a warning level (8-h Time weighted average (TWA); if exceeded risk management measures (e.g. exposure control) have to be taken.
- NRV are provisional limit values (not legally binding) to be replaced by DNEL (derived no affect concentration) in REACH or OEL (occupational exposure limit) if they exist.

P. van Broekhuizen et. al 2012

IV. APPROACHES FOR RISK ASSESSMENT (8)

NRV approach (for occupational health) used in Netherlands based on IFA:

Class	Description	Density	NRV (8-h TWA)	Examples
1	Rigid, biopersistent fibres, effects simmilar to asbestos not excluced	_	0.01 fibres cm^{-3}	SWCNT, MWCNT, metall oxide fibres
2	Biopersistent granular nanomaterial (1-100 nm)	> 6000 $kg\ m^{-3}$	20,000 particles cm^{-3}	Ag, Au, Ce02, Fe
3	Biopersistent granular and fibre form nanomaterial (1-100 nm)	< 6000 $kg\ m^{-3}$	40,000 particles cm^{-3}	Al2O3, SiO2, TiO2, ZnO, carbon black, dendrimers
4	Non-biopersistent granular nanomaterial (1-100 nm)	_	Applicable OEL	Fats, NaCl

Source: P. van Broekhuizen et. al 2012

IV. APPROACHES FOR RISK ASSESSMENT (9)

Multi-perspective approach (expected 2015) (1):

- All available proposals for the grouping of NMs go beyond the determination of mere (quantitative) structure–activity relationships and build a sound scientific basis to advance regulatory provisions for grouping of NM.
- But proposals don´t focus on full nanomaterial life cycle, i.e. NM exposure and use scenarios are only occasionally addressed.
- Multi-perspective approach restricts grouping not to only one aspect (e.g. material properties), but combines all the different tools for grouping at hand.

Source: ECETOC 2014

IV. APPROACHES FOR RISK ASSESSMENT (10)

Multi-perspective approach:

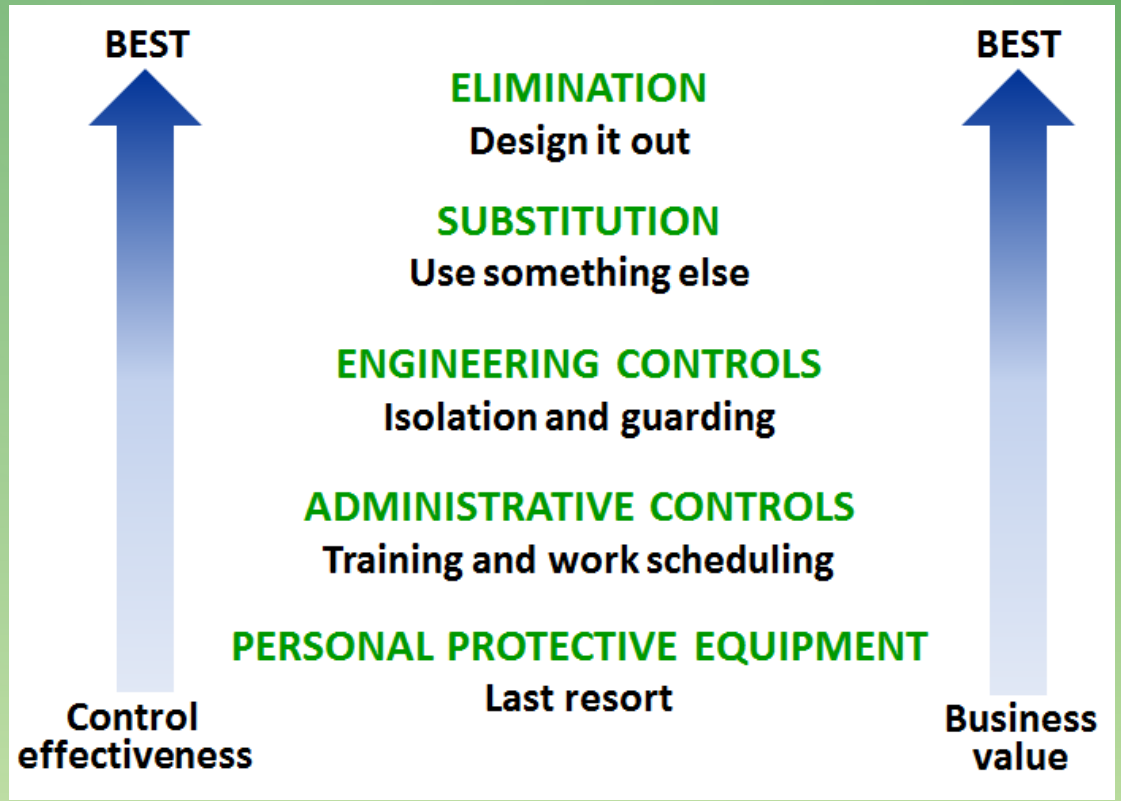
- Linked to IATAs (=Integrated Approaches for Testing and Assessment) by supporting a concern-driven step-wise collection and evaluation of information.
- Aims at a concern-driven ranking of NMs within a group or between different groups of NMs that results in separating safe uses from unsafe uses of NM.
- To justify the assignment of a NM to a group case studies are necessary to verify the quality and robustness of the grouping framework.
- Multi-perspective approach is intended to be flexible and efficient.
- However, approach demands transparency and full understanding of all parameters and decisions (which data is included/ which excluded).

Source: ECETOC 2014 (doi:10.1016/j.yrtph.2014.07.025)

V. HAZARD CONTROL OF NM

V. HAZARD CONTROL (1)

Hierarchy of hazard control in occupational health



Source: National Institute for Occupational Safety and Health (NIOSH)

V. HAZARD CONTROL (2)

- Regulation of hazard control practices only when a critical mass of evidence supports the necessity of such action (weight-of-evidence approach).
- With limited state-of-science for NM & possibility that NM exhibit enhanced or unique properties which may lead to unexpected effects, placing limits on allowable activity is an option (e.g. use of specific NM only under highly controlled conditions).
- When more data available, the scope of the risk assessment could be extended to evaluate potential risk under other conditions of use.

Source: OECD ENV/JM/MONO(2012)8

V. HAZARD CONTROL (3)

In case of limited toxicological information minimizing or eliminating potential exposure:

- NM is not directly available to consumers (e.g. matrix-bound). But Disposing or aging need to be considered in life-cycle analysis and exposure assessment.
- Application is non-dispersible and releases from facilities are fully controlled.
- Personal protective equipment for workers in production & engineering controls for downstream uses.

OECD in 2010 published Compilation of nanomaterial exposure mitigation guidelines relating to laboratories (OECD ENV/JM/MONO(2010).

VI. REGULATORY APPROACHES ON RISK MANAGEMENT

VI. REGULATORY APPROACHES ON RISK MANAGEMENT (1)

- Legal frameworks (EU, USA, Canada, Japan & Australia) dedicated to ensure a high level of safety of NM for workers, consumers & environment.
- But concrete provisions prescribing specific information requirements for the hazard and risk assessment of NMs have not been adopted in legal acts.
- Binding („hard“) or non-binding („soft“) Regulation:
  - „Hard“ Regulation: e.g. Toxical Substance Control Act – TSCA in USA, REACH in EU.
  - „Soft“ Regulation: Code of Conducts, Guidlines (e.g. Swjss Precautionary Matrix, EDF-DuPont NanoRisk Framework, CENARIOS Risk Management).

VI. REGULATORY APPROACHES ON RISK MANAGEMENT (2)

Situation on Test Guidelines (TG):

- Applicability of TG for environmental fate of NM in REACH is questioned:
  - In principle are applicable for assessing the fate of NM. (Hankin et. al. 2011, Kühnel and Nickel 2014).
  - Environmental fate cannot be reliably assessed with existing TG (Schwirn et. al. 2014).
- Majority of OECD TGs for chemicals are generally applicable for NM (OECD 2009).
- **But** new TGs are necessary for specifying dissolution behaviour, adsorption-desorption properties, the determination of dispersion behaviour and transformation processes in environmental media.
- Lack of harmonised methods in sample preparation, characterisation of the test substance.

VI. REGULATORY APPROACHES ON RISK MANAGEMENT (3)

How can the regulator receive further information on registered substances (nanomaterials)?:

- Duty of registrant to update his registation and submit available! data to ECHA („new knowledge of the risks of the substance to human health and/or the environment“) (Art. 22 (1) lit. e REACH; for CSR Art.14 (7)).
- Decision to request further information from registrant (by ECHA, Art. 36 REACH)
- Dossier Evaluation regarding examination of testing proposal and compliance check (by ECHA)
- Substance Evaluation (by Member State Competent Authority)

VII. FINAL REMARK (1)

Regulatory amendments for risk management are necessary:

- Binding definition for nanomaterials in REACH (EU recommendation; and sectoral regulation on Cosmetics, Biocides exist); amendment is discussed.
- Nano-specific information requirements to test substances for environmental fate and behaviour & their (eco-) toxicological hazards (Annexes VII to XI of REACH); amendments are discussed, e.g.:
  - Characterisation of NM,
  - Guidance for grouping of nanomaterial (Annex XI),
  - Separate information on NM in the safety data sheet on: composition, handling, exposure controls, physical and chemical properties and toxicological information

VII. FINAL REMARK (2)

Regulatory amendments for risk management are necessary:

- Any category-approach in the regulatory context must be based on robust scientific justification, i.e.:
  - identify & consider the properties or parameters that drive the specific endpoint;
  - criteria & validation approaches must have a high enough certainty to not jeopardise safe use.
- ECHA needs a (undisputed) legal instrument to withdraw registration in case of incompletness or wrong information (cf. Art. 5 „no data, no market).

THANK YOU

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