Nanoparticle Risk Assessment

A probabilistic approach

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Overview

- Background
- Basics of risk assessment
- Deterministic vs probabilistic approach
- Methods
- Conclusions

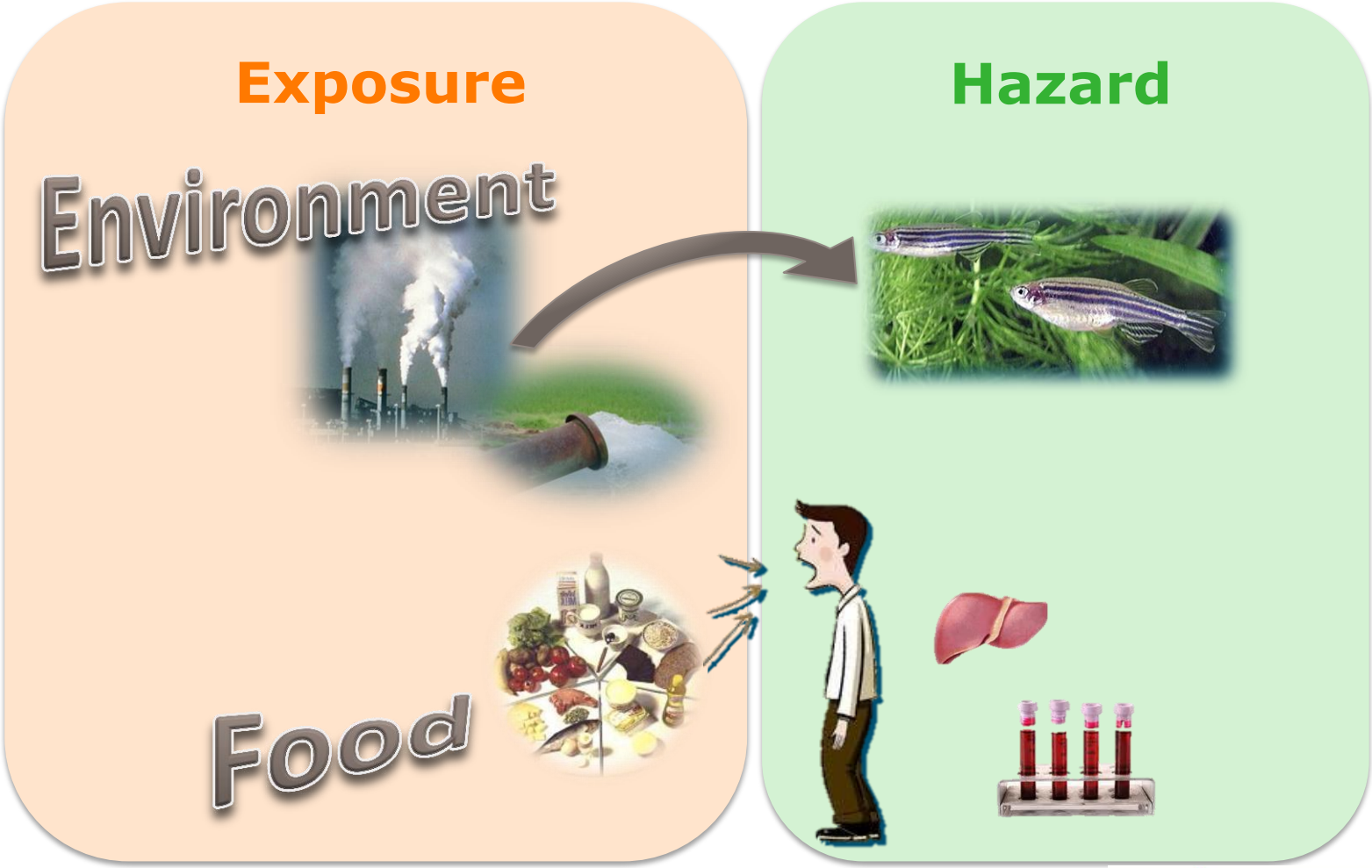
Background

- Risk assessment (RA) of manufactured nanoparticles (MNPs) important for societal acceptance of its applications and for safe use of products on these materials.
- More and more government agencies, research institutes and universities invest time and money on the RA of MNPs

Background

- Approach: Use existing methods of chemical RA on MNPs
- Serious doubts
  - current methods can be used, but with modifications to methodology (Handy et al., 2008)
  - NPs in principal covered by existing legislation frameworks, doubts exist as to the actual applicability to NPs (Hansen, 2012)
  - "distinct lack of nano-specific regulation" (Bowman and Hodge, 2007)
  - "is sufficiently unlike other technologies [so as] to warrant separate consideration" in respect to regulatory frameworks (Hodge and Bowman, 2004)

Basics of risk assessment



Basics of risk assessment

- Environment: Risk Characterization Ratio (RCR):

$$\mathrm{RCR} = \frac{\text{predicted environmental concentration}}{\text{predicted no effect concentration}} = \frac{\mathrm{PEC}}{\mathrm{PNEC}}$$

- Food: Margin of Safety/Exposure (MOS/MOE):

$$\mathrm{MOS/MOE} = \frac{\text{no effect level}}{\text{exposure}}$$

Deterministic vs probabilistic approach

Deterministic

often worst case scenario (accumulative effect of worst cases – not realistic)

vs

Probabilistic

- assess distribution of MOS/MOE/RCR
- uncertainty analysis
- more realistic

"Fundamentally, the EPA [US Environmental Protection Agency] should replace risk values that are built on science-policy assumptions with risk estimates that acknowledge underlying uncertainties. ... The EPA's definitive values are illusions: they conceal uncertainty that cannot be resolved scientifically."

Gray and Cohen, 2012, *Nature*

Deterministic vs probabilistic approach

- In the words of Verdonck et al. (2005, 2006):
  - The PEC and the PNEC are "considered as single, crisp values" while in reality they contain both uncertainty and variability.
  - This uncertainty and variability is accounted for by utilizing worst-case estimates for exposure and toxicity.
  - This leads to an overestimated, worst-case estimate.

Deterministic vs probabilistic approach

Variability

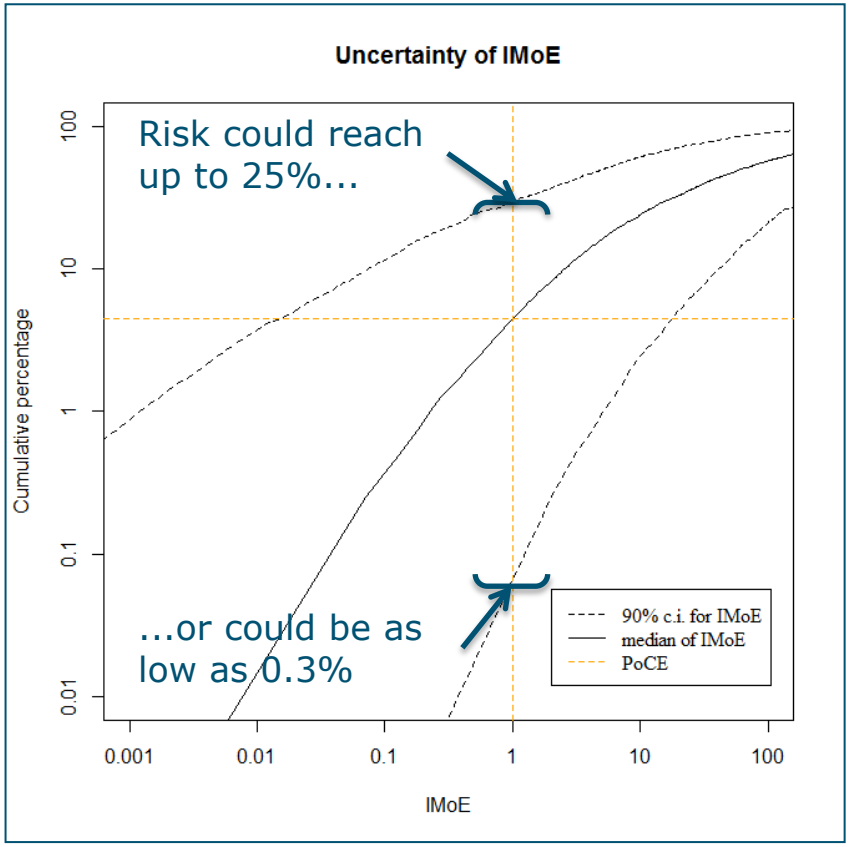
- Truly existing differences between people
- Part of reality
- Examples (REACH):
  - Interspecies variability
  - Intraspecies variability
  - Variability in environmental characteristics
  - Variability in time and space

Deterministic vs probabilistic approach

Uncertainty

- Lack of knowledge
- Can be reduced (in principle)
- Examples (REACH):
  - Measurement uncertainties
  - Model uncertainties
  - Exposure uncertainties (exposure pathways, exposed population, emission sources)
  - Hazard uncertainties (lab to field, inter- and intraspecies factors, dose-response models)

Deterministic vs probabilistic approach



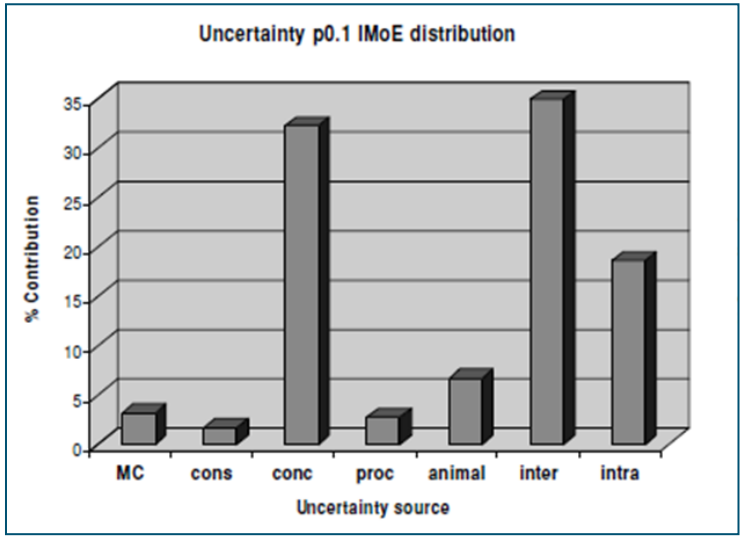


Figure 2. Illustrating areas of uncertainty.

Figure 1. The distribution of the individual margin of exposure (IMoE).
Illustrating the difference between a deterministic and a probabilistic approach.

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Methods

- Using Integrated Probabilistic Risk Assessment (IPRA) (van der Voet & Slob, 2007) on a case study of nano-silica in food (Dekkers, et al., 2011).
- Quantification of uncertainty using Bayesian methods, bootstrapping ect (Verdonck et al, 2003; Aldenberg & Jaworska, 2000; Aldenberg et al., 2002).
- Use expert elicitation (Flari et al., 2011) to better characterize the uncertainty
- Consider environmental exposure modelling using material flow analysis (Gottschalk et al., 2010)

Conclusion

- Need for risk assessment of MNPs
- Current chemical risk assessment possibly not applicable to MNPs
- MNP risk assessment to be approached probabilistically
- Possibilities for a probabilistic approach

References

- Aldenberg, T., & Jaworska, J.S. (2000). Uncertainty of the hazardous concentration and fraction affected for normal species sensitivity distributions. *Ecotoxicology and Environmental Safety,* 46:1-18.
- Aldenberg, T., Jaworska, J.S., & Traas, T.P. (2002). Normal Species Sensitivity Distributions and probabilistic Ecological Risk Assessment. In L. Posthuma, G. W. Suter II & T. P. Traas (Eds.), *Species Sensitivity Distributions in Ecotoxicology* (pp. 49-102). London: CRC Press.
- Bowman, D. M. and Hodge, G. A. (2007). A small matter of regualtion: an international review of nanotechnology regulation. The Columbia SCIENCE AND TECHNOLOGY LAW REVIEW, 8:1-36.
- Dekkers, S., Krystek, P., Peters, R.J., Lankveld, D.P., Bokkers, B.G., van Hoeven-Arentzen, P.H., Bouwmeester, H., & Oomen, A.G. (2011). Presence and risks of nanosilica in food products. *Nanotoxicology,* 5(3):393-405.
- Flari, V., Chaudhry, Q., Neslo, R., & Cooke, R. (2011). Expert judgment based multi-criteria decision model to address uncertainties in risk assessment of nanotechnology-enabled food products. *Journal of Nanoparticle Research,* 13(5):1813-1831.
- Gray, G. M. and Cohen, J. T. (2012). Rethink chemical risk assessments. Nature, 489:27-28.
- Gottschalk, F., Scholz, R.W., & Nowack, B. (2010). Probabilistic material flow modeling for assessing the environmental exposure to compounds: Methodology and an application to engineered nano-TiO2 particles. *Environmental Modelling & Software,* 25:320-332.
- Handy, R. D., Owen, R., and Valsami-Jones, E. (2008). The ecotoxicology of nanoparticles and nanomaterials: current status, knowledge gaps, challenges, and future needs. Ecotoxicology (London, England), 17(5):315-25.
- Hansen, S. F. and Baun, A. (2012). European regulation aecting nanomaterials - review of limitations and future recommendations. Dose-Response, 10(3):364-383.
- Hodge, G. and Bowman, D. (2004). Governing nanotechnology : setting the regulatory agenda. The journal of contemporary issues in business and government. - Perth, ISSN 1323-6903, ZDB-ID13413077. - Vol. 10.2004, 2, p. 18-33.
- van der Voet, H., & Slob, W. (2007). Integration of probabilistic exposure assessment and probabilistic hazard characterization. *Risk Analysis,* 27(2):351-371.
- Verdonck, F.A.M., Aldenberg, T., Jaworska, J., & Vanrolleghem, P.A. (2003). Limitations of current risk characterization methods in probabilistic environmental risk assessment. *Environmental Toxicology and Chemistry,* 22(9):2209-2213.
- Verdonck, F., Sioen, I., Baert, K., Van Thuyne, N., Bilau, M., Matthys, C., De Henauw, S., De Meulenaer, B., Devlieghere, F., Van Camp, J., Vanrolleghem, P., Van Sprang, P., Verbeke, W., and Willems, J. (2006). Uncertainty and variability modelling of chemical exposure through food. Archives of Public Health, 64(4):159-173.
- Verdonck, F., Van Sprang, P., and Vanrolleghem, P. (2005). Uncertainty and precaution in European environmental risk assessment of chemicals. Water science and technology : a journal of the International Association on Water Pollution Research, 52(6):227-344.