Environmental hazard assessment of CeO_2 nanoparticles

How to evaluate the huge amount of available ecotoxicological data in a transparent way for regulatory purposes

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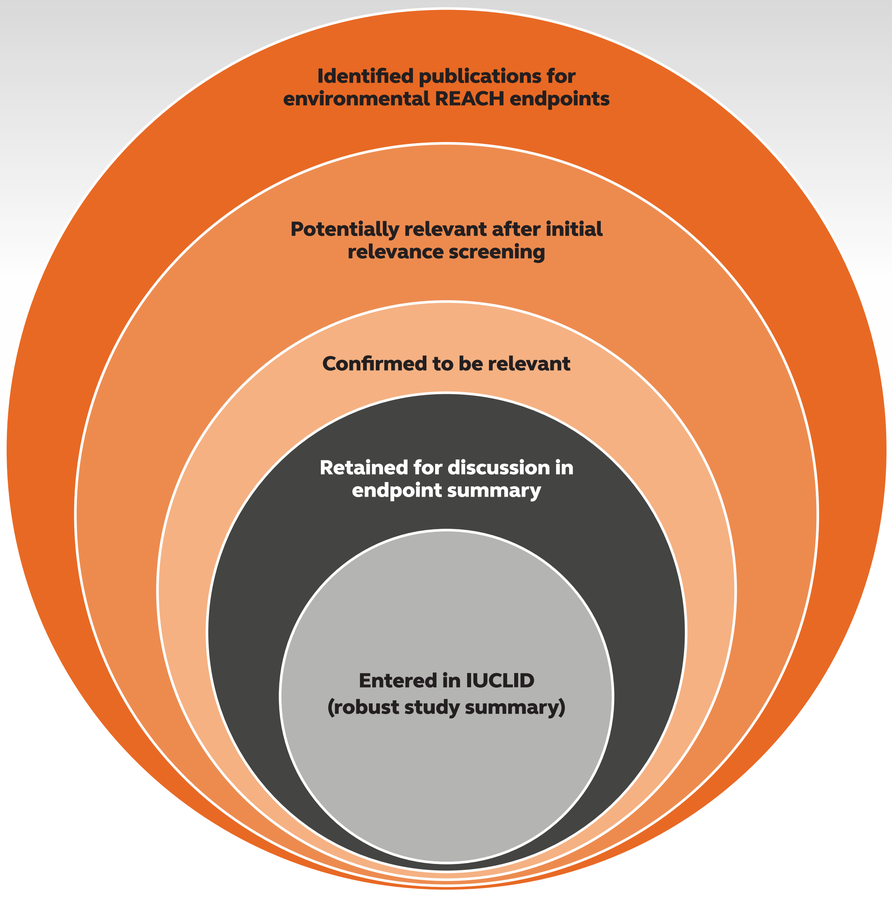
Huge amount of ecotoxicological information published over – predominantly – the past 2 decades

→ Due to absence of harmonised or internationally standardised methodologies for nanomaterial testing, studies were performed according to different methodologies

→ Consequently, a lot of contrasting findings are observed among published literature

→ How to deal with this in view of the update of the REACH dossier for CeO_2?



Methods

Literature search → > 900 publications

Initial relevance screening → ca. 450 publications retained

Combination of sources in weight-of-evidence (WoE) approach that best reflects the findings on the endpoint under consideration → IUCLID entries (robust study summaries)

After relevance confirmation → inclusion in xls table: information on nanoparticles tested, materials and methods, key results and findings → inclusion as Annex in REACH dossier for reasons of completeness

Additional set of sources not retained for the WoE approach but delivering important additional information on the endpoint is not entered in IUCLID but only discussed in the endpoint summary

Screening against criteria for assessing reliability (based on OECD recommendations where available)

- Nanoparticles characterisation
- Dispersion / spiking methodology
- Nanoparticles stability and analytical monitoring during test
- Test species and testing method
- Endpoints investigated (apical and/or sub-apical)

Results

Results (expressed as CeO_2) for uncoated, non-surface treated, mainly spherical nanoparticles

FISH
Acute → 21 studies – 3 WoE
Long-term → 6 studies – 3 WoE

- **No or low toxicity** based on apical endpoints (LC50 > 10 mg/L, NOEC ≥ 100 mg/L)
- Several biochemical/physiological responses observed that may represent evidence for oxidative stress
- **Physical effects of direct interaction with epithelia** especially for longer aspect ratio particles

AQUATIC INVERTEBRATES
Acute → 38 studies – 12 WoE
Long-term → 15 studies – 5 WoE

- In general **no or low toxicity** based on apical endpoints (E/LC50 0.26->5000 mg/L, NOEC/EC10 2.1-56 mg/L
- **Physical effects** resulting in **impaired food intake or movement**

ALGAE/AQUATIC PLANTS
36 studies – 15 WoE

- EC50 values 1.24-1994 mg/L, lowest NOEC/EC10 1 mg/L, other values > 1 mg/L)
- Toxicity was found to be linked to **membrane damage and photosynthesis** impairment caused by **cell-particle interactions** promoting an oxidative stress mechanism
- Indirect effects due to phosphate deprivation cannot be excluded either
- **Higher aquatic plants: no adverse effects** observed

TERRESTRIAL PLANTS
113 studies – 25 WoE

- Typically **no or limited effects on apical endpoints** such as growth, biomass, germination (NOEC 100 - ≥ 1000 mg/kg dw)
- Often stimulation observed
- Some evidence of **effects on nutrient status, oxidative stress and photosynthetic parameters**
- Observed effects heavily dependent on soil properties (e.g. water content, organic carbon)

SEDIMENT ORGANISMS
3 studies – 1 key

- **No effect on apical endpoints**
- Sublethal oxidative damage to tissues in *Corophium volutator* related to CeO_2 NP redox cycling in saline waters
- **Physical effects** (accumulation in digestive tract) were observed in chironomids

AQUATIC MICROORGANISMS
54 studies – 6 WoE

- Effects in the range of 10-50 mg/L reported (not in all studies)
- Similar as for algae, a process of **cell damage** seems to occur **in cells in close contact with CeO_2 aggregates**
- Role of EPS in protecting the cells
- Microbial community composition shifts observed
- Effect on sludge aggregation

TERRESTRIAL INVERTEBRATES
8 studies – 6 WoE

- NOEC ≥ 1000 mg/kg dw
- Some **particle-triggered effects** at the biochemical level, but **not translated in effects on apical endpoints**

TERRESTRIAL MICROORGANISMS
10 studies – 3 WoE

- **No or low toxicity** (no effects at 1 mg/kg dw or below, effect concentrations very variable)
- Microbial community structure shifts observed
- **Particle aggregation plays role** in magnitude of impact → increased contact elicits negative response

AQUATIC VERTEBRATES
3 studies – 3 WoE

- **No effects** of spherical particles **on apical endpoints** growth and mortality of amphibian larvae
- **Genotoxic effects** observed (not fully unravelled, might be ROS related), but **not translated in effects on apical endpoints**

Take home messages

- Depending on species and conditions, no or limited effects are observed on apical endpoints. Effects observed on sub-apical endpoints are not always translated in effects on apical endpoints.
- Observed toxicity was typically the result of physical effects resulting from the direct interaction of the nanoparticles with the organism and are not caused by dissolved Ce. Conditions reducing the possibility for direct interaction seem to alleviate any effects.
- Ecological relevance of the observed effects in aquatic organisms is not entirely clear → CeO_2 nanoparticles tend to agglomerate and partition to sediment in the aquatic environment (see our other **POSTER***). Therefore, their potential to induce physical effects is considered low.
- Long-term effect levels in general > classification threshold of 1 mg/L → no long-term harm expected, but there are no rules specified yet by GHS/CLP for nanomaterial classification in case of physical effects.
- No clear relationship between particle size and toxicity was observed.

* Deleebeeck N, Fratepietro F, Claessens M, Mandrillon AL (2022). Environmental fate of CeO_2 nanoparticles - Critical evaluation of available data and implications for exposure assessment. Poster presented at SETAC Europe 32nd Annual Meeting, Copenhagen, Denmark.