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Environmental risk assessment of engineered nanomaterials

# ENVIRONMENTAL RISK ASSESSMENT OF ENGINEERED NANO-$SiO_2$, NANO IRON OXIDES, NANO-$CeO_2$, NANO-$Al_2O_3$, AND QUANTUM DOTS

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**Abstract:** A lot of research studies have endeavored to investigate the ecotoxicological hazards of engineered nanomaterials (ENMs). However, little is known regarding the actual environmental risks of ENMs, combining both hazard and exposure data. The aim of this study is to quantify the environmental risks for nano-$Al_2O_3$, nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, and quantum dots by comparing the predicted environmental concentrations (PEC) with the predicted no effect concentrations (PNEC). The PEC values of these five ENMs in fresh waters in 2020 for northern Europe and southeastern Europe were taken from a published dynamic probabilistic material flow analysis model. PNEC values were calculated using probabilistic species sensitivity distribution (PSSD). The order of the PNEC values was quantum dots<nano-$CeO_2$<nano iron oxides<nano-$Al_2O_3$<nano-$SiO_2$. The risks posed by these five ENMs were demonstrated to be in the reverse order: nano-$Al_2O_3$> nano-$SiO_2$>nano iron oxides>nano-$CeO_2$>quantum dots. However, all risk characterization values are four to eight orders of magnitude lower than one and no risk was therefore predicted for any of the investigated ENMs at the estimated release level in 2020. Compared to static models, the dynamic material flow model allowed us to use PEC values based on a more complex parameterization, considering a dynamic input over time and time-dependent release of ENMs. The PSSD approach makes it possible to include all available data to estimate hazards of ENMs by considering the whole range of variability between studies and material types. The risk assessment approach is therefore able to handle the uncertainty and variability associated with the collected data. The results of the current study are able to provide a scientific foundation for risk-based regulatory decisions of the investigated ENMs. 

**Keywords:** Hazard/risk assessment, Nanomaterials, Nanoparticles, Nanotoxicology, Risk assessment

## INTRODUCTION

Applications of engineered nanomaterials (ENMs) are ubiquitous in industry and consumer products due to the rapid development of nanotechnology (Schmid and Riediker 2008, Zhang, Leu et al. 2015). The use of these nanoproducts inevitably causes the release of ENMs throughout the whole life cycle of nanoproducts to air, soil, water and sediments (Wiesner, Lowry et al. 2006). It has been demonstrated that ENMs often have special properties, which are more likely to induce hazardous effects compared to conventional materials (Barlow, Donaldson et al. 2005, Handy, van der Kammer et al. 2008). Therefore, it is imperative to evaluate the environmental risks posed by these materials, especially to support regulatory decision making (Hansen, Larsen et al. 2007). The quantitative environmental risk assessment approach is comparing the exposure level of a compound with their hazard by dividing the predicted environmental concentration (PEC) by the predicted no effect concentration (PNEC) (ECHA 2016).

With the current analytical techniques it is difficult to identify specifically engineered nanoparticles in the environment (von der Kammer, Ferguson et al. 2012). This therefore limits the exposure assessment and consequently restricts the environmental risk evaluation of ENMs (Nowack, Baalousha et al. 2015). Currently, environmental exposure assessments are mostly depending on an exposure modelling approach (Hendren, Lowry et al. 2013). Environmental exposure models have been advancing significantly during the last years, going from simplified to more complex models, from deterministic to probabilistic modeling, from regional to local systems, and from static to dynamic models (Hendren, Lowry et al. 2013, Baalousha, Cornelis et al. 2016, Nowack 2017). Gottschalk et al (2010) developed a probabilistic material flow analysis (PMFA) model based on a life-cycle perspective, which is able to include all applications of a specific ENM and handle the uncertainty and variability associated with the input parameters, e.g. production volume or product allocation of ENMs. Based on the same concept, a dynamic probabilistic material flow analysis (DPMFA) model was developed by Bornhöft et al (2016) and used to estimate the environmental release and concentrations of nano-$TiO_2$, nano-Ag, nano-ZnO, and CNT in the EU in different scenarios (Sun, Bornhoft et al. 2016, Sun, Mitrano et al. 2017). Another study has predicted environmental concentrations of nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, nano-$Al_2O_3$, and quantum dots in seven European regions using the same DPMFA model (Wang and Nowack 2017). Compared to the static model, the DPMFA model considered 1) a dynamic input of ENMs to the system from 1990 to 2020, 2) a dynamic release: ENMs release was considered to follow different kinetics for different product categories, resulting in different delayed release schedules, and 3) the differences in waste management systems among European regions. These novel aspects make the PEC values from the dynamic models more realistic than those from the simpler static models.

The other critical point of environmental risk assessment is the hazard evaluation. The species sensitivity distribution method (SSD) is able to derive a PNEC, defined as the $5^{th}$ percentile of the SSD, a threshold concentration so that 95% of species in an ecosystem are protected (ECHA 2016). SSD is a well-established way to estimate the adverse effects of chemical substances by considering all available data instead of just using the lowest response endpoint (Kooijman 1987, Frampton, Jansch et al. 2006, Fox 2010). The challenges of assessing the ecotoxicity of ENMs using the SSD method are manifold: There is only limited availability of ecotoxicological studies: whereas the effects on aquatic organisms have been intensively studied, much less studies are available for soils and sediments. The observed toxic effects also show a very large variability between studies, due to differences in test conditions and the different forms of the ENM that are investigated (Gottschalk and Nowack 2012). To overcome those challenges and handle variability of data, Gottschalk et al (2012) developed a probabilistic species sensitivity distribution (PSSD) method, which was applied later to evaluate hazardous effect of five ENMs (nano-$TiO_2$, nano-Ag, nano-ZnO, fullerenes and CNT) (Coll, Notter et al. 2016). Semenzin et al. (2015) assessed the ecotoxicity of nano-$TiO_2$ using a weighted SSD approach, which includes three weighting criteria: the species relevance, the trophic level abundance and the nanotoxicity data quality. Garner et al. (2015) combined all available data to investigate toxicity of nano-Ag, PVP-coated nano-Ag, nano-$Al_2O_3$, nano-C60, CNT, nano-Cu, nano-CuO, nano-$TiO_2$ , nano-ZnO and nano-$CeO_2$ by also considering the particle characteristics. Another recent study constructed a SSD for metallic nanomaterials based on data, that are grouped according to the characteristics of ENMs, test conditions and types of endpoints (Chen, Peijnenburg et al. 2017).

In the field of environmental risk assessment, early studies have used the lowest response concentration to evaluate adverse effect of nano-$TiO_2$, nano-ZnO, nano-Ag, carbon nanotubes, and fullerenes (Mueller and Nowack 2008, Gottschalk, Sonderer et al. 2009). Later, researchers have also estimated risks posed by ENMs from specific nanoproducts, e.g. a glass cleaner (Dekkers, Krystek et al. 2011, Michel, Scheel et al. 2013, Mahapatra, Sun et al. 2015). However, these studies either calculated the PNEC value using the lowest effect concentration or estimated the release of ENMs only from a single application. Other studies have assessed the risks from all possible applications using a PMFA model and a PSSD for nano-$TiO_2$, nano-Ag, nano-ZnO, fullerenes, CNT, nano-$SiO_2$ and nano iron oxides for fresh waters, soils, and sediments (Gottschalk, Kost et al. 2013, Coll, Notter et al. 2016, Wang, Deng et al. 2016, Wang, Kalinina et al. 2016). In both parts of the risk assessment, the exposure and the hazard assessment, the scientific progress is fast with new exposure models and large numbers of ecotoxicological studies being constantly published that can be used in new risk evaluations.

In light of these issues, the aim of this work was to conduct an environmental risk assessment for ENMs that have not or only marginally been covered (nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, nano-$Al_2O_3$, and quantum dots). The PEC was modeled using the DPMFA model described in Wang & Nowack (2017) and the hazard assessment is based on updated ecotoxicological data using a PSSD approach [32]. The results from the current study provide insights into the possible risk posed by the considered ENMs in the future based on the predicted release level, and contribute to future regulatory risk assessment framework for ENMs (Steinhäuser and Sayre 2017).

## MATERIALS AND METHODS

### *Predicted environmental concentration*

The exposure assessment for nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, nano-$Al_2O_3$, and quantum dots using the DPMFA model has been described in Wang & Nowack (2017). This study shows that the PEC in fresh water compartments in Europe is the lowest in northern Europe and the highest in southeastern Europe (of seven European regions considered). These two regions were therefore selected in the present work. Due to the increase in production over time, the PEC values are constantly increasing in environmental compartments. In order to consider also the near-future increase, we selected the year 2020 as basis for the model. Therefore, the PEC values in northern Europe and southeastern Europe were extracted from Wang & Nowack (2017) for the year 2020. These PEC values represent average concentrations in standard environmental compartments as defined in the REACH guidance (ECHA 2016).

*Ecotoxicological data collection*

Ecotoxicological data for nano-$Al_2O_3$, nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, and quantum dots were collected from peer-reviewed studies published before July 2017. The data screening followed the criteria described in Coll et al (2016). All endpoints from the same study using nanoparticles with different size and/or type (e.g. coating) were considered as individual data points. If tests in one study were conducted under various test conditions, maximal three values were chosen (minimum, median, and maximum). Hence, the collected data covered studies investigating the ecotoxicity of a range of species exposed to varied test materials with different particles sizes and test media. Too little information regarding the hazard of the considered ENMs to soil and sediment organisms was found to build a PSSD for these systems. Hence, the data presented here is restricted to the risk assessment of the targeted ENMs in fresh waters.

The summary of collected ecotoxicological concentrations is given in Table 1 and the detailed information extracted from the studies is presented in Table S1. In total 173 endpoints were collected, including EC10, EC15, EC20, EC50, LC10 LC20, LC50, IC50, lowest observed effect concentration (LOEC), highest observed no-effect concentration (HONEC), and NOEC. Among the five ENMs, nano-$CeO_2$ has the most data available with 71 endpoint concentrations covering 17 species, and the least data is available for quantum dots with 16 data points from 7 species.

*Probabilistic species sensitivity distribution modelling*

According to the European Chemical Agency guidelines, the calculation of PNEC values for fresh waters using the SSD method should be based on all available NOECs from long term studies (ECHA 2008). In this work, two assessment factors (AF) were used to derive chronic

NOEC values from the collected data. One AF is used to derive the no observed concentration from the observed concentration if a NOEC is not available. The other AF is applied to extrapolate long-term effects from short-term studies. The method of assigning the AF was described in detail in the previous studies (Coll, Notter et al. 2016, Wang, Deng et al. 2016), and is based on the REACH guidelines (ECHA 2008). To calculate NOEC values with all uncertainties included, the collected ecotoxicological data were introduced into the model as triangular distributions that are then divided by two AFs, to which triangular distributions were also applied in order to consider the uncertainties associated with the AFs. Triangular distributions are obtained by multiplying or dividing each AF with two. A similar method was first developed by Gottschalk and Nowack (2013) and was applied to generate SSDs in several risk assessment studies (Coll, Notter et al. 2016, Wang, Kalinina et al. 2016). However, the uncertainties of the AFs were not considered in these former studies. With the Monte Carlo approach applied in our model, a probabilistic distribution was derived and an overall PSSD of each ENM was then generated by combining all data of single species. The PNEC was calculated by dividing the 5$^{th}$ quantile of the SSD (considering 50% confidence interval associated with this concentration) by an AF in ECHA guidelines (ECHA 2016). To include the uncertainty derived from the PNEC calculation, we abstracted 3$^{rd}$, 5$^{th}$, and 7$^{th}$ quantiles of the PSSD, and applied a triangular distribution to these three values. In this work, 10,000 random values were used to generate the triangular distributions.

*Risk calculation*

The environmental risks of ENMs were quantified by calculating the risk characterization ratio (RCR) by comparing the exposure level (PEC) with the corresponding PNEC according to the risk assessment guidelines (Equation 1) (ECHA 2016). If the RCR is less than 1, the risk to the environment is controlled at the given exposure scenario. If the RCR is larger than 1, certain risk management measures have to be taken. The RCR distribution was generated by dividing each values of the PEC distribution by all data from the PNEC distribution of each ENM.

$$RCR = PEC / PNEC \quad (1)$$

**RESULTS**

The PEC values for fresh waters are based on the dynamic MFA model by Wang and Nowack (2017) and therefore consider the accumulation of ENMs in stocks and the delayed release from them. The dynamic nature of the model also allows an extrapolation of the release into the future and 2020 has been chosen as reference year to enable a precautionary assessment. The mean concentrations of the five considered ENMs in 2020 in northern Europe and southeastern Europe, as well as the 5$^{th}$ and 95$^{th}$ percentiles of the distribution, are given in Table 2. Quantum dots have the lowest concentration among the five studied ENMs at the level of fg/l and the highest concentrations are observed for nano-$SiO_2$ at the µg/l level. Based on the study by Wang and Nowack (2017), northern and southeastern Europe were chosen because they represent the European regions with the lowest and highest fresh water concentrations of ENMs, mainly caused by their different volume of fresh waters and the different level of wastewater treatment infrastructure.

The NOEC values calculated from the reported endpoints are contained in Table S1 and have been used to construct the PSSD for each material shown in Figure 1. The NOEC values of individual species are indicated with blue triangles, the calculated PSSD with the red line. The NOEC values for one species exposed to the same ENM from different studies can vary a lot.

For example, the highest NOEC value of *P. subcapita* for nano-$CeO_2$ is five orders of magnitude higher than the lowest value. The range of response concentrations between the most and the least sensitive species for all considered ENMs is between four and six orders of magnitude.

The PNEC values, which are derived from the 5th percentile of the PSSD, are given in Table 3. The highest PNEC is found for nano-$SiO_2$ with 1665 µg/l, the lowest one for quantum dots with 0.32 µg/l. Figure 2 shows the comparision of whole PNEC distribution (red line) and the corresponding PEC distributions for each of the ENM in the fresh water compartment in northern Europe (blue line) and in southeastern Europe (green line) in 2020. The PEC distribtution of southeastern Europe is found to be closer to the PNEC compared to the PEC of northern Europe. This is because the concentration of ENMs in 2020 in southeastern Europe is higher than that in northern Europe. Overall, no overlap was observed between PEC and PNEC distributions for any of the considered ENMs. However, the distance between the PEC and PNEC curves of these ENMs varies a lot. For example, for nano-$SiO_2$, the PEC and PNEC curves are quite close to each other, while the gap for quantum dots is much larger. To quantify this gap, we calculated the RCR.

The mean RCR values and the range between the 5th and 95th percentiles are also given in Table 3. The complete probability distributions of the five RCR are shown in Figure 3. All RCR values are at three to seven orders of magnitudes lower than 1, and the order of RCR values among all ENMs is nano-$SiO_2$ > nano-$Al_2O_3$ > nano iron oxides > nano-$CeO_2$ > quantum dots. The risk posed by the considered ENMs in 2020 in northern Europe is smaller than that in southeastern Europe.

**DISCUSSION**

This study is the first to conduct an environmental risk assessment for ENMs using release data based on dynamic material flow modeling. This dynamic model is considering a material input into the environment from 1990 to 2020 and also reflects regional differences in waste management (Wang and Nowack 2017). From previous static models, PEC values are available for nano-$SiO_2$, nano iron oxides, nano-$Al_2O_3$, nano-$CeO_2$, and quantum dots (Gottschalk, Lassen et al. 2015, Wang, Deng et al. 2016, Wang, Kalinina et al. 2016). The concentrations presented in the current paper can be either higher or lower than those from previous studies, depending on the material. This can be explained by the following factors: i) the different input data and methods used to assess production volume and product allocation that are at the basis for the different models; ii) the various time periods or geographic systems considered in the studies; iii) the different modelling approaches used to predict PEC and PNEC. For example, the dynamic model considers both the increasing production of ENMs over time as well as time-dependent releases and accumulation of ENMs in stocks and environmental compartments. Therefore, the PEC values in 2020 in this work are slightly larger than that predicted in the previous study using the same DPMFA model as the production and use of ENMs have been increasing after 2014, the base year in the previous model (Wang and Nowack 2017).

The DPMFA model allows us to predict environmental concentrations considering the changing behavior of the model system over time. However, it does not include one fact, which is the change of nanoapplications over time. Due to an almost complete lack of data on historic product distributions for ENMs, the model is based on the simplifying assumption that the product distribution in the past was the same as currently and that it remains the same in the near future. Sun et al. (2017) have used the dynamic MFA model to predict future scenarios of changing product distributions which could be used in the future in prospective risk assessments.

It is necessary to state that the risk assessment in the current study is generic for each modelled ENM, namely that the exposure and hazard assessments are not specific in terms of type of ENMs. The PNEC values derived in the current study did not distinguish ENMs with various sizes, forms, and test conditions. However, researchers have demonstrated that the type of crystal phase can change the toxic effects of ENMs significantly (Lin, Li et al. 2014). A first study by Gottschalk et al (2015) provides PEC values for different forms of nano-$TiO_2$, which could form the basis to assess the environmental risk posed by the different form of nano-$TiO_2$ (e.g. photocatalytic and photostable) (Gottschalk, Lassen et al. 2015).

The exposure assessment in this study estimated the total flux and concentrations of each considered ENM in the environment without considering the transformation of ENMs. Therefore, the exposure level predicted for 2020 is rather conservative under a worst scenario with no transformations included. ENMs are affected in the environment by a series of reactions such as agglomeration, dissolution, and sedimentation (Klaine, Alvarez et al. 2008, Baun, Sayre et al. 2017). These reactions will decrease the exposure concentration in water and thus decrease the calculated risks even further.

Another aspect determining the PEC values that needs consideration is the fact that the predicted concentration is representing an average level for the target region. One of the possible release pathways of ENMs entry to the environment is from production and manufacturing, with the effluent of sewage treatment plants and by emissions from waste incineration plants. These releases are local point sources and their geographic distribution determines the local PEC values that can vary greatly between different regions (Gottschalk, Ort et al. 2011, Keller and Lazareva

2014, Dale, Lowry et al. 2015, Dumont, Johnson et al. 2015, Sun, Conroy et al. 2015). For example, Dumont et al (2015) modelled nano-Ag and nano-ZnO monthly concentrations in European fresh waters by considering dilution, downstream transport, water evaporation, water abstraction, and nano-particle sedimentation (Dumont, Johnson et al. 2015). High concentrations of ENMs were predicted close to big cities due to the high population density and thus high wastewater production. The concentrations estimated in our work are valid for the regional scale, which implies that the PEC values in a local water system might be higher than the predicted values and consequently may underestimate the environmental risk of the considered ENMs.

Earlier studies have already applied the SSD method to assess the environmental hazards for some of the ENMs covered in our study, e.g. nano-$SiO_2$, nano iron oxides, nano-$Al_2O_3$, and nano-$CeO_2$ (Garner, Suh et al. 2015, Wang, Deng et al. 2016, Wang, Kalinina et al. 2016). The PNEC value of nano-$SiO_2$ predicted in the current study (1665 µg/l) is close to the results presented in the previous study (1028 µg/l) . The updated PNEC for nano iron oxides is at the same concentration level than in a previous study (Wang, Deng et al. 2016). Garner et al. (2015) have built SSDs for nano-$Al_2O_3$, and nano-$CeO_2$ as well and estimated that the PNEC are 2-8 mg/l for nano-$Al_2O_3$, and 0.08-6 mg/l for nano-$CeO_2$ (Garner, Suh et al. 2015). The PNEC range calculated in our work are 48-254 µg/l (nano-$Al_2O_3$) and 2.1-3.2 µg/l (nano-$CeO_2$), which is one to three orders of magnitudes lower compared to the previous study. The reason for this difference is that the SSD built by Garner et al. (2015) was for acute freshwater toxicity using LC50 values whereas we used two different assessment factors to convert acute effect concentrations to chronic NOEC values, thus explaining up to a factor of 100 of difference between these two studies.

The nano-SSD studies performed so far, including the current one, are based on all available studies reporting endpoints such as EC50, LOEC or NOEC although most of these studies have not followed procedures that are based on validated test systems. However, as detailed by Hjorth et al (2017) (Hjorth, Skjolding et al. 2017)., even when tests are performed in accordance with OECD guidelines, the reliability of the outcomes depends on many factors such as a proper characterization of the starting material or during exposure. Whereas there are ongoing activities to develop specific guidelines for ecotoxicity testing of ENM, we should still make use of the large amount of existing data that have been published so far, especially when the context of the study is a scientific evaluation and not within a regulatory decision making.

A handful of studies have investigated the influence of ENMs characteristics on the hazardous effects of ENMs (Botha, James et al. 2015, Garner, Suh et al. 2015, Mahapatra, Sun et al. 2015, Chen, Peijnenburg et al. 2017). Garner et al. (2015) for example built SSDs for metal nanomaterials separated into different forms, e.g. uncoated Ag, Ag-PVP, and Ag+, and only minor differences were observed between coated Ag particles and Ag+, and the uncoated Ag was found to be less toxic than PVP coated Ag. Other factors including size, exposure time, and shape of the nanoparticles were also shown to influence the toxic effects of ENMs (Chen, Peijnenburg et al. 2017). However, according to the REACH guidelines, building an SSD requires at least ten endpoint concentrations from different species for at least eight taxonomic groups (ECHA 2016). If enough data are available for constructing more detailed SSDs, the hazard assessment of the current work could be improved with considering the effect of characterization of ENMs and the experimental conditions. However, at the same time exposure data for the different forms of ENMs would also need to be available, which is currently not the case.

Our risk assessment shows no overlap between the PEC distributions in fresh waters and PNEC distributions in all cases. Therefore, no risk is predicted under the estimated release level in 2020 for the five considered ENMs. RCR values are decided by both the exposure and the effect level and therefore the ENM with the highest hazard to organisms does not necessarily imply the highest associated risk. For example, quantum dots show the smallest risk even though they are the most toxic ENMs among all considered ENMs. Nano-$SiO_2$ is the ENM of the second highest concerns with the largest RCR value although it has the highest PNEC value. This is because the exposure concentration of nano-$SiO_2$ is several orders of magnitude higher than that of quantum dots – it is the ratio of the two values that matters for the risk.

Thousands of nano-ecotoxicological papers have been published since 2004, however, the data is still inadequate to conduct a full risk assessment for every environmental compartment (Hjorth, Skjolding et al. 2017). The soil and sediment compartments were not included in the current study due to a limited number of ecotoxicological studies reporting EC50 or NOEC values to construct an SSD. However, sufficient evidence has proven that ENMs are likely to accumulate in soils and sediments because these compartments constitute sinks for these materials and critical ENMs concentrations might be reached over time (Klaine, Alvarez et al. 2008, Pan and Xing 2012, Gardea-Torresdey, Rico et al. 2014). Because our PEC modeling also provides values for soils and sediments, the risks to the compartments can easily be calculated once enough ecotoxicological data become available to build an SSD.

The results from this study can provide regulators scientific foundations for a risk-based environmental policy regarding ENMs in the future. This work will complement the growing number of risk assessment frameworks that are proposed or under development to deal with the specific challenges existing in the risk assessment process for ENMs (Hristozov, Gottardo et al. 2016, Sayre, Steinhäuser et al. 2017, Steinhäuser and Sayre 2017).

*Supplemental Data*—The Supplemental Data are available on the Wiley Online Library at DOI: 10.1002/etc.xxxx.

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*Data availability*—The original data not contained in the Supplemental Data are available from the corresponding author (nowack@empa.ch).

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Figure 1. Probabilistic species sensitivity distribution (PSSD) for nano-$Al_2O_3$, nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, and quantum dots in fresh water. The blue triangles represent no observed effect concentration (NOEC), which are calculated based on collected endpoint concentrations. The red lines are the PSSD.

Figure 2. Comparison of predicted no-effect concentration (PNEC) (red line) with predicted environmental concentrations (PEC) of nano-$Al_2O_3$, nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, and quantum dots in fresh water in northern Europe (blue line) and in southeastern Europe (green line) in 2020.

Figure 3. Risk characterization ratio (RCR) distribution of nano-$Al_2O_3$, nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, and quantum dots in northern Europe (red line) and in southeastern Europe (green line) in 2020.

**Table 1. Summary of endpoint concentrations collected for the five considered ENMs**

| ENM | Number of species | Number of Endpoints |
|---|---|---|
| nano-$SiO_2$ | 12 | 34 |
| nano iron oxides | 13 | 26 |
| nano-$Al_2O_3$ | 16 | 26 |
| nano-$CeO_2$ | 17 | 71 |
| Quantum dots | 7 | 16 |

**Table 2. Predicted environmental concentrations of five ENMs in the fresh water in 2020 based on the model by Wang and Nowack (2017)**

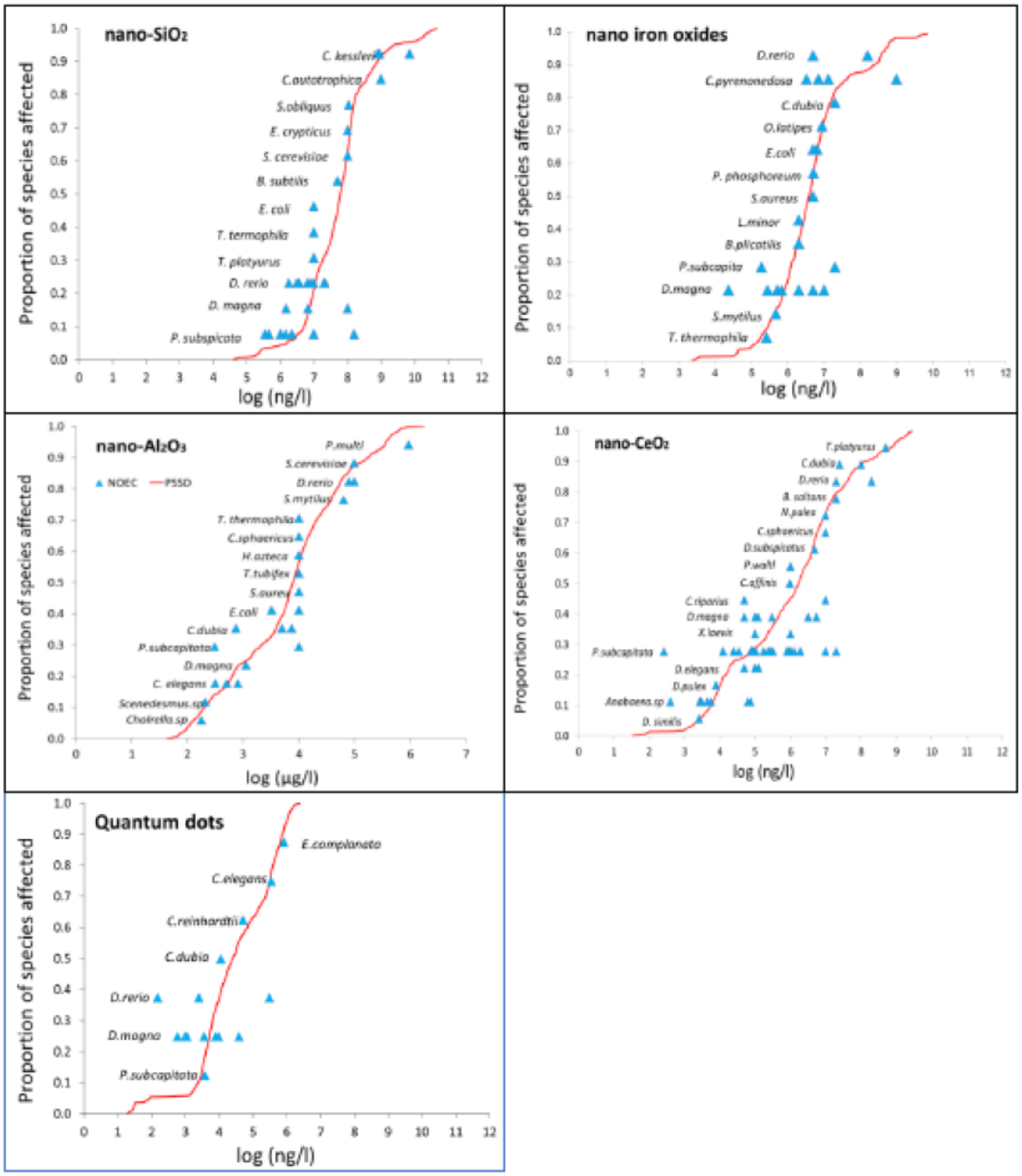
| ENM | Northern Europe | Southeastern Europe | Unit |
|---|---|---|---|
| nano-$SiO_2$ | 562 (5.35 - 1640) | 2600 (21.7 - 8460) | ng/l |
| nano iron oxides | 12.8 (0.271 - 55.5) | 44.2 (0.872 - 171) | ng/l |
| nano-$Al_2O_3$ | 39.6 (0.716 - 99) | 221 (3.48 - 780) | ng/l |
| nano-$CeO_2$ | 268 (5.81 - 1230) | 1130 (23.2 - 5430) | pg/l |
| Quantum dots | 32.8 (10.9- 89.3) | 107 (14.9 - 369) | fg/l |

**Note: Mean values are given, the values in the bracket are the 5$^{th}$ and 95$^{th}$ percentiles.**

**Table 3. Mean values of predicted no effect concentrations (PNEC) and risk characteristic ratio (RCR)**

| ENM | PNEC (µg/l) | RCR (NE) | RCR (SEE) |
|---|---|---|---|
| nano-$SiO_2$ | 1665 (275 - 2995) | 2.55E-04 (2.12E-06 - 9.38E-04) | 1.25E-03 (9.09E-06 - 4.56E-03) |
| nano iron oxides | 128 (38 - 190) | 1.10E-04 (2.56E-06 - 6.12E-04) | 3.84E-04 (8.97E-06 - 1.75E-03) |
| nano-$Al_2O_3$ | 120 (48 - 254) | 2.97E-04 (6.05E-06 - 8.17E-04) | 1.8E-03 (2.41E-05 - 5.3E-03) |
| nano-$CeO_2$ | 2.62 (0.77- 16) | 5.26E-05 (7.36E-07 - 2.29E-04) | 2.11E-04 (2.7E-06 - 1.08E-03) |
| Quantum dots | 0.32 (0.03- 1.57) | 7.19E-08 (1.26E-08 - 2.29E-07) | 2.25E-07 (2.04E-08 - 8.27E-07) |

**Note: the values in the bracket are the 5$^{th}$ and 95$^{th}$ percentiles. NE: Northern Europe, SEE: Southeastern Europe**

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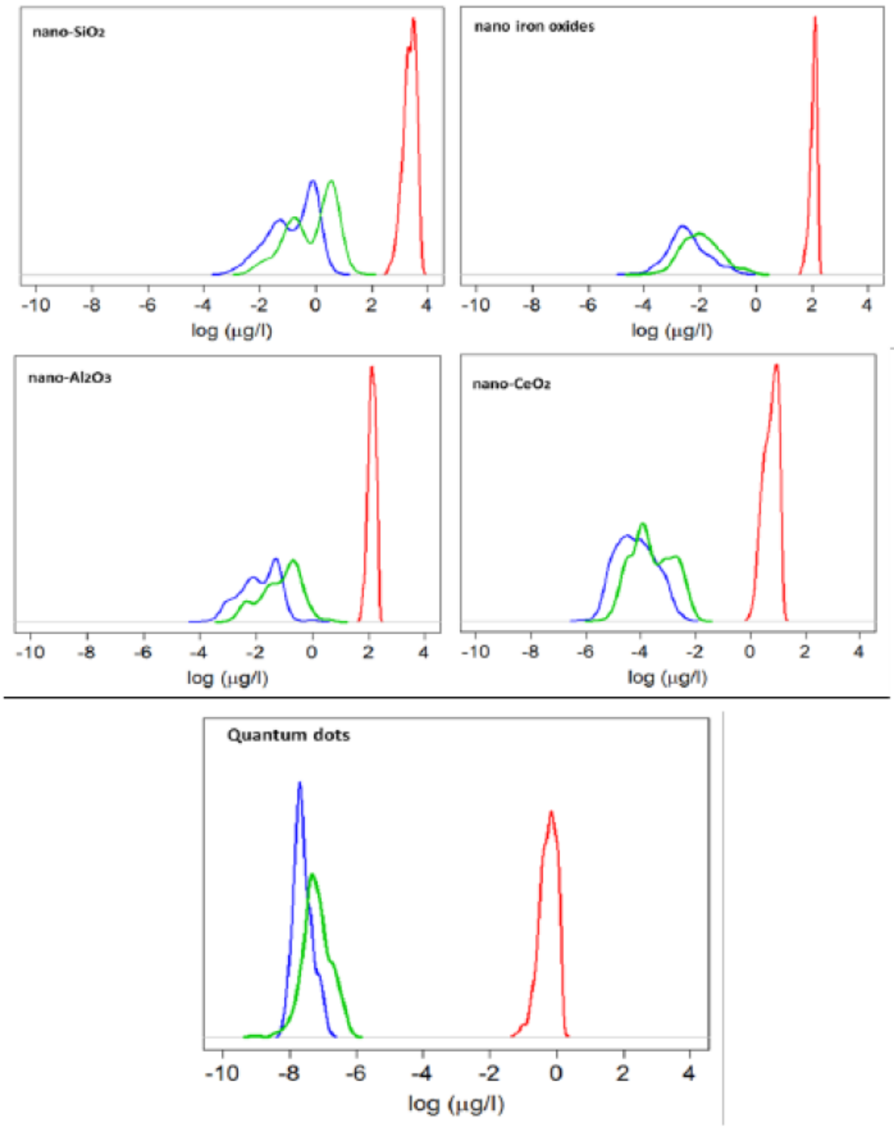


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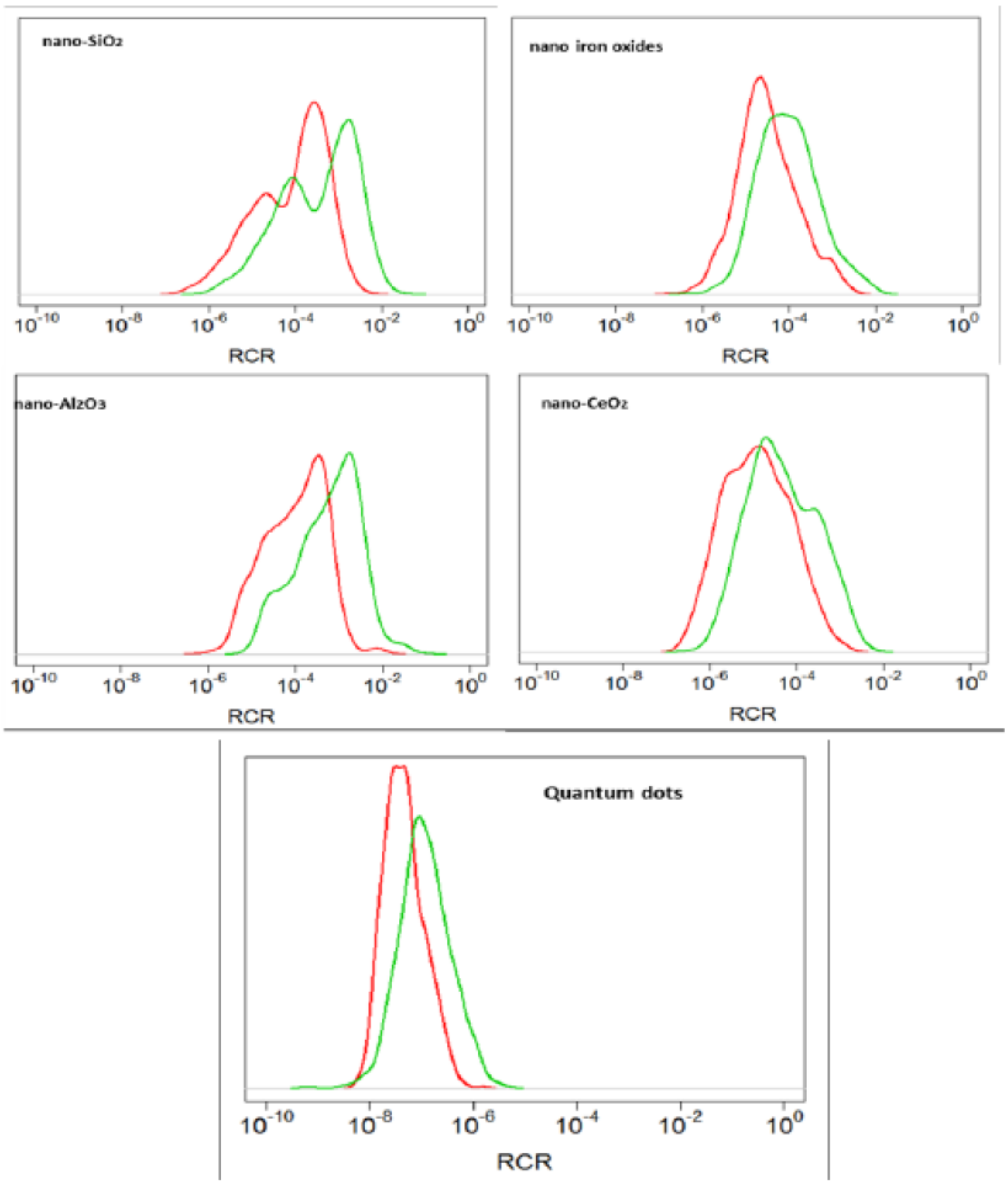


**Figure 3. Risk characterization ratio (RCR) distribution of nano-$Al_2O_3$, nano-$SiO_2$, nano iron oxides, nano-$CeO_2$, and quantum dots in northern Europe (red line) and in southeastern Europe (green line) in 2020.**