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**Probabilistic/stochastic environmental exposure modeling: Methodology and applications to engineered nanomaterials**

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*In memory of my father and for my children Silvana, Flavio & Milena.*





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## Summary

A fundamental step towards a quantitative assessment of the risks of new compounds or pollutants (chemicals, materials) to the environment is to estimate their environmental concentrations. Thus, the calculation of predicted environmental concentrations (PEC) comprises the basis for an initial exposure assessment. Potential risks are assessed in this thesis by means of a comparison of the PEC values with the predicted no effect concentrations (PNEC) derived from published data.

The first part of the thesis presents a probabilistic method of computing distributions of PECs by means of probabilistic/stochastic material flow analysis (PMFA). The evolved model is basically applicable to any substance with a distinct lack of data concerning its environmental fate, exposure, emission and transmission characteristics. The model input parameters and variables consider production, application quantities and the fate of the compounds in natural and technical environments. In order to cope with uncertainties concerning the estimation of the model parameters (e.g. transfer and partitioning coefficients, emission factors) as well as uncertainties about the exposure, and the causal mechanisms (e.g. level of compound production and application) themselves, we utilized and combined the following probabilistic methods: sensitivity and uncertainty analysis, Monte Carlo simulation, Bayesian and Markov Chain modeling. The model developed is programmed and carried out with the computational tool R, and implemented and validated with data for an exemplary case study of flows for the engineered nanomaterial (ENM) nano-TiO<sub>2</sub> in Switzerland.

Engineered nanomaterials are already used in many products and consequently released into environmental media. Hence, in the second part of the thesis, we calculated predicted environmental concentrations (PEC) for different ENMs based on the probabilistic material flow analysis developed and from a life-cycle perspective of the ENMs and ENM-containing products. The model considered as input parameters the production volumes of the ENMs, the manufacturing and consumption quantities of products containing those materials, and the fate and pathways of ENMs in natural and technical environments. We modeled nano-TiO<sub>2</sub>, nano-ZnO, nano-Ag, carbon nanotubes (CNT), and fullerenes for the USA, Europe and Switzerland. The environmental concentrations were calculated as probabilistic density functions and were compared to data from ecotoxicological studies. The simulated modes (most frequent values) ranged from 0.003 ng L<sup>-1</sup> (fullerenes) to 21 ng L<sup>-1</sup> (nano-TiO<sub>2</sub>) for surface waters and from 4 ng L<sup>-1</sup> (fullerenes) to 4 µg L<sup>-1</sup> (nano-TiO<sub>2</sub>) for sewage treatment effluents. For Europe and the USA, the annual increase of ENMs on sludge-treated soil ranged from 1 ng kg<sup>-1</sup> for fullerenes to 89 µg kg<sup>-1</sup> for nano-TiO<sub>2</sub>. The results of this part of the thesis indicate that risks to aquatic organisms may currently emanate from nano-Ag, nano-TiO<sub>2</sub> and nano-ZnO in sewage treatment effluents for all regions considered and for nano-Ag in surface waters. For the other environmental compartments for which ecotoxicological data were available, we conclude that no risks to organisms are to be expected at this point in time.

In the third part of the thesis a sensitivity analysis and a comprehensive discussion of the uncertainties of the simulation results and the limitations of the developed approach are presented. As case studies predicted environmental concentrations (PEC) were modeled for

nano-TiO<sub>2</sub>, carbon nanotubes (CNT) and nano-Ag in Switzerland. The PEC values of the ENMs in the different environmental compartments varied widely due to the different ENM production volumes and different life cycles of the nanoproducts. The use of ENM in products with high water relevance led to higher water and sediment concentrations for nano-TiO<sub>2</sub> and nano-Ag, compared to CNTs, where smaller amounts of ENM reached the aquatic environment. For nano-TiO<sub>2</sub> and nano-Ag the sensitivity analysis showed that changes in the parameters STP inflow, STP overflow, and STP removal efficiency covered at least 98% of the source of variation of the ENM concentrations in water. The variation of the parameters STP overflow and STP removal efficiency explained to a probability of 88% how the CNT concentrations in water responded to changes in input parameters. Summing up the key limitations of the results, we see a general lack of input data, the focus on one unique region (Switzerland) and the steady state calculations for only one time period (2008). Especially data found in the literature for the annual production volumes of ENMs vary widely, sometimes by a factor of 100. Additional key limitations exist in the lack of data on the ENMs' fate in nature. In particular the exchange between water and sediment through re-suspension and burial processes could not be considered in detail. Accumulation in sediments was equated to sedimentation/aggregation.

In the fourth part of the thesis two models, one based on probabilistic material flow analysis (PMFA) and one based on graph theory were combined to calculate PECs of engineered nanomaterials (ENMs) in Swiss rivers at high spatial resolution. PECs for nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag were calculated for 742 river sections at base flow conditions Q<sub>95%</sub> (flow reached or exceeded annually in 95% of the time). Additionally, flow measurements for 20 selected locations over a 20-year period (1988–2007) were used to assess temporal variations. At base flow the highest PECs (modal values) were found for nano-TiO<sub>2</sub> where the concentrations at Q<sub>95%</sub> ranged from 0.1 ng L<sup>-1</sup> to 7.8 µg L<sup>-1</sup>, followed by nano-ZnO (0.004 ng L<sup>-1</sup> to 0.5 µg L<sup>-1</sup>) and nano-Ag (0.3 pg L<sup>-1</sup> to 0.03 µg L<sup>-1</sup>). Comparing PECs with PNEC values (predicted no effect concentrations) revealed that based on the hydrological data used and averaged for all 20 stations and scenarios (scenario with and scenario without sedimentation) the PNEC was exceeded for nano-Ag using modal concentrations at 234 days annually. The equivalent results for nano-ZnO and nano-TiO<sub>2</sub> were 150 and 109. This part of the thesis showed that linking a probabilistic material flow analysis to a geo-referenced model fills two gaps: the PEC calculations for rivers were improved compared to calculations at regional level by considering geographical distribution of the ENM emissions and a clear distinction between input uncertainty and natural water flow variations could be achieved. Variability in the stream flow variation influenced the ENM concentrations up to a factor of 5, the uncertainty in the ENM loads caused a difference in the PEC calculations up to a factor 10.

Summing up, we may state that currently attention is paid to potential life cycle impacts and toxicity of engineered nanomaterials. However, there is still limited data available on the environmental fate and effects of ENM, and consequently a lot of questions are still around concerning the possible risks caused to the environment and human health. In addition, there are almost no analytical methods available for such material. Hence, the discussion of ENM and the environment differs completely, e.g. from that on organic micropollutants, where advances in analytical detection of the compounds in the environment have been the starting point for scientific and public discussions. As a consequence, predictions of the concentrations to be found in the environment and studies on potential exposure pathways based on mathematical modeling

are needed and, as shown in this thesis, a valuable first tool to evaluate and predict risks posed by ENM to the environment.





## Zusammenfassung

Ein grundlegender Schritt in Richtung einer quantitativen Bewertung der Risiken neuer Verbindungen oder potenzieller Schadstoffe (Chemikalien, Materialien) für die Umwelt ist es, ihre Konzentrationen in der Umwelt zu schätzen. So bilden in dieser Arbeit berechnete PEC-Werte (Predicted Environmental Concentrations) die Basis einer ersten Bewertung der Umwelt-Exposition bzw. -Risiken, welche von künstlich hergestellten Nanomaterialien ausgehen können. Solch potenzielle Risiken werden durch einen Vergleich von PEC-Werten mit aus veröffentlichten Daten abgeleiteten PNEC-Werten (Predicted No Effect Concentrations) ermittelt.

Im ersten Teil dieser Arbeit wurde in der statistischen Programmiersprache R ein probabilistisch-stochastisches Stoffflussanalyse-Modell entwickelt (probabilistic material flow analysis (PMFA)) und programmiert, welches zur Simulation von Emissions- und Umweltverhalten von sogenanntem Engineered Nanomaterial (ENM) dient. Dieses Modell ist basierend auf eine Formalisierung und Programmierung von Monte-Carlo- und Monte-Carlo-Markov-Ketten-Algorithmen entwickelt worden. Das Modell eignet sich, um Schadstoffkonzentrationen in der Umwelt zu berechnen oder vorherzusagen. Es sollte angewendet werden bei schwacher Datenlage bezüglich Herstellung und Verwendung, Emissionsvolumen sowie bezüglich des Verhaltens der Kontaminanten in technischen Anlagen und in der natürlichen Umwelt. Es liefert Simulationsresultate in der Form von Wahrscheinlichkeitsverteilungen. Aus solchen Verteilungen können z. B. Modalwerte (die am häufigsten vorkommenden Simulationswerte) und Konfidenzintervalle der Simulationsergebnisse extrahiert werden. Um die unterschiedlichen Unsicherheiten hinsichtlich der Schätzung der Modellparameter sowie Unsicherheiten über die kausalen Mechanismen der Exposition (Dauer, Höhe, Häufigkeit, Pfade) zu modellieren, wurde zusätzlich eine Methode der Sensibilitäts- und Unsicherheitsanalyse für probabilistische Berechnungen entwickelt. Das Modell wurde mit Daten für eine exemplarische Fallstudie zu Stoffflüssen (Schweiz) von künstlich hergestelltem nano-TiO<sub>2</sub> ein erstes Mal angewendet.

Im zweiten Teil dieser Arbeit wurden mit Hilfe der probabilistisch-stochastischen Stoffflussanalyse (PMFA) Stoffflüsse zu nano-TiO<sub>2</sub>, nano-ZnO, nano-Ag, Kohlenstoff-Nanoröhren (CNT) und Fullerene für die USA, Europa und die Schweiz simuliert. Umweltkonzentrationen (PEC) wurden aus einer vollständigen Lebenszyklus-Perspektive von ENM und ENM-haltigen Produkten modelliert. Die Konzentrationen in der Umwelt wurden als Wahrscheinlichkeits-Dichte-Funktionen berechnet und mit Daten zu ökotoxikologischen Untersuchungen verglichen. Die simulierten Modi (häufigste Werte) umfassten einen Bereich von 0,003 ng L<sup>-1</sup> (Fullerene) bis 21 ng L<sup>-1</sup> (nano-TiO<sub>2</sub>) für Oberflächengewässer und einen solchen von 4 ng L<sup>-1</sup> (Fullerene) bis 4 µg L<sup>-1</sup> (nano-TiO<sub>2</sub>) in Abflüssen von Kläranlagen. Für Europa und die USA wurde der jährliche Anstieg der ENM-Konzentration in Böden und in mit Klärschlamm behandelten Böden berechnet. Die Werte der jährlichen Zunahme reichen von 1 ng kg<sup>-1</sup> für Fullerene bis 89 µg kg<sup>-1</sup> für nano-TiO<sub>2</sub>. Die Ergebnisse dieser Studie zeigen, dass derzeit Risiken für aquatische Organismen in Klärschlamm ausgehend von nano-Ag, nano-TiO<sub>2</sub> und ZnO für alle betrachteten Regionen möglich sind. Überschreitungen des kritischen Werts von eins bei Risikoquotienten (PEC/PNEC) wurden auch für nano-Ag in Oberflächengewässern beobachtet. Daraus lässt sich zumindest schliessen, dass weitere Untersuchungen dringend erforderlich sind, um das Risiko für die

aquatische Umwelt genauer zu bewerten. Für die übrigen Umweltkompartimente, für die ökotoxikologische Daten vorliegen, sind derzeit keine Risiken zu erwarten.

Im dritten Teil dieser Arbeit wurden eine Sensitivitätsanalyse und eine umfassende Diskussion über Möglichkeiten und Grenzen des in der ersten Studie entwickelten Modellierungsansatzes durchgeführt. Dies erfolgte basierend auf modellierten Fallstudien zu Konzentrationen in der Umwelt von nano-TiO<sub>2</sub>, Kohlenstoff-Nanoröhren (CNT) und nano-Ag in der Schweiz. Die PEC-Werte der ENMs in den verschiedenen Umweltkompartimenten variierten sehr stark. Diese Differenzen sind aufgrund von Unterschieden in den ENM-Produktionsmengen und den Lebenszyklen der verwendeten Nanoprodukte zu suchen. Die Verwendung von ENM in wasserrelevanten Produkten führt zu höheren Wasser- und Sediment-Konzentrationen für nano-TiO<sub>2</sub> und nano-Ag verglichen mit CNTs, von denen kleinere Mengen die aquatische Umwelt erreichen. Für nano-TiO<sub>2</sub> und nano-Ag ergab die Sensitivitätsanalyse, dass Änderungen in den Parametern STP Zufluss Kläranlage, Überlauf Kläranlage und Abscheideleistung von Kläranlagen mindestens 98 % der Variation der ENM-Konzentrationen in Wasser abdecken. Die Variation der Parameter Überlauf Kläranlage und Abscheideleistung von Kläranlagen erklärte mit einer Wahrscheinlichkeit von 88 %, wie die CNT-Konzentrationen in Wasser auf Veränderungen von Modellparametern reagieren. Die Grenzen der Methode bzw. der Simulationsergebnisse zeigten sich einerseits im Umgang mit einer sehr ausgeprägten Lücke von empirischen Input-Daten, welche auch durch differenzierte Expertenbefragung oder ausgeklügelte Monte-Carlo-Algorithmen nicht gänzlich zu schliessen ist. Andererseits ist die Limitierung auf eine einzige Region (Schweiz) und auf Steady-State-Berechnungen für eine einzige Zeitspanne (2008) eine weitere Schwäche der Modellierung, welche z. B. die Dynamik zukünftiger Verwendungen von kommerziell verfügbaren ENM-haltigen Produkten nicht zulässt. Insbesondere die Daten in der Literatur für die jährliche Produktion von ENM sind mit grossen Unsicherheiten behaftet, manchmal mit einem Faktor von 100. Weitere wichtige Limitationen der Simulationsergebnisse sind im Mangel an Wissen über Verbleib und Verhalten der ENM in der Umwelt zu sehen. Insbesondere der einflussreiche Parameter Austausch zwischen Wasser und Sediment durch Sedimentation und Resuspension konnte aufgrund der kaum vorhandenen empirischen Datenbasis nicht im Detail betrachtet werden.

Im Rahmen des vierten Teils dieser Arbeit wurden zwei Modelle, eines auf probabilistische Materialflussanalyse und eines auf der Grundlage von Graphentheorie beruhend, kombiniert. Somit konnten zum ersten Mal Konzentrationen von künstlich hergestellten Nanomaterialien in Schweizer Flüssen mit hoher räumlicher Auflösung berechnet werden. PECs wurden für nano-TiO<sub>2</sub>, nano-ZnO und nano-Ag für 742 Flussabschnitte unterhalb von 742 Kläranlagen auf der Basis von Strömungsverhältnissen (Q<sub>95%</sub>), welche in 95 % der Zeit überschritten werden, berechnet. Darüber hinaus wurden auch Durchflussmessungen zu 20 ausgewählten Standorten über einen Zeitraum von 20 Jahren (1988–2007) verwendet, um die zeitliche Variation der Abflussmenge zu berücksichtigen. Basierend auf Q<sub>95%</sub>-Flussstände wurden die höchsten Belastungen (Modal-Werte) für die nano-TiO<sub>2</sub> mit PEC-Werten zwischen 0,1 ng L<sup>-1</sup> und 7,8 µg L<sup>-1</sup> beobachtet, gefolgt von nano-ZnO (0,004 ng L<sup>-1</sup> und 0,5 µg L<sup>-1</sup>) und nano-Ag (0,3 pg L<sup>-1</sup> und 0,03 µg L<sup>-1</sup>). Der Vergleich von PECs mit PNECs ergab, dass basierend auf die verwendeten hydrologischen Daten und im Durchschnitt für alle Perioden und 20 Stationen und Szenarien (Szenario mit und Szenario ohne Sedimentation) der PNEC für nano-Ag bei Modal-Konzentrationen an 234 Tagen pro Jahr überschritten wurde. Die entsprechenden Ergebnisse für

nano-ZnO und nano-TiO<sub>2</sub> betragen 150 und 109. Diese Studie zeigt, dass eine Verknüpfung der probabilistischen Materialflussanalyse mit einem georeferenzierten Modell zwei Lücken füllt: Die PEC-Berechnungen für Flüsse wurden gegenüber Berechnungen auf regionaler Ebene unter Berücksichtigung der geografischen Verteilung der ENM-Emissionen verbessert und eine klare Unterscheidung zwischen Unsicherheit im ENM-Eintrag und Unsicherheit im natürlichen Wasserfluss erreicht. Variabilität im Abfluss beeinflusst die ENM-Konzentrationen bis zu einem Faktor von 5, die Unsicherheit in der ENM-Belastung verursacht einen Unterschied in der PEC-Berechnung bis zu einem Faktor von 10.

Zusammenfassend lässt sich sagen, dass derzeit potenzielle Umweltauswirkungen und Toxizität von synthetisierten Nanomaterialien diskutiert werden. Allerdings sind noch immer nur sehr begrenzt Daten zu Umweltverhalten und möglichen negativen Auswirkungen von synthetisiertem Nanomaterial auf die Umwelt verfügbar. Auch stehen im Fall von ENM nahezu keine analytischen Methoden zur Verfügung. Daher muss die Diskussion rund um ENM in der Umwelt völlig anders geführt werden als z. B. diejenige über organische Mikroverunreinigungen, bei denen Methoden der Identifizierung und der Mengenbestimmung in der Umwelt zur Verfügung stehen und die somit Ausgangspunkt der wissenschaftlichen und öffentlichen Diskussion sein können. Infolgedessen sind im Fall von ENM Vorhersagen zu Konzentrationen in der Umwelt und Studien zu potenziellen Expositionspfaden basierend auf mathematischer Modellierung nötig, und, wie in dieser Arbeit gezeigt, ein wertvolles erstes Instrument zur Bewertung und Vorhersage von möglichen Risiken für die Umwelt.



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## Acronyms

<b>Acronym</b>	<b>Description</b>
AFM	Atomic force microscope
CNT	Carbon nanotubes
ECB	European Chemicals Bureau
EC50	Median effect concentration
ENM	Engineered Nanomaterial
LCA	Life Cycle Assessment
LC50	Median lethal effect concentration
MC	Monte Carlo
MCMC	Markov Chain Monte Carlo
MFA	Material flow analysis
NOEC	No observed effect level or concentration
PEC	Predicted environmental concentrations
PMC	Production, manufacturing and consumption process
PMFA	Probabilistic material flow analysis
PNEC	Predicted no effect concentrations
STM	Scanning tunneling microscope
STP	Sewage treatment plant
TC	Transfer coefficient
R	Recycling process
RQ	Risk quotient
Q <sub>95%</sub>	Stream flow reached or exceeded annually in 95% of the time
WIP	Waste incineration plant



# 1. Introduction

## 1.1 Background of the thesis

### 1.1.1 Invention

December 29, 1959, annual meeting of the American Physical Society at the California Institute of Technology, Richard Feynman gives a talk: “There’s Plenty of Room at the Bottom: An invitation to enter a new field of physics” (Feynman 1960). This sufficed for Feynman (Nobel Prize laureate in physics, 1965) to be credited by a lot of people and scientists as being the first person to see the enormous potential of manipulating matter at the nanoscale (e.g. Drexler 1986 and over 1200 Feynman speech citations in Google as of February 2010). However, this is a fairy tale! Feynman’s speech was only cited seven times (Toumey 2005) in the first two decades after it was first published in the Caltech magazine “Engineering and Science” in 1960. The truth is that when nanotechnology finally became a major area of research following the invention of the scanning tunneling microscope (STM) in 1981 (Binnig et al. 1982), some authoritative account of its origin was needed in idealized form (Nature Nanotechnology (Editorial) 2009; Toumey 2005).

In contrast to the modern achievements, the historical beginnings of nanotechnology and the application of nanoscience are almost unknown. There are only a few scientific/technical advances that may be listed (Table 1), most of them relating to insights of the 20th century to atomic and molecular structures. Nevertheless, what we may state is that rather than chemists and physicists of the 20th century or workers in a modern semiconductor plant, the first “noteworthy” nanotechnologists were probably medieval glass workers that produced gold nanodots for Victorian and medieval churches (famous for marvelous stained glass windows) (Ratner and Ratner 2003; Shong et al. 2010). However, as stated above the “real” nanotechnology and nanoscience started in the early 1980s with the invention of the STM, followed by the discovery of fullerenes and carbon nanotubes (CNT) and the commercial use of metal oxide particles (e.g.  $\text{TiO}_2$ ,  $\text{ZnO}$ , Ag, Fe), e.g. for cosmetics, exterior coatings, plastics, textiles, or electronics (Hornyak et al. 2008).

### 1.1.2 Promised chances and unknown risks

There is some consensus that manipulation of matter at such small scales could lead e.g. to the development of unimaginably lightweight and strong materials, electrical devices that utilize spin properties of electrons in addition to their electrical charge, or e.g. to novel biomedical healthcare and disease treatment, for instance, significant improvements in finding a cure for cancer (Morose 2010; Shong et al. 2010). Nanodevices promise a future in which less material would be required during production and as a by-product of manufacturing processes also a reduction in the need for raw and manufactured material, a minimization of wastes and effluents and e.g. a reduction in the amount of toxins entering the environment. In addition, significant benefits for the environment are also expected from green manufacturing, pollution prevention, treatment, mitigation and remediation (e.g. Hornyak et al. 2008; Nowack 2008).

Table 1. Some historical events in the development of nanoscience and nanotechnology (Shong et al. 2010, Institute 2010, Ratner & Ratner 2003).

5th Century B.C.	Democritus and Leucippus stated that matter was made up of tiny, indivisible particles in constant motion.
1803	John Dalton, English chemist and physicist, developed the first relevant atomic theory of matter.
19th Century	Application of gold nanodots for Victorian churches.
1914	Niels Bohr, Swedish physicist, advanced atomic theory further in discovering that electrons traveled around the nucleus in fixed energy levels.
1959	Feynman gives after-dinner talk describing molecular machines building with atomic precision.
1974	Taniguchi uses term “nano-technology” in paper on ion-sputter machining.
1977	Drexler originates molecular nanotechnology concepts at MIT.
1981	Scanning Tunneling Microscopy (STM) invented by Gerd Binnig and Heinrich Rohrer at IBM Zurich.
1985	Buckyball discovered by Robert Curl, Harold Kroto and Richard Smalley.
1986	Atomic Force Microscopy (AFM) invented by Gerd Binnig, Calvin Quate and Christoph Gerber.
1988	First university course, Nanotechnology and Exploratory Engineering (Stanford).
1989	IBM logo spelled in individual atoms by Don Eigler at IBM Almaden.
1990	Nanotechnology: first nanotechnology journal founded by Institute of Physics UK.
1991	Carbon nanotubes discovered by Sumio Iijima at NEC, Japan.
1997	First nanotechnology company founded: Zyvex.
2000	President Bill Clinton announces US National Nanotechnology Initiative.

However, the development of such technologies and materials also raises concerns regarding environmental and human health hazards. Let us illustrate two realistic examples by way of introduction: i) CNTs are e.g. of great interest to researchers and industry because of their remarkable structural, mechanical and electronic properties (Gottschalk 2008). Since these tubes have tunable electronic properties, they are being investigated as possible new material for coming generations of microelectronics (Shong et al. 2010). Used as an intercalation medium to increase the electrical storage capacity of lithium ion batteries, CNTs could be released into the environment (Koehler et al. 2008). During battery manufacturing, for instance, nanotubes could be emitted before battery cells are sealed. In this case emissions during product use e.g. in the case of irregular recharge attempts or from recycling or disposal activities are imaginable. Recycling processes may break down the structure or matrix in which the CNTs are fixed within a battery. Sophisticated technologies that involve shredding, milling, mechanical sorting or thermal

processing such as pyrolysis or smelting could generate dust and emissions to the air. ii) There are also examples to illustrate direct unintended and intended releases of nanomaterial to the environment. The US Environmental Protection Agency (2009) emphasizes e.g. two different applications of nanoscale titanium dioxide (nano-TiO<sub>2</sub>). Cosmetic industry uses undoubtedly significant amounts of nanoscale titanium dioxide as an active ingredient e.g. in tropical sunscreen. Direct release is also caused by the use of such TiO<sub>2</sub> to remove e.g. arsenic from drinking water.

Based on such technical and scientific achievements made in recent decades on the one hand, positive impacts of nanotechnology are expected to be enormous and numerous for society (e.g. Drexler 1992; Hornyak et al. 2008; Shong et al. 2010); on the other hand, the same applies to negative effects as well (e.g. Oberdorster et al. 2007; Roco 2005). Hence, there is currently a lot of excitement and controversy concerning the potential and the risks of nanotechnologies (Hewitt and Goldstein 2008): advocates emphasize the enormous potential of applications and advantages of nanoparticulate material, while at the other end of the spectrum, others see unrealistic prognoses and a simple rush into hazardous technologies without ways to assess potential risks to humans and the environment.

Roughly speaking, we may state that from an environmental perspective it will not be essential to predict to what degree nanotechnology will become a mature and well-accepted technology, or in what way there may be disappointment due to unrealized promises (Shong et al. 2010) and negative impacts. Scientific engagement in assessing risks does not depend on cycles of public hype that are eventually followed by disappointment or simply loss of interest (Arie 2006).

## **1.2 The case of nanotechnology**

### **1.2.1 Engineered nanomaterial**

Nanotechnologies involve, roughly speaking, the study and the control of matter in dimensions of approximately 1–100 nm, where unique physico-chemical material properties enable novel applications in industry and academia (Hornyak et al. 2008; Nikulainen and Palmberg 2010). For reference, often the diameter of a human hair (about 80,000 nm) is mentioned (Morose 2010).

Human and environmental exposure to nanoparticles is not new; nanostructured materials have been present on earth for millions of years and have been used by humankind for millennia (Buzea et al. 2007; Nowack and Bucheli 2007): volcanic ash, dust storms, soot as part of the carbon black continuum (product of the incomplete combustion of fossil fuels and vegetation with a particle size partially in the nanometer range) or e.g. virus and bacteria (nanosized and around since prehistoric times). Another example is nanoparticulate indoor pollution as a result of badly ventilated stoves combined with the use of biomass fuels (wood, crop residue, coal etc.) that causes annually e.g. estimated 1.6 million deaths worldwide (Buzea et al. 2007).

However, as mentioned in the introduction, it is a fact that manufactured nanosized matter/material did not attract scientific (and public) attention until recent decades when our ability to produce and manipulate matter on such a scale increased (Moriarty 2001). Noteworthy research in nanotechnology began in the 1980s with inventions in the field of microscopy (STM and the atomic force microscope (AFM) (Heinze 2004; Nikulainen and Palmberg 2010; Palmberg and Nikulainen 2006)). Since then great efforts in industry and academia have been observed for

developing novel products and applications in a wide range of industrial and consumer sectors (Helland et al. 2006; Som et al. 2010). Such “explosive” (Moriarty 2001) growth in interest arises mainly from new variations in fundamental electrical, optical and magnetic properties and large surface areas per unit volume that occur when particles of a particular material consist only of a countable number of atoms (Boverhof and David 2010; Moriarty 2001). Such properties can in the case of nanosized material be associated with a particular type of agglomeration behavior, dissolution rate, surface chemistry or reactivity, altered optical or magnetism properties, increased flexibility, strength or e.g. improved electrical conductivity or absorption – all factors which, however, have thus far not been studied much (Boverhof and David 2010). In addition to such promised “new” functionalities/material characteristics for products and substances, a reduction in the use of hazardous chemicals, of energy consumption, material and waste generation is also expected (Gottschalk 2008; Nowack 2007; Som et al. 2010). Furthermore, such engineered nanomaterials (ENM) are often coated e.g. with a surfactant, polymer or polyelectrolyte that can affect e.g. the above-mentioned ENM aggregation behavior in order to make them, for instance, water soluble or biocompatible (Lowry and Casman 2009; Nowack and Bucheli 2007). As the inner material is not allowed to be either water soluble or biocompatible, such new compounds are not very likely to have any analogues in nature, e.g. quantum dots containing heavy metals (Lowry and Casman 2009).

ENM are already applied in a wide range of areas such as e.g. pharmaceutical, biomedical, cosmetic, electronic, energy, environmental, catalytic and material applications (Nowack and Bucheli 2007). As a consequence, impressive application prospects of nanosized materials could lead to a significant increase in the ENM production, manufacture and use of them in products, and consequently to a relevant ENM human and environmental exposure to them (Andreev et al. 2009).

The same physico-chemical characteristics that make ENM desirable for a lot of applications could pose a risk for organisms exposed to such material and its properties (Boverhof and David 2010). No doubt, there is currently a distinctive data gap concerning such potential health and environmental effects (Alvarez et al. 2009; Andreev et al. 2009; Borm et al. 2006; Chaudhry et al. 2008; Handy et al. 2008; Helland et al. 2006; Hund-Rinke and Simon 2006; Klaine et al. 2008; Nowack 2009; Nowack and Bucheli 2007; Oberdorster et al. 2007; Scheringer 2008; Wiesner et al. 2006). As a result potential negative effects of ENM are worldwide under discussion in governments, the public or the private sector (Helland et al. 2006; Hudson and Orviska 2009; Roco 2005; Siegrist et al. 2007a; Siegrist et al. 2007b). Hence, as seen e.g. in the cases of asbestos, CFCs, DDT, PCBs, mercury, and other former “wonder” substances and technologies (Kimbrell 2009), it does not take a prophet to predict that manufactured nanoparticulate material could also have significant unintended negative consequences on human and environmental health and that thus public reaction might have a strong influence on the development, funding and acceptance of these technologies and materials (Scholz and Siegrist 2010). However, in contrast to these negative past examples and e.g. to the fields of nuclear power and gene technology, in the case of nanotechnology researchers are trying to anticipate – probably for the first time (Donaldson 2009) – potential risks and public reaction/perception in advance (Scholz and Siegrist 2010; Siegrist et al. 2007a; Siegrist et al. 2007b).

## 1.2.2 Environmental risk assessment

### 1.2.2.1 Concepts and estimation procedures

Since the early days of industrial chemistry (toward the end of the 18th century) the control of the potential risks and hazards of chemical processes and products for human health – and later also for the natural environment – was discussed in research and development (Hungerbuehler et al. 1998; Leeuwen and Vermeire 2007). However, an equivalent importance of the process and products health and environmental security – comparable to process and products efficiency and quality – was not observed until the 70s and 80s of the last century (Hungerbuehler et al. 1998). As a consequence today, in fact for long-term success, products also have to ensure the non-existence of unacceptable health and environmental risks in addition to offering high quality and economic efficiency.

Environmental and/or ecological risk assessment addresses anthropogenic adverse effects on the environment (SETAC 1997; Suter 2007) such as e.g. chemical pollution, habitat destruction, invasion of exotic species, infection with disease organisms etc. (Sergeant 2002). Risk is a basic concept of environmental literacy used to study uncertainty and negative impacts that derive from human action (Hungerbuehler et al. 1998; Scholz 2010; Scholz and Siegrist 2010; Scholz and Tietje 2002). Scholz (2010) refers to Kant as seeing in risk an elementary or primitive concept (Scholz and Tietje 2002; Sokolowska 2006). Based on this conceptualization, risk is denoted as a function  $(r(P,E))$  of the probability  $P = (p_1, \dots, p_n)$  and the valuation of the outcomes  $E = (E_1, \dots, E_i, \dots, E_n)$  and related to a decision, where at least one of the outcomes may have a negative value (Scholz and Tietje 2002). Adapted from such a conceptualization, risk is often analyzed based on a technical view focused on a cause-effect framework. Thus, risk characterization is seen as the process of selecting and quantifying possible negative consequences (frequency and magnitude) that result from some action (or inaction) (McKone 1999; Scholz and Tietje 2002).

As shown in Scholz and Siegrist (2010) until the 1970s such technological risks were almost exclusively characterized by definitions of risk in which only losses were considered (pure risk). However, the environmental and health risk assessment methodologies developed since the 1970s differ from such simple approaches (Paustenbach 2002b) providing risk estimations that relate a valuation of unwanted, negative effects to their likelihood of occurrence (Scholz 2010; Scholz and Tietje 2002). In addition, risk assessors also broadened their framework from pure risks to speculative risks (Brachinger and Weber 1997; Scholz and Tietje 2002) to avoid focusing solely on negative effects and their likelihood and neglecting potential benefits that may result from development and application of a particular technology. Scholz and Siegrist (2010) illustrate also how vital risk assessment, risk perception, and risk management are today, and how risk is dealt with in a wide breadth of disciplines (“risk sciences” (Bernard et al. 1995)) ranging from natural to technical, medical, social sciences and humanities. The authors emphasize in particular that environmental risk assessment gained a new dimension with the mastery of nuclear fission (Krohn and Weingart 1987) that provided our human species with the ability to damage not only microcosmic systems but also global ones (Beck and Sznaider 2006). Understanding this, we have to emphasize that no one can keep new technologies – genetic manipulations in a plant or animal, new organic compounds, or e.g. manufactured nanomaterial

(Scholz and Siegrist 2010) – from posing also intolerable risks for society and for the environment.

Hungerbuehler et al. (1998) encapsulate a generic risk assessment procedure into three main steps: i) define a system whose potential damage should be considered (protective regulations); ii) design possible damage scenarios that should in principle be assessable quantitatively; iii) estimate the probabilities for such scenarios by means of relative frequencies of events in the past as well as using forward-looking probabilistic considerations. Such an assessment framework covers uncertainties of the choice of appropriate model structure/geometry and uncertainty and variability of the risk model input parameters. Whereas variability arises from true diversity across temporal, spatial or inter-individual differences in the model parameters, uncertainty is a measure of knowledge incompleteness about unknown input values whose true magnitude could be measured if measuring methods were available (Cullen and Frey 1999; Paustenbach 2002a). As a consequence, analyzing risks requires sufficient empirical data and may become cloudy if designing the assessment framework e.g. for nanomaterial is associated with several distinctive parametric and structural uncertainties.

#### 1.2.2.2 Dealing with uncertainties

Scholz (2010) illustrates comprehensively the scientific inter-relationships among uncertainty, probability/stochasticity and risk assessment. Uncertainty derives from incomplete knowledge or data regarding the state of a particular object (model input parameters such as e.g. in this thesis nanomaterial emission and transmission characteristics) or of the system (e.g. framework and geometry (structure) of the nanomaterial exposure modeling). Probability is seen as a concept of the language of such uncertainty (Scholz 1987), whereas stochastic processes are denoted as sequences of events (e.g. nanomaterial concentrations in the environment) where there is indeterminacy about future states. Therefore, risk links the behavioral dimension of human systems' actions (e.g. commercial use of engineered nanomaterial) with uncertain (however mostly negatively) evaluated environmental impacts resulting from such actions.

One possible approach to risk estimation that one can use when faced with such uncertainties is *inductive-stochastic risk assessment* (Scholz et al. 1992), where the impacts from the source of risk (e.g. nanomaterial release into rivers from commercially used nanoproducts) to safeguard objects in a critical compartment (e.g. aquatic organisms) have to be considered. Thus, for exposure assessment one must model parameters such as nanomaterial production and integration into products, the amount of products consumed or nanomaterial released from such products. One critical issue is now that for each of those input parameters a probability distribution (Hoffmann et al. 2004; Scholz 2010) must be defined which covers the uncertainty in each specific parameter. Doing this means that the insecurity in such a modeling has been considered conceptually (Scholz and Schnabel 2006) and not corrected subsequently by the use of safety factors. At every stage of the path of the nanomaterial flows insecurities are considered. Input and output flows, transfer coefficients and environmental concentrations are modeled as probability distributions.

One of the most critical points of such probabilistic/stochastic modeling is then the use of adequate input distributions (McKone and Bogen 1991; Nothbaum 1997; Scholz 2010; Scholz et al. 1991). The construction of such distributions depends on different types of knowledge (Scholz et al. 1992). If we have data, e.g. on the quantity of a compound produced daily, we can take a



statistical, frequentist approach, best when smoothing or adapting a given frequentistic distribution. If this is not the case, we can construct a subjectivist probability distribution, based on our own, or on experts' best knowledge. There is, in principle, also the possibility of constructing distributions based on logical probability concepts, e.g. if frequentist distributions from other cases are available and transferable by weighted arguments (Carnap 1950; Scholz et al. 1992).

In general, one should follow a two-step procedure when determining such probability distributions. The first step consists of defining the shape of the variable (e.g. normal, log-normal, trapezoid, triangular, uniform). The choice of the form of the distribution depends on the knowledge about the process. Then in a second step the parameters (e.g. mean/median/mode, standard deviation, range, kurtosis) are modeled. Form and mathematical parameters of the input distributions may be determined considering available empirical data or based on unstructured expert questioning without formal procedures. However, methodical (group) processes are also conceivable. The Delphi method e.g. (Brown 1968) is a forecasting method using independent experts. Other structured expert panel methods using a facilitator to elicit assessments concerning input distributions from the experts in attendance are e.g. Consensus Development Conferences (Murphy et al. 1998), or procedures for defining parameters by group decision making (Scholz and Hansmann 2007).

#### 1.2.2.3 Treating nanomaterials as particular chemicals?

An established approach of dealing with uncertainties in conventional chemical risk assessment is the use of hazard indicators, in particular for properties such as persistence, bioaccumulation, and toxicity (Scheringer et al. 2006). However, often such hazard indicators are not available for most of new chemicals, although in the chemical industry it has become common to identify possible environmental impacts in an early stage in the chemical design process to avoid costly process changes later (Hoffmann et al. 2004; Hungerbuehler et al. 1998). However, early risk assessments are frequently faced also in the case of new chemicals with high uncertainty around possible economic, ecological, and technical parameters that have to be estimated. There are different approaches for assessing chemical process hazards at early design stages. Hoffmann et al. (2004) developed e.g. a method based on approximating flowsheets (as modeled e.g. in commercial flowsheet simulators) by using response surfaces to select promising process alternatives while taking explicit account of uncertainties. Shah et al. (2005) have also provided a systematic tool to support decision makers in evaluating chemical processes in early process phases. This approach covers the characteristics of the single chemical substances, possible interactions between substances (reactivity assessment), possible hazard scenarios resulting from the combination of substances and operating conditions in the different equipment and necessary safety technologies required to run a particular process safely and according to legal regulations.

Such approaches have been developed for conventional chemicals and do not address the question if nanomaterials should be treated as particular chemicals due to their particular size and structural properties. Nanomaterials are covered by the definition of a "substance" in REACH<sup>1</sup>, although there is currently no explicit reference to nanomaterials. The first registration deadline under REACH (November 30, 2010) applies to substances manufactured or imported at

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<sup>1</sup> REACH is the Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals of the European Union (EU).

1000 tons or more per year (REACH 2010). The registration of nanomaterials in this tonnage band will then undoubtedly create more information that may be used for the risk assessment.

Nevertheless, expeditious evolution in the area of nanotechnologies has raised questions as to the applicability and adequacy of the established risk assessment paradigm and regulatory framework for chemicals (Gottschalk 2008; McKone 2010; Som et al. 2010). A critical point is that available experience with inorganic and organic chemicals may not be relevant to nanoparticulated materials (Linkov et al. 2007) due to unique physical and chemical properties that do not primarily depend on the chemical composition but on the material size, structure, surface modification and functionalization. ENM may, for instance, have large surface areas per volume unit and novel electronic properties relative to conventional chemicals. Their surface may be coated to improve material properties for specific applications (EPA 2007). Incorporating also potential environmental relevancies of such physical and chemical properties within a risk assessment framework for nanoparticulate material is difficult. Thus, conventional risk assessment tools for chemicals that are based mainly on chemical composition of the materials may not be applied directly to ENM.

As a consequence, established risk assessment procedures for chemicals must be analyzed concerning the applicability also for ENM in order to propose a risk assessment framework for studying environmental risks to ENM and ENM containing products. ENM containing products are usually defined as commercially available products that either contain ENM, or that derive specific functions from nanostructured material with or without ENM (Som et al. 2010). Examples are textiles containing nano-silver, batteries with carbon nanotubes (CNTs), cosmetics or sunscreen with nano-TiO<sub>2</sub> or nano-ZnO etc. However, also ENM-free emitters that contain nanostructures such as nm-thin coatings and that could thus lead to nanoscaled pollution are considered as well.

As discussed in Som et al. (2010) currently there is a total absence of nano-specific regulations in the EU (Fuehr et al. 2007) or elsewhere in the world (Hodge et al. 2007) in addition to a distinct scarcity of available risk reports to ENM. Existing policies are focused on conventional chemicals and do not consider the particular physico-chemical properties of ENM (e.g. small size, reactivity, special surface chemistry and structure) (Chatterjee 2008; Franco et al. 2007). In addition, there is almost no reliable data on ENM application volumes in industry and households (Schmid and Riediker 2006; Schmid and Riediker 2008). However, some first studies to potential human and environmental health implications of ENM are available. Nowack and Bucheli (2007) reviewed recent works and found that attention is devoted more to toxicological studies (Helland et al. 2007; Iavicoli et al. 2009; Kreyling et al. 2006; Lam et al. 2006; Norppa and Greim 2009; Xia et al. 2009) than to environmental behavior and ecotoxicological aspects (Biswas and Wu 2005; Helland et al. 2007; Klaine et al. 2008; Moore 2006; Wiesner et al. 2006). However, to conduct exposure (and risk) assessment apart from toxicological and ecotoxicological effects also the concentrations organisms are exposed to in environmental media and technical compartments have to be considered.

### **1.2.3 Exposure assessment**

Generally speaking, exposure assessment denotes the description/quantification of a contamination source, the pollutant's transport and transformation within natural or technical environments, and the organism's contact with pollutants (McKone and Daniels 1991). Exposure

assessment within its total framework includes at least for human populations time and activity patterns and microenvironmental (e.g. indoor concentrations) data providing a comprehensive view of exposure pathways and identifying main sources of uncertainty in addition to the estimation of potential pollutants' environmental concentration in air, water etc. (McKone 1999).

McKone and Small (2007) provide an overview of the state of the art in exposure assessment that is seen as a key element in estimating the environmental and public health impacts from chemical release in the life cycle of industrial products (McKone et al. 2006). The authors distinguish four main approaches: regulatory assessments for health protection, chemical-transfer and individual activity based models and models integrating environmental concentrations and human exposure. *Regulatory assessments* are intended for modeling human behavior in the environment and are focused on the variability of the time spent of individuals e.g. at maximal concentrations (exposure). Several methods for the United States are listed, e.g. the Total Exposure Assessment Methodology (TEAM) studies and the National Human Exposure Assessment Survey (NHEXAS).

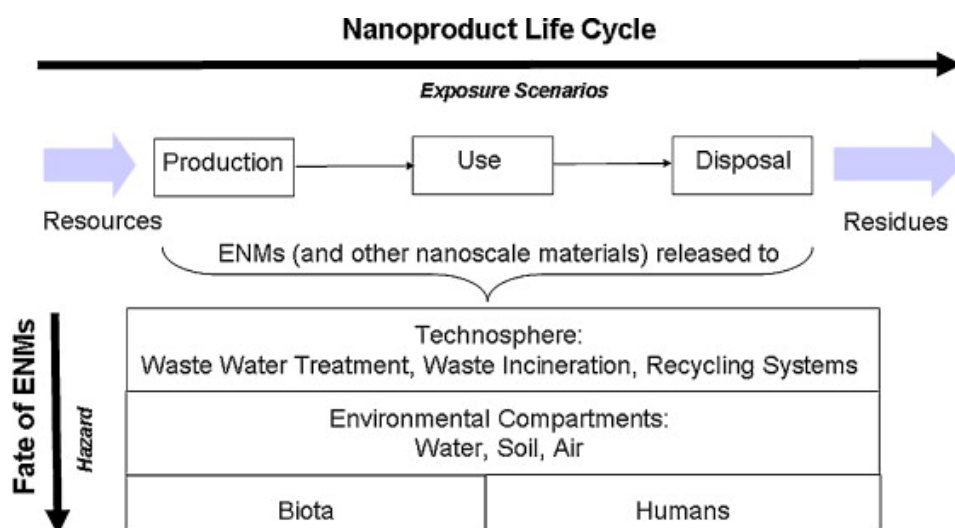


Figure 1. Simplified stages of the nanoproduct life cycle and the fate of ENMs (Som et al. 2010).

These methodologies were created to study the relationship between environmental and indoor air concentrations and had been applied for different pollutants such as e.g. nitrogen oxides, volatile organic compounds (VOCs), fine particulate matter. *Chemical transfer-based models* focus on partitioning and mass transfer (McKone and MacLeod 2003) and may include also intake or uptake of pollutants. *Individual activity* models cover time allocation to individuals' exposure in microenvironments (e.g. home workroom; office or factory). An example of models integrating estimations of environmental concentrations and human exposure is the CalTOX model (McKone 1993a; McKone 1993b; McKone 1993c) that estimates human exposure through 23 potential exposure pathway scenarios for pollutants in the air, soil, or water.

Since we know that several negative effects caused by exposure to some chemical substances and technologies did not come to light until years after the initial use and introduction of chemicals and technologies (Gottschalk 2008; Koehler et al. 2008; Renn 2002), it is imperative to address issues arising from nanotechnologies holistically and as early as possible (Som et al.

2010; Som et al. 2009). Hence, the exposure assessment for ENM has to include currently a wide range of ENM applications that are poorly researched and that may lead to diffuse release of such material into the environment. Thus such an assessment has to be done including all life stages (Fig. 1) of ENM and ENM containing products (von Gleich et al. 2008). In order to do this, Davis and Thomas (2006) propose a basic structure for a comprehensive environmental assessment (CEA) approach that allows one to identify and prioritize research efforts for ENM and ENM containing products (Fig. 2). The ambiguity between ENM<sup>2</sup> and ENM containing products is clarified by Som et al. (2010): ENM (e.g. TiO<sub>2</sub>) can form part of nanomaterials (such as polymer-ENM composites, e.g. polyamid-TiO<sub>2</sub> composite). However, such nanomaterials can in turn form part of products (e.g. a T-shirt, sun lotions, food packaging, etc.). Compared to the mentioned exposure assessment approaches listed above, the ENM exposure assessment planned in this work may be seen as a *Chemical transfer-based model* in terms of a material flow modeling that does, however, not include intake or uptake of ENM.

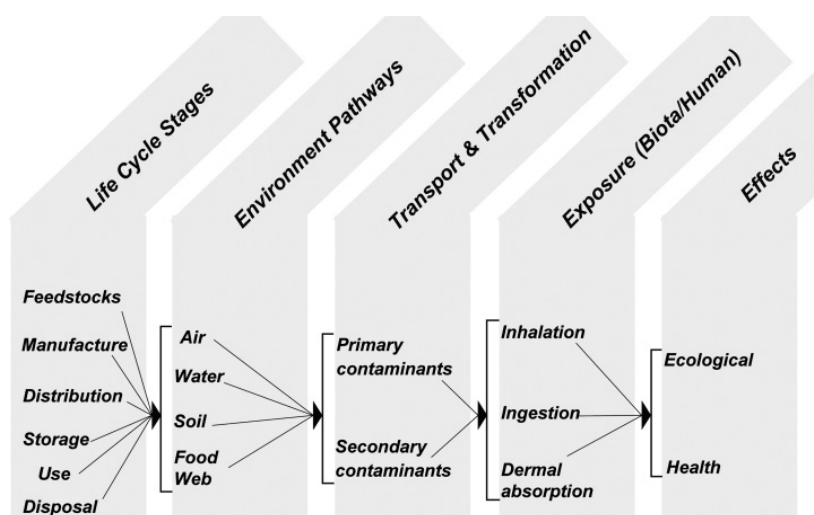


Figure 2. Basic structure of the Comprehensive Environmental Assessment (CEA) approach to identifying and prioritizing research efforts for a nanoscale product (Davis & Thomas 2006).

#### 1.2.4 (Nano-)Material flow analysis

Material Flow Analysis (MFA) is often described by means of the metaphor that material and energy illustrate the metabolism of a system (Scholz and Tietje 2002), e.g. as metabolism of the anthroposphere (Baccini and Brunner 1991) or as industrial metabolism (Tukker et al. 1997). Apart from initial input-output models with simple engineering or economic objectives, MFA was first applied to study the metabolism or physiology of cities (Wolman 1965), or in developed countries to reflect on systems such as densely populated regions (Brunner and Baccini 1992). However, MFA also became an approach to study flow dynamics of environmental pollutants. Binder (2007) mentions first studies on instance trace contaminants through watersheds or urban

<sup>2</sup> Due to the novelty and great interdisciplinarity of the field of nanotechnologies the terms “engineered nanomaterials (ENMs)”, “nanoparticles (NP)”, “engineered nanoparticles (ENPs)” and “nanoproducts” are not used in a uniform manner in the literature (Som, C., Berges, M., Chaudhry, Q., Dusinska, M., Fernandes, T. F., Olsen, S. I., and Nowack, B. (2010). “The importance of life cycle concepts for the development of safe nanoproducts.” *Toxicology*, In Press, Corrected Proof.).

regions (e.g. Bergback et al. 1994; Kleijn et al. 1994) and in developing countries (e.g. Binder et al. 1997). In recent years and stimulated e.g. by industrial ecology approaches (Allenby 2006) the study of material flows between production of raw materials, manufacture and use of products, and their fate and behavior at their end of life became very popular to illuminate (Harper et al. 2006) e.g. global and local material scarcity, energy and water consumption, waste management strategies, and the impacts of pollutants on human health and ecosystems (e.g. Chang et al. 2009; Jiang et al. 2001; Lu et al. 2007).

In the latter context MFA may form a subset of exposure assessment that can be used to model environmental concentrations of a particular pollutant. Standard MFA may e.g. be extended to a probabilistic/stochastic modeling to cope with model uncertainties. Such a mathematical approach might be a useful tool providing quantitative information to the flows of pollutants through and to economic and environmental compartments, in cases where only few empirical data on almost all model input parameters are available. A particular property of MFA is adequate to incorporate the spirit of Life Cycle Assessment (LCA) – and its uncertainty and variability (Geisler et al. 2005) – in the sense that the whole life cycle of a studied material (e.g. nanomaterial production, incorporation into products, products consumption, disposal and recycling phase etc.) may be considered.

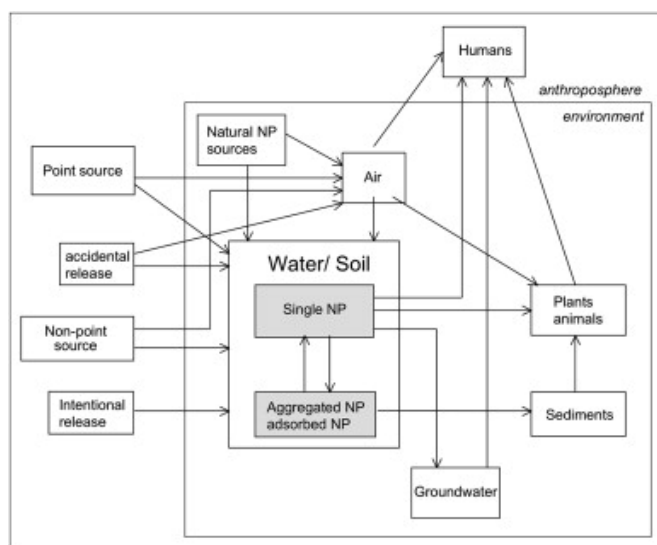


Figure 3. Nanoparticle pathways from the anthroposphere into the environment, reactions in the environment (Nowack & Bucheli 2007).

There are various multimedia models that cover the fate and transport of contaminants in the environment differing only in structural characteristics such as spatial and temporal resolution and the processes and compartments considered (von Waldow et al. 2008). However, such multimedia transport models (an overview is given in Fenner et al. 2005) address only persistent organic pollutants whose calculations are mainly based on molecular weight and octanol-water and air-water partitioning coefficients. However, the use of the listed partitioning coefficients is obviously not adequate for an inorganic material such as ENM. Material transport between the model media has to be modeled using other partitioning characteristics e.g. by means of standard mass balance transfer coefficients as used in typical MFA.

Nowack and Bucheli (2007) illustrate potential ENM transfers from the anthroposphere into the environment (Fig. 3) considering the two main forms of released nanomaterial as crucial for exposure modeling: ENM may enter the environment as individual particles or agglomerates, e.g. silica nanoparticles used as solid lubricants, or fullerenes added to cosmetics, or e.g. metal oxide particles injected for groundwater remediation; second ENM in composites or mixtures would probably be released to the environment in an encapsulated form (attrition from products containing ENM e.g., CNT composites used in tires, brake pads, tennis rackets etc. (Koehler et al. 2008)). Furthermore, accidental release may also come from point sources such as nanomaterial production and manufacturing facilities or transport processes, landfills wastewater treatment or waste incineration plants or e.g. storm-water runoff from manufacturing facilities or city roads and highways (Lowry and Casman 2009; Nowack and Bucheli 2007). Intentional release is possible as well, e.g. nZVI injected into groundwater contaminated with chlorinated solvents (Nowack and Bucheli 2007). However, as with many pollutants, non-point sources of ENM – such as wearing or washing clothes containing nanomaterial, or using nanomaterial containing cosmetics, sunscreen etc. – are probably more important and the most difficult to control (Nowack and Bucheli 2007).

Summing up, in the case of environmental risk assessment for ENM we have to cope with multiple emission sources, unknown ENM fate and behavior in nature and technical environments, complex exposure pathways that could vary significantly among organisms and individuals, and with high uncertainties (due to the lack of appropriate ecotoxicological information) regarding possible negative effects caused to organisms exposed to such material. Obviously it is a challenge for risk assessors to consider how such “events” can be captured best (McKone 2010), how addressing epistemic uncertainty (lack of knowledge in mechanisms and models) as well as parameter uncertainty and variability (lack of data) (McKone 2010; Scholz and Siegrist 2010). Epistemic uncertainties cannot be covered by standard quantitative uncertainty analyses only, but rather can only be addressed taking an interactive approach that enables one to incorporate timely detection, analysis, and correction of the model’s insufficiencies (McKone 2010). Consequently, the discussion of methodological limitations of the developed risk assessment framework is crucial and a necessity to make progress from an epistemological point of view.

## **1.3 Research design and methodology**

### **1.3.1 Frame of the PhD thesis**

This thesis is part of the EMPA project “Quantitative risk assessment of nanoparticles in the environment: Exposure modeling and ecotoxicological considerations”. The project aims to estimate quantitatively the risks that ENM may pose to the environment. PECs will be contrasted to PNECs. Such PECs will be derived from modeling realistic scenarios of ENM release to fate, transport and distribution in the environment, PNECs from analyzing results from ecotoxicological assays. In order to calculate and integrate the distinctive uncertainties concerning the estimation of the model input parameters (e.g. transfer and partitioning coefficients, emission factors) into the modeling, probabilistic/stochastic algorithms will be conceptualized and programmed.

### 1.3.2 Goals and methods

In order to conduct environmental risk assessment for ENMs and to gain more knowledge on the occurrence, fate and behavior of these materials in the environment, the following questions were asked:

- What are the relevant ENMs used in industry and household, and what are the ENM production and use amounts (worldwide, in Switzerland, Europe and the United States)?
- What are the ENM emission volumes to and concentrations in the environment (surface waters, soil, sediments, air etc.) we have at present and what to expect in the near future?
- What are the most crucial parameters that influence ENM concentrations in the environment?
- Does the modeled exposure to ENM cause negative effects for organisms in the environment?

Thus, the goals of this thesis are:

- 1) to evaluate available exposure models for chemicals regarding their potential to model also ENM release into and fate in the environment in order to develop a suitable modeling framework for coping with high ENM specific uncertainties of the model input parameters;
- 2) to conceptualize and program the developed model in an appropriate computational software;
- 3) to collect data on use, products, amounts of release, fate and behavior in natural and technical environments for relevant ENMs;
- 4) to use the model to calculate regional PEC values for Switzerland, Europe and the United States;
- 5) to calculate local PEC values for rivers in Switzerland based on a high geographical resolution incorporating spatial information and water flow level measurement data;
- 6) to evaluate PNECs;
- 7) to estimate environmental risks (on regional and local level);
- 8) to discuss potentials and limitations of the developed and implemented method.

Methods used:

- 1) System analysis: Based on literature, web review and personal communications (ENM producers, ENM containing product producers, operators of waste incineration and sewage treatment plants, operators of recycling facilities, scientists and governmental bodies), production volumes, ENM mass flows into the environment, environmental behavior and ecotoxicity of the selected ENM are identified.
- 2) Mathematical formalization and computational programming of an exposure assessment model to derive ENM flows to and expected concentrations in the environment.
- 3) Risk calculation according to the ratio PEC/PNEC.

## 1.4 Papers included in the thesis

### Paper I (Chapter 2)

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-TiO<sub>2</sub> particles. *Environmental Modelling & Software* 25(3), 320–332.

### Paper II (Chapter 3)

Gottschalk, F., Sonderer, T., Scholz, R. W., Nowack, B. (2009). Modeled environmental concentrations of engineered nanomaterials (TiO<sub>2</sub>, ZnO, Ag, CNT, fullerenes) for different regions. *Environmental Science & Technology* 43(24), 9216–9222.

### Paper III (Chapter 4)

Gottschalk, F.; Sonderer, T.; Scholz, R. W.; Nowack, B. (2010). Possibilities and Limitations of Modeling Environmental Exposure to Engineered Nanomaterials by Probabilistic Material Flow Analysis. *Environmental Toxicology & Chemistry* 29(5), 1036–1048.

### Paper IV (Chapter 5)

Gottschalk, F., Ort, Ch., Scholz, R. W., Nowack, B. (submitted). Engineered nanomaterials in rivers – an exposure assessment at high spatial and temporal resolution for nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag. *Environmental Science & Technology*.

## 1.5 Outline

In *Chapter 2* a model framework to derive predicted environmental concentrations (PEC) based on probabilistic/stochastic calculations that are combined with substance/material flow modeling is developed. The evolved model is basically applicable for any possibly environmentally hazardous substance with a distinct lack of data concerning environmental fate, exposure and emission characteristics. As case study the exposure in the Swiss environment to nano-TiO<sub>2</sub> is presented.

*Chapter 3* shows simulation results of predicted environmental concentrations (PEC) for soils, sludge treated soils, surface waters, sewage treatment plant effluents, sewage sludge, sediments, and air. These calculations were done for nano-TiO<sub>2</sub>, nano-ZnO, nano-Ag, carbon nanotubes (CNT), and fullerenes for the USA, Europe and Switzerland. The environmental concentrations are calculated as probabilistic density functions and are compared to data from ecotoxicological studies.

*Chapter 4* discusses based on a case study of nano-TiO<sub>2</sub>, CNTs and nano-Ag for Switzerland and based on a comparison with the scenario analysis presented in Mueller and Nowack (2008) the possibilities and limitations of modeling environmental exposure to engineered nanomaterials by means of probabilistic material flow analysis. This study extends the exposure modeling of Mueller and Nowack (2008) by using a probabilistic/stochastic approach and by considering the environmental compartments sediment and groundwater as well as production, manufacturing and recycling processes.



In *Chapter 5* two models, one based on probabilistic material flow analysis and the other based on graph theory are combined to calculate predicted environmental concentrations (PEC) of engineered nanomaterials in Swiss rivers at high spatial resolution. PECs for nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag were calculated for 742 river sections at base flow conditions Q<sub>95%</sub> (flow reached or exceeded annually in 95% of the time, averaged in Switzerland over a 10-year period) and using historical hydrological data (flow measurements for 20 selected locations over a 20-year period (1988–2007)). In addition, the river sections where PECs are expected to exceed PNECs at different water levels are identified.

In the *Appendix A* to Chapter 3 a description of the system compartments used for the case studies in Chapter 3 and 4 is given. Furthermore, information to the model input parameters (ENM production volumes, allocation of these volumes to product categories and release of ENM from products, production and manufacturing processes and to the considered ecotoxicological studies) is presented.

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## 2. Probabilistic material flow modeling for assessing the environmental exposure to compounds: Methodology and an application to engineered nano-TiO<sub>2</sub> particles

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### Abstract

An elementary step towards a quantitative assessment of the risks of new compounds or pollutants (chemicals, materials) to the environment is to estimate their environmental concentrations. Thus, the calculation of predicted environmental concentrations (PEC) builds the basis of a first exposure assessment. This paper presents a probabilistic method to compute distributions of PECs by means of a stochastic stationary substance/material flow modeling. The evolved model is basically applicable to any substance with a distinct lack of data concerning environmental fate, exposure, emission and transmission characteristics. The model input parameters and variables consider production, application quantities and fate of the compounds in natural and technical environments. To cope with uncertainties concerning the estimation of the model parameters (e.g. transfer and partitioning coefficients, emission factors) as well as uncertainties about the exposure causal mechanisms (e.g. level of compound production and application) themselves, we utilized and combined the following probabilistic methods, sensitivity and uncertainty analysis, Monte Carlo simulation, Bayesian and Markov Chain modeling. The combination of these methods is appropriate to calculate realistic PECs when facing a lack of data. The proposed model is programmed and carried out with the computational tool R and implemented and validated with data for an exemplary case study of flows of the engineered nanoparticle nano-TiO<sub>2</sub> in Switzerland.

Keywords: Probabilistic material flow analysis (PMFA); Monte Carlo (MC); Markov Chain Monte Carlo (MCMC); Uncertainty; Engineered nanomaterial (ENM); Exposure assessment; Predicted environmental concentrations (PEC).

### 2.1 Introduction

An elementary step towards a quantitative assessment of the risks of new compounds or pollutants (chemicals, materials) to the environment is to estimate their environmental

concentrations. Model input parameters describing production volumes, emissions, and fate in the environment have to be estimated to model environmental concentrations. An important example of a new class of environmental pollutants are engineered nanomaterials (ENM). The increase in the use and production of ENMs leads presumably to increased human and environmental ENM exposure. The discussion about potential risks of ENMs has a high priority in governments and the public (Roco, 2005; Helland et al., 2006; Siegrist et al., 2007). However, the adequacy of conventional tools for assessing health and environmental risks from the use and production of nanomaterials is unknown at the time (Kandlikar et al., 2006; Katao, 2006; Nowack and Bucheli, 2007; von der Kammer and Hofmann, 2007). Available experience with inorganic and organic chemicals may not be relevant to nanoparticulated materials (Linkov et al., 2007) because of the particular chemical and physical properties of ENMs. These physical and chemical properties depend on size, structure, surface modification and functionalization of the ENM. Furthermore, even rough estimations of production and application quantities of ENMs are difficult to obtain.

Material flow analysis (MFA) is an established method to study material and energy flows into, throughout, and out of a system (Baccini and Brunner, 1991; Baccini and Bader, 1996; Scholz and Tietje, 2002; Brunner and Rechberger, 2004). To model the fate of chemicals after discharge to the environment, mass balance multi-compartment models are the most commonly used approach (Cowan et al., 1995; Mackay et al., 1996; Mackay, 2001; McKone and MacLeod, 2003; Scheringer et al., 2004; Arnot, 2009). Examples of such models are the Berkeley-Trent (BETR) model (MacLeod et al., 2001) and the Climate Zone Model for Chemicals (CliMoChem) (Scheringer et al., 2000).

Normally for new compounds, there is a lack of data about the parameters needed for these material flow and fate models. For many environmental contaminants such data gaps are filled using assumptions, extrapolations or safety factors (Kandlikar et al., 2006; Mueller-Herold et al., 2006). Estimating risks of new compounds, e.g. of the currently intensely discussed nanomaterials (Alvarez et al., 2009), demands approaches to handling the inherent uncertainties and to simulate the compounds' environmental fate under various possible conditions. A particular challenge is that risk estimation of new compounds has to integrate the uncertainty about the accuracy of the calculated modeling parameters and the natural variability of these parameters. An extreme lack of empirical data cannot be treated only statistically, because we often need predictions about parameter values that have not yet been measured. As a result, some judgments, e.g. technically informed judgments or predictions in form of probability or frequency distributions, are required (Whitfield and Wallsten, 1989; Frey, 1992).

Whereas *variability* arises from true diversity across temporal, spatial or interindividual differences in the input values of a modeled system, *uncertainty* is associated with the knowledge of the data. Uncertainty about the knowledge is a measure of knowledge incompleteness about a quantity whose true value could be measured if perfect measuring methods were available (Cullen and Frey, 1999; Paustenbach, 2002). A detailed overview of the various sources of such epistemic uncertainties and variabilities in a modeling study is given in Refsgaard et al. (2007).

Probabilistic methods of risk and exposure assessment to cope with such uncertainty and variability have been broadly discussed (McKone and Bogen, 1991; Finley and Paustenbach, 1994; Cullen and Frey, 1999; Maddalena et al., 2004; Caldas et al., 2006; Fryer et al., 2006; van der Voet and Slob, 2007; Mutshinda et al., 2008). All these existing approaches can be roughly

characterized as human intake assessment models (Fryer et al., 2006), which simulate exposure as intake resulting e.g. from inhalation, ingestion or dermal absorption of pollutants. Such intake assessment models use as target variable the probability of adverse effects in response to environmental contamination (Mutshinda et al., 2008) and not the probability of environmental concentration of a pollutant as precondition for adverse effects. The main sources of uncertainty within such studies stem from quantifying human physical and behavioral characteristics, which have to be determined to model rates of intake e.g. of air or agricultural products.

In addition, methods for the probabilistic assessment of environmental levels within environmental fate models were developed as well. MacLeod et al. (2007) developed a multimedia model to assess diel variability of persistent semivolatile contaminants (SVOC) concentrations in the air. In this work a Monte Carlo (MC) analysis was applied to estimate uncertainty in the model output by means of confidence factors. Schenker et al. (2008) described the environmental fate of Perfluorooctanoate (PFO) using MC analysis to calculate the uncertainties in the model due to different pathways for Arctic contamination, and to estimate the relative importance of such pathways to the total contamination levels. MacLeod et al. (2002) provided an analytical approach to calculate the relationship between uncertainty in input parameters and uncertainty in output parameters. Applications to a regional contaminant fate and a food web bioaccumulation model showed that this approach may lead to results that are consistent with equivalent modeling outputs of a MC analysis.

The goal of our study was to develop a probabilistic material flow analysis (PMFA) framework to derive probability distributions of PEC values for any compound or material. The PMFA aims at calculating from a whole life cycle perspective concentrations of potential contaminants in complex systems, covering all environmental compartments and life stages of these contaminants. Our model goes further than simple probabilistic exposure assessments (Cullen and Frey, 1999), which cover the contaminants' concentration exclusively in produce or e.g. in indoor air to model intake (ingestion or inhalation) quantities of such materials. We simulate the emission of pollutants into the environment, which generates pollutant concentrations in natural compartments. However, compared to generic chemical fate models, the here presented material flow analysis includes besides the natural compartments also technical compartments (pollutant production; manufacturing of pollutant containing products; use, recycling and disposal of such products and pollutants fate in waste incineration and sewage treatment plants). Based on a material flow analysis, which covers the whole life cycle of a studied contaminant substance, the flows of the contaminant from the source to the natural compartments where organisms are exposed to are modeled. Thus, environmental concentrations of possibly environmentally hazardous substances are calculated considering uncertainty and variability within all input data by means of probability distributions. The results of the calculations are probability distributions representing the range and likelihood of possible concentrations. The uncertainty in this model is accounted for already conceptually (Scholz and Schnabel, 2006) and hence does not need to be corrected by the use of safety factors. At every point on the path of the compound flows uncertainties are considered. Input and output flows, transfer coefficients and environmental concentrations are modeled as probability distributions. As case study the simulation of PECs of engineered nano-TiO<sub>2</sub> particles in Switzerland has been chosen.

## 2.2 Methodology and modeling

First the modeling steps are defined. Based on this modeling procedure we then discuss how the model parameters are linked to input variables and outputs (modeled responses) and how such responses may be validated. Key aspects concerning model building, testing and verification have been presented e.g. in Jakeman et al. (2006).

### 2.2.1 Conceptualization

The proposed exposure assessment is based on a material flow modeling and involves: 1) characterization of sources and production volumes, 2) estimation of emissions to environmental compartments, 3) specification of the fate in the environment, and 4) derivation of distributions of PECs for the studied compounds.

*Table 2. Main steps of the developed modeling approach.*

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Step 1: Goal definition, including system boundaries constituted by the studied compounds, time and space
Step 2: System modeling, definition of goods, products, processes and functions/relations (transfer coefficients)
Step 3: Stochastic/probabilistic modeling of the input parameters using distributions
Step 4: Calculation/computation
<ul style="list-style-type: none"> <li>▪ Deterministically with point values (e.g. for model validation), (MFA standard)</li> <li>▪ Monte Carlo simulation with the modeled distributions                             <ul style="list-style-type: none"> <li>• Bayesian optimization</li> <li>• Monte Carlo Markov Chain modeling</li> </ul> </li> </ul>
Step 5: Sensitivity analysis
Step 6: Interpretation, assessment of pollution potential (PEC)

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The method of substance/material flow analysis (Baccini and Brunner, 1991; Baccini and Bader, 1996; Scholz and Tietje, 2002; Brunner and Rechberger, 2004) is used to determine flows to and amounts of compounds within the studied environmental compartments and is extended to a probabilistic material flow analysis (PMFA). We combine sensitivity and uncertainty analysis, MC simulation, Bayesian and Markov Chain modeling to propose a PEC modeling approach for cases characterized by a distinct lack of data (see Table 2). The simulated PECs for compounds in air, landfill, surface water, groundwater, soil, and sediment provide the basis for the quantitative exposure assessment and are derived from the results of the probabilistic material flow analysis.

### 2.2.2 System analysis

Compounds can be released from point sources such as production facilities, manufacturing plants, wastewater treatment or waste incineration plants, landfills or from line sources such as emissions during transportation or as components of personal care products or during aging of

materials. Accidental release during production and transport cannot be excluded, e.g. during product finishing. Compounds can also be released intentionally directly into the environment, e.g. from applications in agriculture. We structured the release to the environment as a three level emission. The quantity of compound synthesis is estimated in order to calculate direct emissions from production facilities to the environment. As second level, the emissions from the utilization phase of the compounds when manufacturing other products is modeled. Finally, calculations related to utilizing, wasting, and disposing available products are computed. Such emissions are estimated by grouping the products in product categories, which are supposed to have similar emission coefficients.

The system flow chart (Fig. 4) for a regional analysis of ENMs comprises 11 processes (volumes, boxes), the first one is subdivided in production, manufacturing of products and consumption of products, 27 internal flows, 1 input flow (generation flow within the first process), 3 elimination flows and 3 output flows. The system includes flows between and within production-manufacturing and consumption, wastewater treatment plant, waste incineration plant, lower atmosphere, landfill, soil, surface water, groundwater and sediments. Transfer coefficients imply the exchange of compounds between and within the compartments. As mentioned above this material exchange is triggered by a triple and simultaneous release of compounds (from the production, manufacturing and usage process) to the environmental and technical compartments.

The mathematical structure of the system consists for the stationary input-output model of a set of  $n$  linear equations containing  $n$  unknowns. Matrix algebra is applicable and solutions to the linear system are in principle and for the deterministic case findable straightforward building inverse matrices.

In case of a probabilistic approach, the construction of density functions representing the uncertainty introduces additional uncertainty and is part of the system analysis. The construction of such distributions depends on different types of knowledge (Scholz et al., 1992). If we have (some) data, e.g. about the daily quantity of production of a compound, we can take a *statistical, frequentist* approach, best when smoothing or adapting a given frequentistic distribution. If this is not the case, we can construct a *subjectivist probability distribution*, based on our or on experts' best knowledge. There is, in principle, also the possibility to construct distributions based on the logical probability concept, e.g. if frequentist distributions from other cases are available and transferable by weighted arguments (Carnap, 1950; Scholz et al., 1992).

For the case study presented, all probabilistic simulations including MC and MCMC simulations, uncertainty and sensitivity analysis have been implemented and programmed in R (R Development Core Team, 2008).

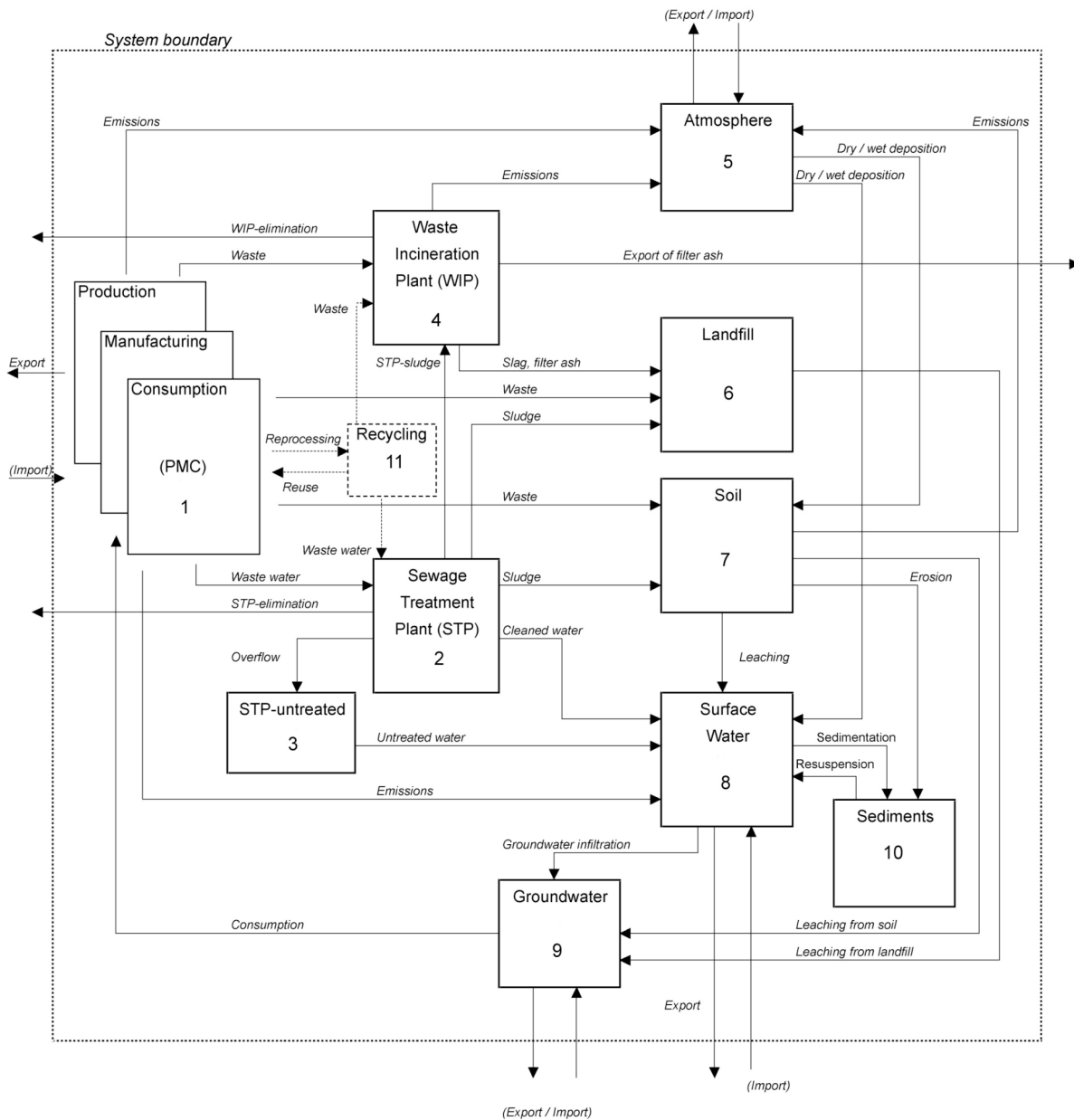


Figure 4. Basic structure of the model with the environmental compartments that are considered and the flows between them (the dotted flows concerning recycling processes were not relevant for the implementation case, import and export flows written in brackets were considered to be equal, small and/or not quantifiable).

### 2.2.3 Mathematical model

Our mathematical model describes the processes by rates of change of stocks and flows by transfer coefficients (e.g.  $TC_{rs}$ , the transfer coefficient concerning the flow from box  $r$  to  $s$ ). The transfer coefficients of output flows depend on the total input into the process. To avoid confusion we distinguish between variables and parameters. The term parameter refers to the constants e.g. transfer coefficients characterizing the probability density function of the random variables e.g. storage within the processes. The programmed probability density functions describe the probability that parameters and random variables fall within the estimated interval.

### 2.2.3.1 System of equations

The investigated linear system is mapped mathematically on a mass flow modeling, which combines the law of mass and energy conservation principle with phenomenological model approaches based on experimental data or assumptions. It links the source, the metabolism paths and the sinks of compounds and allows modeling the pathway of compounds in the environment. According to the balance principle the mass of all inputs into a process equals the mass of all outputs of the process included accumulation or depletion (transformation) of mass:

$$\frac{dM_i^{(j)}(t)}{dt} = \sum m_{rj}^{(i)}(t) - \sum m_{jr}^{(i)}(t) + G_i^{(j)} \quad (1)$$

$M_i^{(j)}$  is the mass amount of the compound  $i$  in  $V_j$ ,  $m_{rj}^{(i)}$  the mass/energy flow from  $V_r$  to  $V_j$  and  $G_i^{(j)}$  the mass production/transformation in  $V_j$ .

The compound flows are induced by the compound flows or by the flow of compounds containing goods, which are calculated from the compound concentrations  $c$  in these goods:

$$m = m_i = m^{product} \cdot c^{(i)} \quad (2)$$

The couple “goods/substances” (Brunner and Rechberger 2004) is decisive when developing an appropriate strategy for reduction or prevention of emissions from used goods. If potentially hazardous compound flows have to be reduced, we must know their concentration in the relevant goods. For constant stock change rates the studied system was mapped mathematically on a semi stationary model:

$$M_{(i)}^{(j)}(t) = M_{(i)}^{(j)} + \dot{M}_{(i)}^{(j)} \cdot t \quad (3)$$

Transfer coefficients (TC) describe the transfer of compounds from input flows into output flows:

$$TC_{rj} = \frac{m_{rj}}{\sum_s m_{sr}}, \quad (4)$$

where the transfer coefficient  $TC_{rj}$  describes the partitioning of the process  $V_r$  which is transferred to the process volume  $V_j$  by the flow  $m_{rj}$ .

The linear equation system to calculate flows to and deposition within the examined processes of the system was formalized mathematically with the matrices  $T$ ,  $A$  (see Fig. 5), and the vectors  $I$  and  $X$ . The  $n \times n$ -matrix  $T$  (left) involves the transfer coefficients and the  $n \times n$ -matrix  $A$  (right) determines the equality of the input- and output-amount of compounds in the volumes (processes).  $V_1$  to  $V_n$  represent production, manufacturing and environmental processes and  $V_{m+1}$  to  $V_n$  sinks, elimination and removal processes.

The column vector  $I$  determines the periodic input into the system, in this case study into the first process (left) and the column vector  $X$  (right) the unknown variables of amount of compounds in every process.

	$V_1$	...	$V_m$	$V_{m+1}$	...	$V_n$		$V_1$	...	$V_m$	$V_{m+1}$	...	$V_n$
$V_1$	$TC_{11}$	...	$TC_{m1}$	0	0	0	$V_1$	1	...	$-TC_{m1}$	0	0	0
$\vdots$	$\vdots$	$\ddots$	$\vdots$	0	0	0	$\vdots$	$\vdots$	1	$\vdots$	0	0	0
$V_m$	$TC_{1m}$	...	$TC_{mm}$	0	0	0	$V_m$	$-TC_{1m}$	...	1	0	0	0
$V_{m+1}$	$TC_{1m+1}$	...	$TC_{mm+1}$	0	0	0	$V_{m+1}$	$-TC_{1m+1}$	...	$-TC_{mm+1}$	1	0	0
...	...	...	...	0	0	0	...	...	...	...	0	1	0
$V_n$	$TC_{1n}$	...	$TC_{mn}$	0	0	0	$V_n$	$-TC_{1n}$	...	$-TC_{mn}$	0	0	1

Figure 5. Matrices of transfer coefficients (left) and compound quantities.

$$I = \begin{pmatrix} G \\ 0 \\ 0 \\ 0 \\ \vdots \\ n \end{pmatrix} \text{ and } X = \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ \vdots \\ x_m \\ x_{m+1} \\ \vdots \\ x_n \end{pmatrix}, (I, X \in \mathbb{R}^{n \times 1}) \quad (5)$$

Thus,  $A$  defines a linear map from  $\mathbb{R}^n$  to  $\mathbb{R}^n$  by sending the column vector  $X \in \mathbb{R}^{n \times 1}$  to the column vector  $AX \in \mathbb{R}^{n \times 1}$ . As a result

$$A \cdot X = I \quad (6)$$

leads to the steady state of the studied system.

## 2.2.4 Computing and model calibration

### 2.2.4.1 Modeled distributions

Table 3 presents the types of probability distributions used for modeling the nanomaterial case. They are restricted to uniform, triangular, and lognormal distributions. The uniform distribution is used for modeling most of the transfer coefficients. This is done as they are very poorly studied and there are no data for suggesting a specific distribution. The triangular distribution is used if the most probable outcome (mode or modal value) is vaguely known (guessed), it provides a less pronounced valuation of uncertainty and standard deviation as the uniform distribution. The triangular distribution may be applied when a lognormal distribution is not appropriate because of too little data and a uniform distribution not justified because of the “known” mode. Due to some available data lognormal distributions, which in principle may extend from zero to infinity, could be used to simulate the annual ENM production.



Table 3. Types of probability density functions of the model parameters programmed to run the MC and MCMC simulations.

	Lognormal distribution	Triangular distribution	Uniform distribution
Modeled parameters	Logarithmic mean (m), log. standard deviation (sd).	Mode, minimum and maximum value.	Minimum and maximum value.
Modeling characteristics	Exponential modeling of a normal distribution of random variables, multiplicative standard deviation.	Most likely outcome modeling, multiplicative standard deviation.	Intervals of the same range are equally likely, additive standard deviation.
Shape	Skewed	Skewed-symmetrical	Symmetrical
Epistemological approach	statistical frequentist	statistical frequentist/ subjectivist	statistical frequentist/ subjectivist

#### 2.2.4.2 Monte Carlo (MC) simulation

MC methods within this study denote first the modeling of probability distributions of all model input parameters and second the repeated computation of a proposed linear equation system (Fig. 6). As a first step sequences of independent uniform random numbers  $U_n$  on the interval  $[0,1]$  are constructed in order to build functions  $(u_1, \dots, u_q) \mapsto F(u_1, \dots, u_q)$  such that the uniform sequences of random variables  $X = F(U_n)$  follow the required distributions of the model input parameters (see Appendix A). Within the second step the algorithm to produce outcome scenarios (iterations) is performed solving thousands of systems of linear equations (see Appendix B).

#### 2.2.4.3 Number of iterations and smooth density curves

The basic approach within this study to estimate a sufficient number of repetitions or iterations in MC simulations  $S_n$  to get statistically acceptable results is based on the central limit theorem, which implies that the difference between the average of the observed output and the true mean is

$$\frac{S_n}{n} - \mu = \frac{\sigma}{\sqrt{n}} \left( \frac{S_n - n\mu}{\sigma\sqrt{n}} \right), \quad (7)$$

thus, the variation in the observed means tend to zero as fast as  $1/\sqrt{n}$  (Meerschaert, 2007). We performed test simulations with different numbers of repetitions to test the stability of the method.

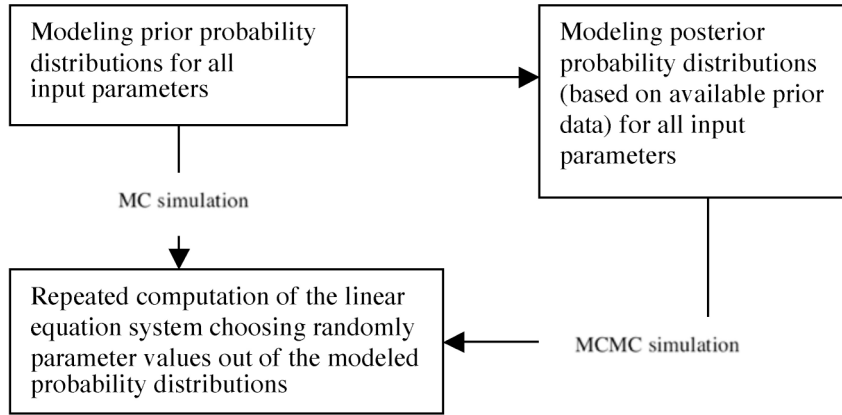


Figure 6. Basic structure of the proposed Monte Carlo (MC) and Markov Chain Monte Carlo (MCMC) modeling approach.

The output distributions of the MC simulations are initially computed as a scatter of data points, which are then smoothed. The size of the bandwidth chosen for kernel density estimation controls the smoothness of the density curves. The choice of a reasonable bandwidth is a concession between smoothing as far that insignificant bumps are rubbed out and that real peaks are not eliminated. A principle with acceptable application in R is a bandwidth  $b$  calculated and controlled as

$$b = \frac{\max(x) - \min(x)}{2(1 + \log_2 n)}, \quad (8)$$

where  $n$  is the number of data points,  $x$  the simulation output variable (Crawley, 2007).

#### 2.2.4.4 Markov Chain Monte Carlo (MCMC)

Bayesian inferences provide in this study posterior distributions  $p(\theta|y)$  defining what is known about unobservable model input parameters  $\theta$  given measured or simulated data  $y$ :

$$p(\theta|y) = p(y|\theta)p(\theta) / \int p(y|\theta)p(\theta)d\theta \propto p(y|\theta)p(\theta) \quad (9)$$

Markov Chain Monte Carlo (MCMC) algorithms are straightforward solutions to sample from such posterior distributions. Metropolis algorithms (Albert, 2007) with symmetric proposal distribution are used to build Markov Chains with the target posterior density as stationary distribution. MCMC packages containing Metropolis sampling routines for R are freely available (<http://cran.r-project.org>). The algorithms can be described as follows:

1. Pick a candidate  $\theta^*$  from the proposal density  $p(\theta^* | \theta^{t-1})$ .
2. Compute  $r = p(\theta^* | y) / p(\theta^{t-1} | y)$ .
3. Accept  $\theta^t = \theta^*$  with probability  $P = \min(r, 1)$ , otherwise  $\theta^t = \theta^{t-1}$ .

The normalizing constant of  $p(\theta | y)$  (see equation 9) is canceled out due to the ratio, which is computed in each iteration step.

The MCMC outputs may be interpreted using graphical and numerical techniques. Once the simulation algorithm is performed it is necessary to check the convergence of the simulated sequences and if the chains have explored the entire posterior distribution. One informal possibility is to plot the posterior traces (Mutshinda et al., 2008) of  $\theta^{(t)}$  against the iteration number to evaluate convergence visually.

High correlation between successive iterates prevents the algorithm from exploring the entire parameter range. A method (Albert, 2007) to assess the mixing of the chains, the degree of dependence between successive iterations in the chain, is to measure the correlation between the sets  $\theta^t$  and  $\theta^{t+N^{(i)}}$  where  $N^{(i)}$  is the difference of iterates between the two sets of generated values. A standard approach is to plot the values of the correlation against the log  $N^{(i)}$ . In the case of a well mixing chain, the values of the described correlation will decrease to zero by increasing of the difference of the number of iterations.

#### 2.2.4.5 Sensitivity analysis

The influence of individual input parameters on system output variables is examined showing the relative differences of the variables changing the parameters. Thus, sensitivity analysis allows to identify e.g. the compound flows that contribute most significantly to the variance of the calculated concentrations. If the most influential parameters are calculated on the most uncertain data, then the confidence in the results may be considered poor, otherwise if those parameters have a robust data basis, the confidence in the exposure assessment might be higher.

Adapted from (Page et al., 1991; Finley and Paustenbach, 1994; Norton, 2008) sensitivity is defined as the ratio of the relative change in the output produced by a unit relative change in the input parameters. Thus, a baseline point value, in this case study the true mean of each distribution, is calculated for each output variable and input parameter of the MC simulation. Then a differential value is calculated for each output variable  $X_i$  by decreasing the baseline input parameter  $P_j$  value by 10%

$$S_{ij} = \frac{(\Delta X_{i,mean} / X_{i,mean})}{(\Delta P_{j,mean} / P_{j,mean})} \times [\sigma_j]. \quad (10)$$

In order to consider the parameter uncertainty the normalized sensitivity is multiplied by the standard deviation of the parameters, which describes the spread of the probability distribution of the analyzed parameters. Such a Gaussian approximation allows to consider both sensitivity and uncertainty (Finley and Paustenbach, 1994; Paustenbach, 2002).

Additionally all sensitivity values are summed to calculate each parameter's relative and percental contribution to the total sensitivity. Thus, the sensitivity analysis ranks the modeling parameters in order of importance and augments the confidence in the model output values comparing the calculated sensitivity to the order of uncertainty of the input parameters. This allows identify the most important inputs that should be studied with priority in order to reduce uncertainty and to improve the exposure modeling.

### 2.2.5 Implementation of a case study (nano-TiO<sub>2</sub>)

As case study and to test computational performance of the model we simulated the behavior of nano-TiO<sub>2</sub> in the environment. Amounts of application of nano-TiO<sub>2</sub> and characteristics of the ENM translocation to and within the environment such as emission factors from products and transfer coefficients were required to run the model. Data to implement the simulations was principally taken from Mueller and Nowack (2008), if not other sources are indicated explicitly (Adam et al., 2006; Schmid and Riediker, 2006; Schmid and Riediker, 2008). For the environmental compartments sediment and groundwater which were not included in the study of Mueller and Nowack (2008) and where data was not available, the estimation of the transfer coefficients was based on assumptions. Recycling processes were not relevant for the implementation case and therefore not considered within the exemplary case study.

The spatial boundary was the geographical boundary of Switzerland. Although most of Switzerland's resident population is concentrated in urban centres, no internal geographical differentiation was assumed. Cosmetics consumption which are e.g. for the case study of nano-TiO<sub>2</sub> the most relevant sources are e.g. assumed to be in tourist destinations in the alpine and pre-alpine region about the same size as in urban regions. The following assumptions were made: a) Environmental compartments are homogenous and well mixed. b) The natural background concentration of particles is neglected. c) Biodegradation of ENMs is not relevant for the case study, nano-TiO<sub>2</sub> as metal oxide is not biodegradable. d) For the reason of feasibility it is assumed that the system is stationary. e) Sludge application on soil and landfill is not admitted in Switzerland and therefore these flows are not considered.

Table 4 shows the assumed ranges of the input parameters. These range values were used to simulate prior and posterior parameter distributions in order to run the model and calculate ENM concentrations. These so called initial values for the transfer coefficients between the studied compartments were taken a) from the literature where few data was available or b) calculated based on estimations within this work. Most of the uniform distributions were derived from Mueller and Nowack (2008) and are based on the mean value of the realistic and the high exposure scenario used in that work. We increased and decreased these mean values by 10% in order to calculate the so-called initial range of the concerned transfer coefficients. The range of the periodical ENM input into the system was modeled as a lognormal distribution based on indications (n = 4) from different sources. Having some indications about the ENM fate within the waste incineration plant (WIP), the transfer coefficient between WIP and atmosphere could be estimated based on a triangular distribution. For this case the uncertainty was reduced in comparison to all the uniformly distributed transfer coefficients where there was at the most one unique indication of parameter value available.

Table 4. Probability distributions of the modeling parameters used to simulate nano-TiO<sub>2</sub> flows. *I* is the annual input of nanoparticles into the production, manufacturing and consumption process (PMC), TC12 represents e.g. the transfer coefficient of nanoparticles between process 1 (PMC) and process 2, the sewage treatment plant (STP) (see for numbering and nomenclature also Fig. 4). The column references indicates the sources from which the prior mean values are derived: (1) Mueller and Nowack (2008), (2) Schmid and Riediker (2006), (3) Schmid and Riediker (2008), (4) Adam et al. (2006), (5) this work.

Parameter	PDF	Minimum or Logarithmic Mean	Maximum or Mode	References
<i>I</i> , Input	lognormal	5.45959		(1),(2),(3)
TC12, Wastewater	uniform	0.58536	0.66075	(1)
TC14, Waste	uniform	0.06795	0.08305	(1)
TC15, Emissions	uniform	0.00131	0.00160	(1)
TC16, Waste	uniform	0.11250	0.13750	(1)
TC17, Waste	uniform	0.05625	0.06875	(1)
TC18, Emissions	uniform	0.02565	0.03135	(1)
TC111, Export	uniform	0.07560	0.09240	(1)
TC23, Overflow	uniform	0.06750	0.08250	(1)
TC24, STP sludge	uniform	0.85233	0.87918	(1)
TC28, Cleaned water	uniform	0.05333	0.06518	(1)
TC45, Emissions	trigonal		0.00050	(1),(4),(5)
TC46, Slag, filter ash	uniform	0.79480	0.97143	(1),(4)
TC411, Export of filter ash	uniform	0.01857	0.20519	(1), (4)
TC57, Particle emissions	uniform	0.96700	0.97300	(1)
TC58, Deposition (dry/wet)	uniform	0.02700	0.03300	(1)
TC69, Leaching	uniform	0.0000009	0.0000011	(5)
TC66, Storage	uniform	0.9999989	0.9999991	(5)
TC75, Emissions	uniform	0.00090	0.00110	(1)
TC78, Leaching	uniform	0.00090	0.00110	(1)
TC79, Erosion	uniform	0.0000009	0.0000011	(5)
TC710, Leaching	uniform	0.00090	0.00110	(5)
TC77, Storage	uniform	0.99670	0.99730	(5)
TC89, Groundwater infiltration	uniform	0.00090	0.00110	(5)
TC810, Sedimentation	uniform	0.45000	0.55000	(5)
TC811, Export	uniform	0.44890	0.54910	(5)
TC91, Consumption	uniform	0.00090	0.00110	(5)
TC99, Storage	uniform	0.99890	0.99910	(5)
TC108, Resuspension	uniform	0.00090	0.00110	(5)
TC1010, Storage	uniform	0.99890	0.99910	(5)

The calculations of the ENM concentration in surface water (rivers and lakes) were performed based on the relevant mixing depth of 3 m (ECB, 2003), which were multiplied with 3% (ECB, 2003) of the total area of Switzerland. This leads to a relevant water volume of 3.7 km<sup>3</sup>. The average concentration of ENMs in the soil was calculated based on the soil mixing depth which depends on the type of soil and is 0.2 m for agricultural soil and 0.05 m for natural and urban soil; the agriculturally used fraction is 0.27, natural ground 0.6 and urban ground 0.1 (ECB, 2003). This leads to a calculated soil volume of 6.2 km<sup>3</sup>. The soil density was taken to be 1.7 kg/l (ECB, 2003). The volume of the relevant sediment compartment was derived from the water surface, which was first assumed to be equal to the surface of the sediment and second multiplied with an average sediment depth of 0.04 m. This leads to an estimated relevant sediment volume of 0.05 km<sup>3</sup>. The bulk density of the relevant sediment was taken to be 1.3 kg/l (ECB, 2003). The computation of the ENM concentration within the air compartment was based on the retention time of 10 days of superfine particles (Anastasio and Martin, 2001) and on the calculated relevant air volume (41, 285 km<sup>3</sup>) obtained by multiplying the total area of Switzerland with the relevant air height for terrestrial ecosystems of 1 km (ECB, 2003). Based on the assumed retention time of 10 days about one thirty-sixth of the ENM input into the air compartment is constantly in the air. In addition to the compartments used by Mueller and Nowack (2008), the secondary compartments groundwater and sediments were included as well in this work. However, calculations of flows from and to these compartments e.g. sedimentation, resuspension, surface erosion or water-sediment partitioning of ENMs are based on very crude assumptions, since currently there is no data available concerning ENM transfer to and from these two compartments.

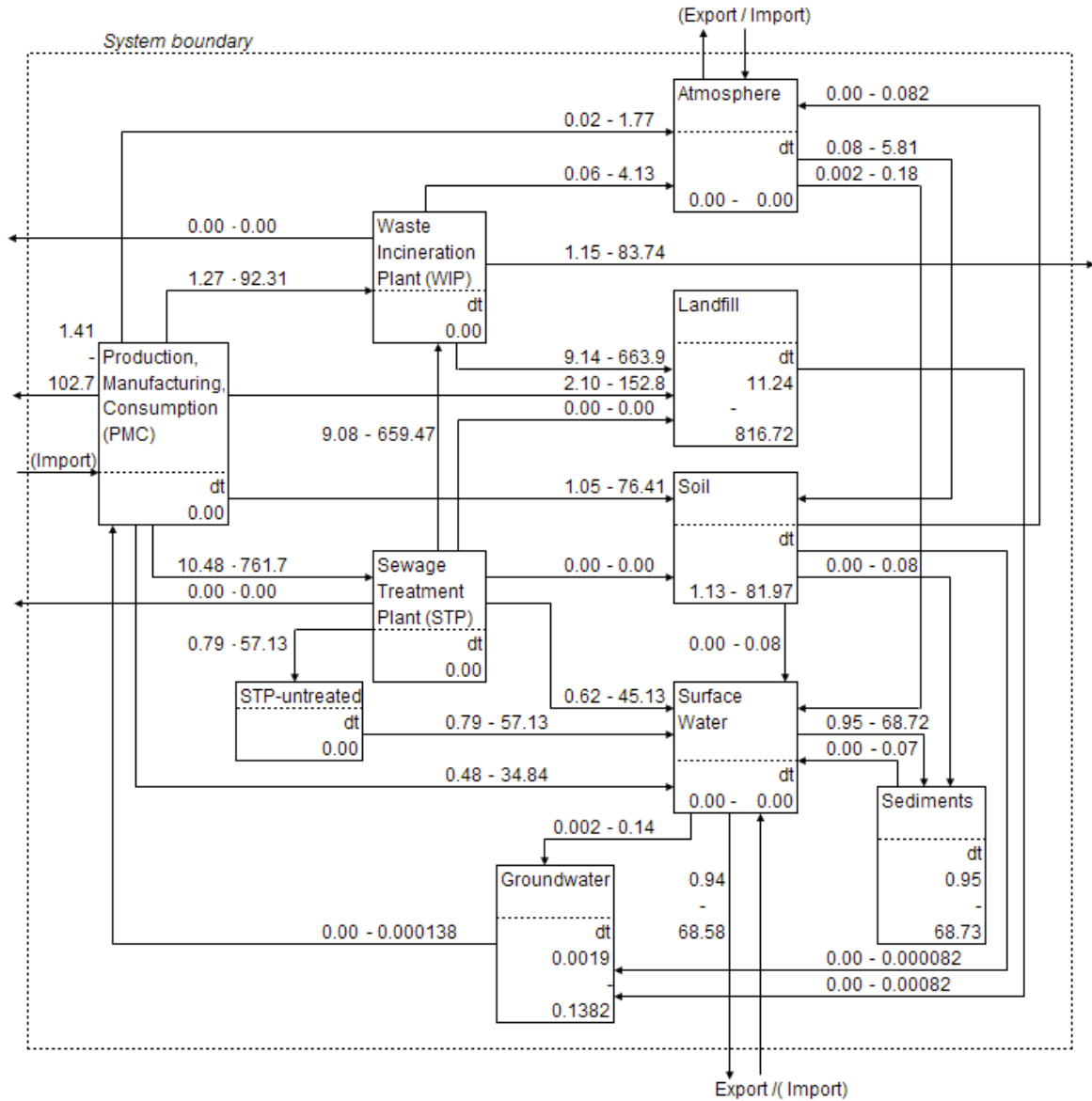


Figure 7. Mass flows between the environmental compartments for nano-TiO<sub>2</sub> and accumulation rates within the compartments in t/year (shown as 95% confidence intervals).

## 2.3 Results and discussion

### 2.3.1 Algorithmic performance of the model

To test the mathematical/computational correctness of the model we recomputed exactly the high exposure scenario of nano-TiO<sub>2</sub> flows presented in Mueller and Nowack (2008). First, the deterministic case was recomputed using the same model input values. All simulation outcomes rounded to 2 significant digits corresponded exactly to the values shown in the mentioned study. The same applied for the computation of the same scenario by means of the MC approach. We ran 100,000 iterations assuming the input parameters to be uniformly distributed (+/-10%) around the given input data in

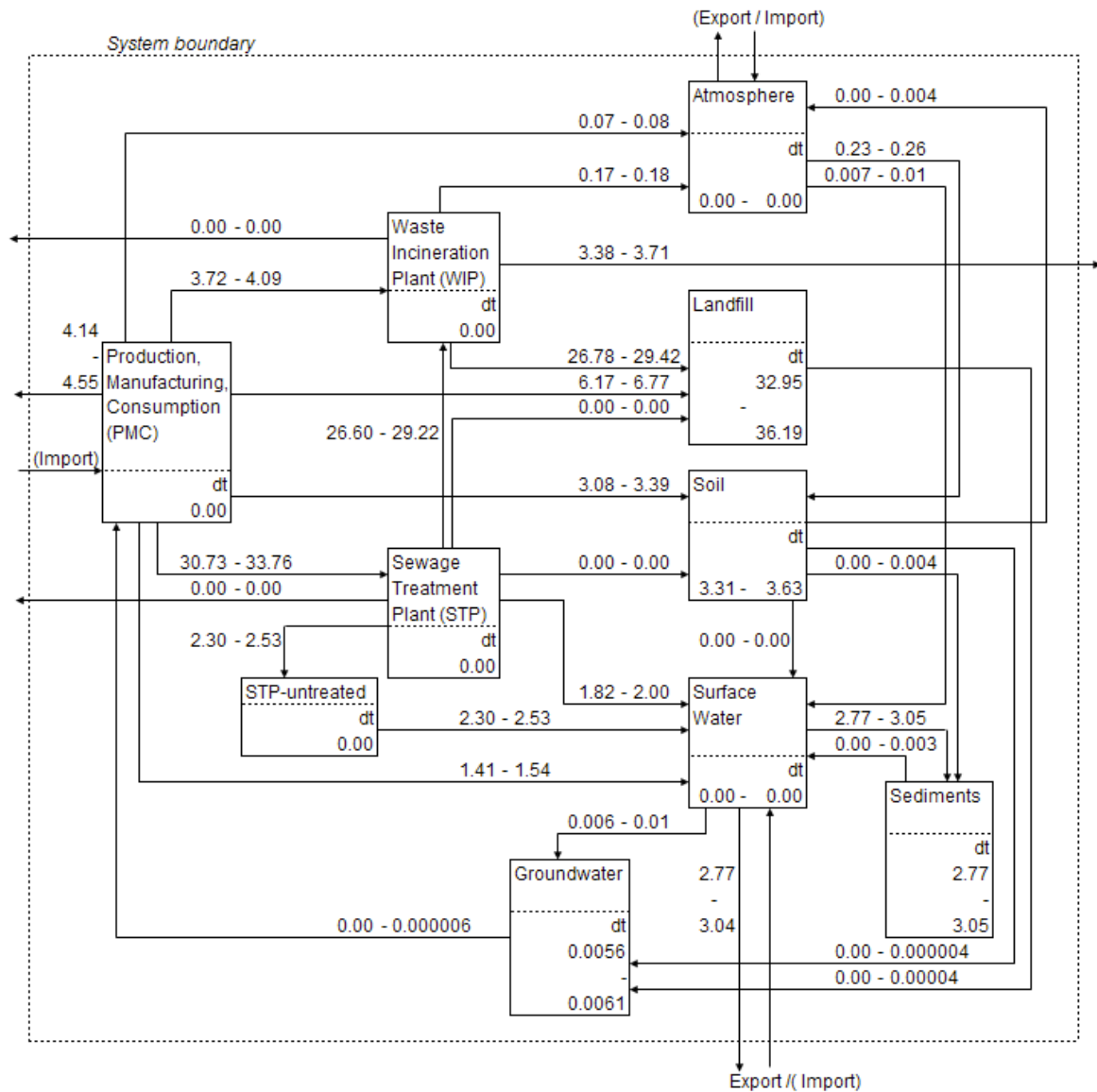


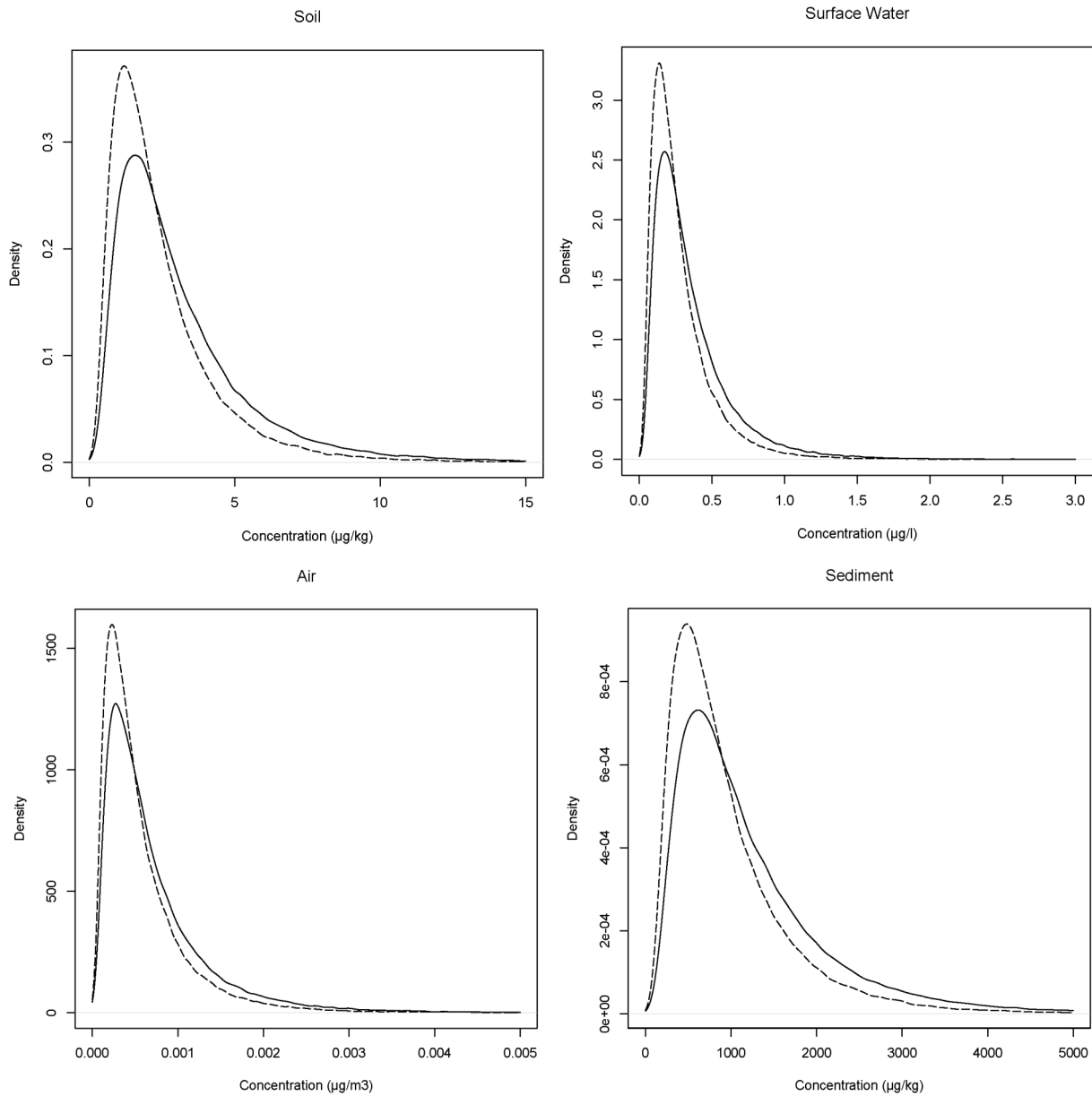
Figure 8. Modes of the mass flows between the environmental compartments for the nano-TiO<sub>2</sub> study and the accumulation rates within the compartments in t/year. The mode is the most frequently computed probability (shown is the 95% confidence interval).

Mueller and Nowack (2008). Eleven of the 14 flows, rounded to two significant digits, corresponded exactly to the values given by Mueller and Nowack (2008). Three of the 14 values corresponded exactly to the values of Mueller and Nowack (2008) if rounded to one significant digit. This shows that even with more complex systems (10 processes, 23 internal flows, 1 input flow, 3 elimination flows and 3 output flows) the programmed MC simulations solve the equations correctly providing results, which fit even as mean values available deterministic data.

### 2.3.2 Modeling results

A sampling size of 100,000 was chosen for all simulations. Numerical stability of MC techniques for exposure assessment is commonly reached or accepted at  $\geq 10,000$  repetitions (Burmaster and Anderson, 1994). To test the numerical performance of the procedure, the stability of mean, median, standard deviation and kurtosis was tested starting from small statistics to arrive at a





**Figure 9.** Probability densities from Monte Carlo (line) and Monte Carlo Markov Chain (dotted lines) simulations of the predicted annual increase of nano-TiO<sub>2</sub> concentrations in µg/kg in soil and sediment and of the concentrations in air in µg/m<sup>3</sup> and surface water in µg/l.

sufficient number of iterations making larger ones. Above 10,000 iterations the mentioned central moments (mean, median) were insofar stable that there was no observable difference between the computed middle values of simulations with the same quantity of iterations and such with higher number of repetitions. It takes more iterations to stabilize the tails of the output distributions and to locate potential extreme events in those tails. Above 100,000 iterations even the standard deviations of the output variables were stable so that there was no significant difference between the computed values of simulations with the same quantity of repetitions and such with more iterations. From the collected data the mean, the range and the probability distribution for the input variable and parameters were calculated. The computed nano-TiO<sub>2</sub> flows and accumulation rates in Fig. 7 indicate the 95% confidence interval within which the output probability distributions of the ENM flows are included when repeating the MC simulations. Fig. 8

shows the 95% confidence interval within which the modes of the computed output probability distributions of the ENM flows and accumulation rates are included when repeating these simulations. The mode is the value that appears most frequently in the computed probability distribution. It is regarded as the highest probability  $p(x)$  for a discrete distribution or as the highest probability density  $f(x)$  for a continuous case. Thus, the range of the flows within Fig. 8 may be interpreted as the most probable indications for the expected ENM flows based on a relative probability, whereas the range of the values within Fig. 7 may be regarded as a range which covers with a very high probability the whole range of possible values. The most relevant ENM flows (95% confidence interval of the mode value) are wastewater (30.7–33.8 t/a), sludge from STP to WIP (26.0–29.2 t/a), filter ash from WIP to landfill (26.8–29.4 t/a), direct deposition from PMC to landfill and soil (6.2–6.8 t/a and 3.1–3.4 t/a), export from PMC and WIP outside the system boundary (4.1–4.6 t/a and 3.4–3.7 t/a) and waste from PMC to WIP (3.7–4.1 t/a). Figure 9 shows the simulated PEC values for soil, water, air and sediments. Noteworthy are the very small concentrations in the air compartment compared to the simulated concentrations in surface water and to the annual increase of the concentrations in soil and sediments.

*Table 5. Examples of the modeled prior and posterior distributions of the parameters (mean values, standard deviation, reduction coefficient and percentiles) used to simulate nano-TiO<sub>2</sub> flows and to calibrate the evolved model.*

Parameter	PDF	Prior distribution		Posterior distribution			50th	75th	97.5th
		Mean	SD	Mean	SD				
<i>I, Input</i>	lognormal	303.31	245.69	235.083	191.950	182.14	294.64	743.49	
		300	44	70	6				
<i>TC810, Sedimentation</i>	uniform	0.5000	0.0289	0.48984	0.0277	0.4853	0.5111	0.5451	
<i>TC12, Wastewater</i>	uniform	0.6231	0.0218	0.62340	0.0217	0.6235	0.6422	0.6589	
<i>TC58, Deposition (dry/wet)</i>	uniform	0.0300	0.0017	0.03000	0.0017	0.0300	0.0315	0.0328	
<i>TC57, Particle emissions</i>	uniform	0.9700	0.0017	0.97001	0.0017	0.9700	0.9715	0.9729	
<i>TC24, STP sludge</i>	uniform	0.8657	0.0078	0.86575	0.0078	0.8658	0.8725	0.8785	
		0.0035							
<i>TC45, Emissions</i>	trigonal	0	0.0023	–	–	–	–	–	

### 2.3.2.1 MCMC simulations

The MCMC simulation results provide the highest posterior probabilities, which may be regarded as the “best” simulations. Prior data do not represent measured data in this case study, but the results of the Monte Carlo simulations. Insofar, the information in the data is small and the posterior distributions do not differ greatly from the prior. In such cases the prior distribution  $p(\theta)$  corresponds strongly to the distribution  $p(y|\theta)$ , which indicates the probability of observing randomly the data  $y$  for a given value of  $\theta$ . Hence, the posterior simulation results

(Fig. 9) are not so much “best” estimations as rather an example how to improve and calibrate simulations in the future when more and more secure data concerning the input parameters will be available.

Table 5 shows exemplarily results of the parameter conditioning based on the modeled Markov Chain properties (see section 2.4) and conducted for the MCMC simulations. For the prior distributions the mean values and the standard deviation are indicated, for the posterior distributions mean values, standard deviation and quantiles are given. For the parameters with downright small uncertainty space and transfer coefficient, no MCMC simulations were performed. To judge convergence by the mixing between the chains, several chains were run simultaneously from different initial states. Markov Chains that converge to the equilibrium indicate that they have approximated the target distribution. In Fig. 10 we see exemplarily the degree of mixing and convergence of Markov Chains from the last 3,000 of 100,000 posterior draws. The upper figure shows draws from the parameter range of the flow coefficient sewage treatment plant (STP) to WIP (STP sludge) (uniformly distributed) and the lower one posterior draws from the periodical ENM input (lognormally distributed) into the system. The chains have converged. The MCMC sampler jumps freely within the whole parameter space. The target mean value is 0.87 for the TC between STP and WIP and 233.22 t/a for the ENM input into the system.

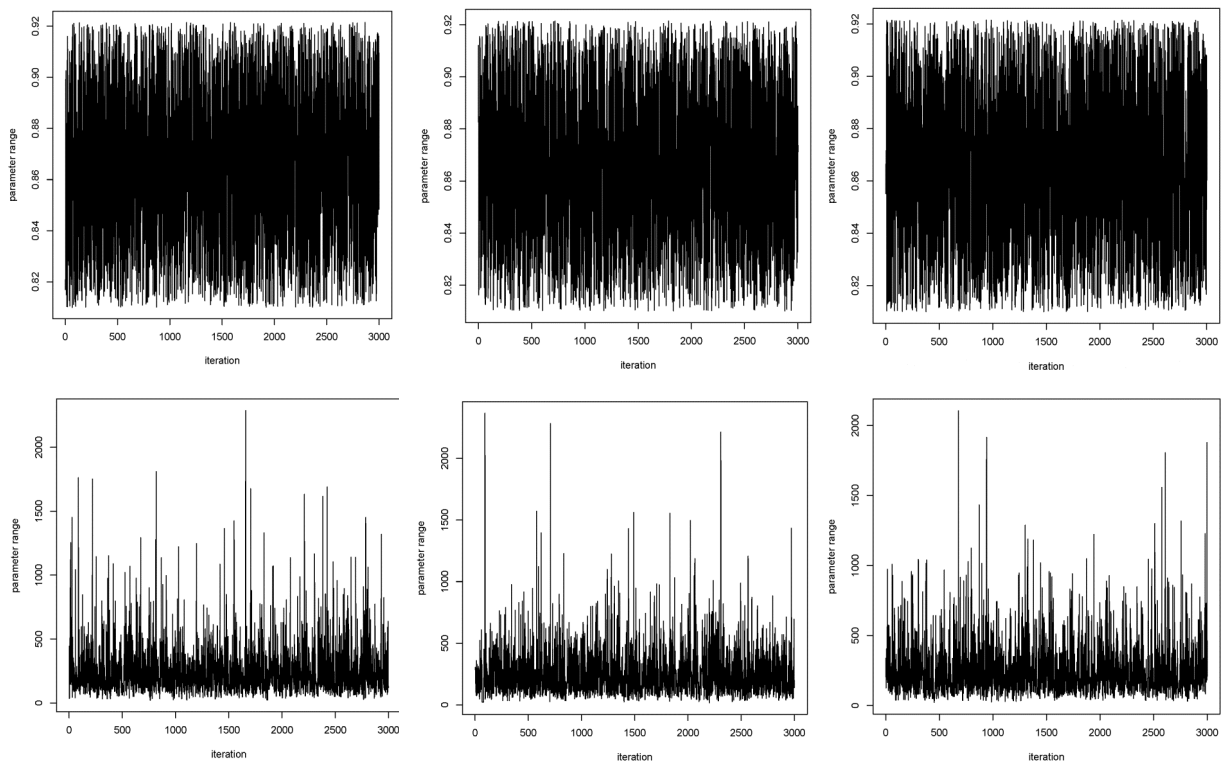


Figure 10. Trajectory plots of posterior draws from Monte Carlo Markov Chain simulations of the transfer coefficient sewage treatment plant to waste incineration plant (uniformly distributed, target mean: 0.87) and the periodical ENM input (bottom) into the system (lognormally distributed, target mean: 233.22 t/a) illustrated as Monte Carlo Markov Chain steps against the iteration number.

### 2.3.2.2 Sensitivity analysis

First, the unitless results (see Table 6) show how a relative change of the input parameters produces a relative change of the simulation output values. Second, the results show the relative contribution of each parameter to the total sensitivity. In addition, the confidence in the simulation results may be estimated by comparing the sensitivity results with the robustness of the influential parameters. If the most influential parameters were based on very uncertain data, the confidence in the simulation output would be small. However, for this case study this estimation is not straightforward. The reason is that most of the probability distributions of the input parameters were computed based on the same data basis (Mueller and Nowack, 2008), and that most of the remaining distributions were calculated based on similar assumptions made within this work (Table 4). Insofar, the ranges of uncertainty of the model input parameters differ only slightly from each other. However, we may at least state that the most influential parameters to the compartments surface water and sediment (ENM flows from or to the sewage treatment plant) were estimated based on information taken from Mueller and Nowack (2008) and not exclusively based on assumptions. The most influential flows for surface waters are sludge from STP to WIP (83.2%), particle emissions from PMC to surface waters (6.6%), the STP overflow (4.1%) and the STP effluent (3.9%). The increase of concentrations in sediment is mostly influenced by the sludge flow from STP to WIP (60.1%), the sedimentation of ENMs in water (15.8%) and by the water flows leaving the system (11.8%). These results underline in accordance with the simulated flows that the parameters describing the flows of nano-TiO<sub>2</sub> from the PMC process to the STP, the STP effluent and overflow, the sludge from STP to WIP, and the sedimentation process in water need a closer look.

### 2.3.2.3 Implications of the simulated case (nano-TiO<sub>2</sub>)

The very small concentrations of nano-TiO<sub>2</sub> in the air compartment compared to the simulated concentrations in surface water and to the annual increase of the concentrations in soil and sediments are mainly due to the high volume of the compartment and the short residence time of the ENMs. Furthermore, ENMs reach the atmosphere during the usage of products or via emissions from waste incineration plants only at very low amounts. However, the simulated concentrations in surface water and the remarkable high annual increase of concentrations in sediments show that a further look at the nano-TiO<sub>2</sub> concentrations in waters is needed to assess potential risks posed from these ENMs to aquatic organisms. Thus, the fate and behavior of nano-TiO<sub>2</sub> in STPs (and STP sludge) and the sedimentation process of this nanomaterial need to be studied in more detail. Sludge application on landfills and soils is prohibited in Switzerland and thus the STP sludge mostly incinerated in WIPs. However, for other regions (e.g. USA, EU) where sludge application on soils is admitted, the sludge concentrations and as a result also the concentrations in STP sludge treated soils need to be studied as well. The results obtained with the new PMFA may be used to guide ecotoxicological research of these compounds as they provide a range of probable environmental concentrations.

Table 6. Results of the analysis of the model parameters sensitivity to the output variables.

Exposure variable	Sensitivity (unitless)	Percentage of sensitivity
<i>Surface Water:</i>		
F24, STP sludge	0.109615559	83.22%
F18, Particle emissions	0.008690587	6.60%
F23, Overflow	0.005422365	4.12%
F28, Cleaned water	0.005208635	3.95%
F16, Waste	0.001094578	0.83%
F111, Export	0.000467249	0.35%
F14, Waste	0.000370735	0.28%
F12, Wastewater	0.000281325	0.21%
F17, Waste	0.000247969	0.19%
F46, Slag, filter ash	0.00016312	0.12%
<i>Groundwater:</i>		
F810, Sedimentation	3.600084654	49.10%
F811, Export	3.586067196	48.91%
F24, STP sludge	0.108806519	1.48%
F717, Storage	0.015171825	0.21%
F18, Particle emissions	0.008626953	0.12%
<i>Sediments:</i>		
F24, STP sludge	0.109483392	60.12%
F810, Sedimentation	0.02885319	15.84%
F811, Export	0.02158482	11.85%
F18, Particle emissions	0.008678748	4.77%
F23, Overflow	0.005415827	2.97%
F28, Cleaned water	0.005202355	2.86%

Furthermore, the results of this case study point out that the probabilistic material flow analysis (PMFA) is applicable i) to predict concentrations of compounds in the environment when little data are available, ii) to program and use any kind of probability distribution functions for the input variables incorporating a large number of processes and flows in order to compute probabilistically compound flows and deposition rates and iii) to improve at any time and any part of the system prior data to posterior results by formulating and incorporating e.g. MCMC algorithms and by starting from new available e.g. simulation or measured data.

However, even sophisticated probabilistic techniques do not create more empirical data than what is available and empirical information is needed to generate model input distributions. In the case of ENMs such a data basis is often missing and thus, the use of uniform distributions unavoidable. In cases where no data are available, the borders of the distributions have to be

determined by experts, which in turn may lead to even higher uncertainties in the input parameters.

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## 2.5 Appendix

### Appendix A

#### R-code for input data generation

(exemplified triangular distribution of the emission coefficient WIP to atmosphere)

```

triangulsim_WIP <- function(vecabc) {
  min <- vecabc[1]
  mode <- vecabc[2]
  max <- vecabc[3]
  u <- runif(1,0,1)
  if (u <= (mode-min)/(max-min) ){
    r = min+sqrt(u*(max-min)*(mode-min)) }else{
      r = max-sqrt((1-u)*(max-min)*(max-mode))
    }
    r
  }

  a = 0.00001
  b = 0.0005
  c = 0.01

  M <- matrix(c(rep(a,10^5),rep(b,10^5),rep(c,10^5)),10^5,3)
  tri <- apply(M,1,triangulsim_WIP)

```

## Appendix B

### R-code for MC simulations

```

N <- 100000
V <- matrix(NA,n,N)
  for (k in 1:N){

      I <- c(rlnorm(1,μ,σ),rep(0,n-1))
      A <- matrix(0,n,n)
      A[2,1] <- -(TCpmcstp[k]) # Exemplified transfer coefficienta from PMCb to STPc

      ...
      A[n,1] <- -(1+T[2,1]+T[4,1]+T[5,1]+...+T[n-1,1])
      ...
      V[,k] <- solve(A,I)

  }

```

---

<sup>a</sup>Transfer coefficient PMC to STP that includes: TC<sub>production to sewage treatment plants</sub> + TC<sub>manufacturing to sewage treatment plants</sub> + TC<sub>production to product category 1</sub> \* TC<sub>product category 1 to sewage treatment plants</sub> + TC<sub>production to product category 2</sub> \* TC<sub>product category 2 to sewage treatment plants</sub> + TC<sub>production to product category 3</sub> \* TC<sub>product category 3 to sewage treatment plants</sub> + ... + TC<sub>production to product category n</sub> \* TC<sub>product category n to sewage treatment plants</sub>.

<sup>b</sup> Production, manufacturing and consumption process.

<sup>c</sup> Sewage treatment plants.



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### 3. Modeled environmental concentrations of engineered nanomaterials (TiO<sub>2</sub>, ZnO, Ag, CNT, fullerenes) for different regions

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#### Abstract

Engineered nanomaterials (ENM) are already used in many products and consequently released into environmental compartments. In this study, we calculated predicted environmental concentrations (PEC) based on a probabilistic material flow analysis from a life-cycle perspective of ENM-containing products. We modeled nano-TiO<sub>2</sub>, nano-ZnO, nano-Ag, carbon nanotubes (CNT), and fullerenes for the USA, Europe and Switzerland. The environmental concentrations were calculated as probabilistic density functions and were compared to data from ecotoxicological studies. The simulated modes (most frequent values) range from 0.003 ng L<sup>-1</sup> (fullerenes) to 21 ng L<sup>-1</sup> (nano-TiO<sub>2</sub>) for surface waters and from 4 ng L<sup>-1</sup> (fullerenes) to 4 µg L<sup>-1</sup> (nano-TiO<sub>2</sub>) for sewage treatment effluents. For Europe and the USA, the annual increase of ENMs on sludge-treated soil ranges from 1 ng kg<sup>-1</sup> for fullerenes to 89 µg kg<sup>-1</sup> for nano-TiO<sub>2</sub>. The results of this study indicate that risks to aquatic organisms may currently emanate from nano-Ag, nano-TiO<sub>2</sub> and nano-ZnO in sewage treatment effluents for all considered regions and for nano-Ag in surface waters. For the other environmental compartments for which ecotoxicological data were available, no risks to organisms are presently expected.

#### 3.1 Introduction

Engineered nanomaterials (ENM) are applied in many commercially available consumer products such as in cosmetics, textiles and paints. Due to the increasing production volumes, an environmental exposure to ENMs is likely (1). Whereas toxic effects of nanomaterials on different organisms have already been described (2, 3), measurements of environmental concentrations of ENMs are almost completely absent. The first study in this field reported the detection of nano-TiO<sub>2</sub> in water leaching from exterior facades (4). Despite the fact that the release of ENM from products is a very important entry pathway for ENMs into the environment, studies examining this process are very rare (5). One recent study quantified the release of silver ENM from socks during washing (6).

Because of the nearly absent information about environmental concentrations of ENMs, modeling of predicted environmental concentrations (PEC) currently constitutes a necessary and valuable substitute for measurement studies. ENMs may reach the environment during production of the material, incorporation into products or during the use-phase of such nanotechnology based goods (5). Only a few studies (7–9) have predicted environmental ENM concentrations. For instance, Mueller and Nowack (7) found that nano-TiO<sub>2</sub> may currently pose a threat to organisms living in the aquatic environment, whereas the current concentrations of nano-Ag and CNT seem non-hazardous. But a major drawback for assessing the risk of ENM is not only the lack of information about fate and behavior but also the inconsistency of the available data (1). Mueller and Nowack (7) have modeled two scenarios to address this lack of available data. Still, some important environmental compartments such as sediments were not included in their study, and consideration of the three nanomaterials (TiO<sub>2</sub>, CNT, Ag) analyzed was limited to the geographical boundaries of Switzerland.

Probabilistic methods of environmental exposure analysis (10–13) allow one to account for the inconsistency and variability of model input parameters by using probability (or density) distributions. Those input distributions may be constructed based on empirical data, on expert judgment or on a combination of these sources. Compared to a scenario analysis, this probabilistic/stochastic approach is not restricted to the use of single input values, but aims at considering all possible model inputs covering also extreme events. It provides in contrast to scenario estimations also an insight into the frequency probability of each simulated outcome. Such a probabilistic modeling approach (14) has been used to describe nano-TiO<sub>2</sub>, CNT and nano-Ag flows in Switzerland (15).

The aim of this paper was to use the probabilistic material flow analysis proposed by Gottschalk et al. (14) to model the environmental concentrations of nano-TiO<sub>2</sub>, nano-ZnO, nano-Ag, CNT and fullerenes for the USA, Europe and Switzerland, considering all environmental compartments including sediments. To assess the risks posed by the ENMs, the simulated PEC was compared to the predicted no effect concentration (PNEC) based on toxicity data for the corresponding environmental compartment.

## **3.2 Materials and methods**

### **3.2.1 Model information**

The modeling was performed based on a probabilistic material flow analysis approach developed by Gottschalk et al. (14). This mass balance and multi-compartment model allows one to treat all parameters throughout the modeling as probability distributions. Thus, the model outcome represents an ENM flow system, depicted by probability (or density) distributions. Model input and output distributions were derived from Monte Carlo (MC) and/or Markov Chain Monte Carlo (MCMC) simulations programmed and executed in R (16), an open source and open development software for statistical computing. For each region, the corresponding geographic boundaries were used as the spatial system boundary. The system was described by 11 boxes which represented environmental compartments (water, air, soil, sediment and groundwater) and technical compartments (production, manufacturing and consumption (PMC), sewage treatment plant (STP), waste incineration plant (WIP) landfill and recycling processes). The environmental compartments were considered homogeneous and well mixed as suggested for modeling the

regional PEC (17). Deposition and elimination/degradation of ENM within the compartments were modeled as constant annual flows into a sub-compartment of each box considered. The derivation of the sizes of the air, water, soil and sediment compartments is given in the Supporting Information (section A). These volumes were used to calculate the respective concentrations of the ENMs in these compartments.

The worldwide annual production amounts of the studied ENMs were scaled to regional production volumes in proportion of the population of the high income countries to the total population of a particular region (18). Then, lognormal distributions were modeled based on logarithmic means and standard deviations derived from these data. For allocating ENM production volumes to the different products, the same method as described in Gottschalk et al. (15) was used. The details are given in the Supporting Information (section B). ENM containing products were grouped into different categories according to similarities in lifecycle by means of Internet based research for each ENM.

Depending on the ENM-containing product, different release pathways of ENMs to the environment were assumed during the products' life cycle. Section C in the Supporting Information gives a complete overview of the transfer coefficients (TC) used to model the ENM emission flows from PMC to other system compartments. For composites and plastics, complete disposal was assumed. For glass & ceramics and light bulbs, the main pathway was also disposal. For cosmetics, coatings & cleaning agents and dietary supplements, the major release of ENM to the environment was via sewage treatment plants. Released ENMs from paints were assumed to end up in STP, landfill, soil and surface waters. Metals, batteries & capacitors, filter aggregates, textiles and consumer electronics were considered as either recycled or discharged to waste incineration plants or to landfills. Furthermore, some of these recycled products were also exported abroad. For textiles, abrasion and emissions during the washing process were considered. The release of nanoparticles from Ag containing textiles was modeled using data from an experimental study (6). The dissolution of nano-ZnO and nano-Ag was modeled as elimination within the different compartments. For nano-ZnO the dissolution was modeled as elimination and calculated by means of a uniform distribution, which ranged from 0% to 100%. It has been shown that under natural conditions readily soluble minerals can be protected from dissolution by a corrosion layer (19, 20). Dissolution of nano-Ag was quantified based on information given in Blaser et al. (9) for the release of Ag from biocidal plastics and in Benn and Westerhoff (6) for release from textiles. No continuous dissolution was considered for natural waters, as little quantitative information was available. It has been shown that nano-Ag dissolves by less than 1% in various natural waters (21).

The sedimentation rate of nano-TiO<sub>2</sub> in water was derived using the sedimentation curves in Fang et al. (22) as measurement data to run MCMC iterations, which produced a distribution for the sedimented fraction with a minimum of 0.29 and a maximum of 1. Although a lot of research has been conducted to understand the behavior of fullerenes in aquatic systems or suspensions (23), most of the results were not applicable to our purpose because they yielded qualitative rather than quantitative data. We assumed almost complete dispersion (90–100%) for derivatized fullerenes and almost complete sedimentation (90–99.99%) for non-derivatized fullerenes based on Terashima et al. (24) in which fullerenes were added to water containing different amounts of humic acids. This range of sedimentation covers also the results provided by Li et al. (25). For CNT the MCMC sampling to calculate a posterior distribution of the deposited fraction was

carried out from data presented in Kennedy et al. (26) and Hyung et al. (27). A range of sedimentation between 79% and 99.9% was modeled. For nano-ZnO sedimentation, a constant probability distribution was chosen with a lower and upper boundary of 6% and 74%, respectively, based on a study in which nano-ZnO was flocculated by  $MgCl_2$  (28). No sedimentation studies were available for nanosized silver and thus a uniform distribution from 0% to 100% was assumed.

A further pathway for nanomaterials to enter the environment is through the air via flue gas cleaning of waste incineration plants. For the efficiency of these filter systems, we used measurements on the removal of ultrafine particles during flue gas cleaning (29), which suggest a cleaning efficiency for nanoparticles between 99.6% and 99.9%. Combustible ENMs (i.e. CNT and fullerenes) should theoretically be completely burned unless they have no contact with oxygen, such as in batteries which may be intact in the bottom ash (5, 30). Therefore, a triangular probability function for elimination was chosen between 0% and 100% with a peak at 98% according to a typical carbon mass flow for incineration plants (31). The remaining part was then distributed randomly either to the slag or to the flue gas cleaning. Incombustible nanoparticles (i.e. nano-Ag, nano-TiO<sub>2</sub> and nano-ZnO) were randomly distributed either to the slag or to the flue gas cleaning but without elimination. Expecting only small differences in the efficiency of waste incineration plants due to the highly developed technology commonly used, processes leading to nanoparticle outputs were modeled similarly for each region with the sole exception of Switzerland, which exports about 80% (32) of the filter ash. The EU and the USA were assumed to landfill all their incineration residues.

For nano-Ag, nano-TiO<sub>2</sub>, and nano-ZnO a removal efficiency during wastewater treatment between 90.6% and 99.5% (uniform distribution) was used based on Limbach et al. (33). For CNT, a removal between 96.3% and 99.7% (uniform distribution) was assumed based on settling studies in water containing 100 mg L<sup>-1</sup> NOM (26, 27). Because of the different types (functionalizations) of fullerenes, a quantification of treatment efficiency was not possible. Therefore, a distribution with constant probability from 0% to 100% was taken to account for this lack of knowledge. During and after heavy rainfall, untreated wastewater is discharged into surface water. For the EU and USA, 20% storm water overflow was assumed (17), and a uniform distribution between 3% and 16% (15) was used for Switzerland. Sewage sludge is used in different ways in the studied regions. In Switzerland it ends up entirely in waste incineration plants, whereas the majority of it is applied to soils in the EU and USA (EU: 55% (9), USA: 63% (34)). The remaining fraction is incinerated (EU: 25% (9) USA: 19% (34)) or landfilled (EU: 20% (9), USA: 18% (34)). Application of sewage sludge to soil is only relevant for 1% (35) of the agricultural area. The percentage of sources connected to sewage treatment facilities is 80% for the EU (17), 71% for the USA (36) and 100% for Switzerland. The treatment efficiency and ultimate fate of the sludge from other treatment systems such as septic tanks was assumed to be the same as for sewage treatment plants. For calculating the water volume in the effluent, a daily water consumption per inhabitant of 200 L for Switzerland and the EU was assumed (17); for the US 388 L (37).

Due to the deposition of nanomaterials in soils and sediment, the simulation results for these two compartments show annual increases in the nanomaterial concentrations. In order to obtain current concentrations in these compartments, the time course of the annual deposition needs to be known. Based on estimations of both public sector expenditures to promote nanotechnology



(38) and the worldwide market value for products incorporating nanosized materials (39) for the period 2001–2012, the modeled increase (base year 2008) of ENM concentrations in sludge treated soil and sediment was scaled to calculate annual increases of these concentrations for each year within the indicated period. No market and thus zero deposition of ENM was assumed for the year 2000.

### 3.2.2 Toxicity assessment

Calculations of the predicted no effect concentration (PNEC) were based on ecotoxicological data from literature and were conducted according to established procedures on risk assessment (17). Due to the low accuracy of available data, an assessment factor of 1000 was applied to the lowest concentration for calculating the appropriate PNEC values that are listed in section D in the Supporting Information. The risk quotient (RQ) was calculated according to the European approach by dividing the PEC (mode value of the PEC density distribution) by the PNEC. If the RQ was greater than or equal to 1, further testing was required; less than 1 meant that no risk was currently posed to the environment and therefore further testing or risk reduction measures were not needed (17).

## 3.3 Results

### 3.3.1 Material flow

In Figure 11, the calculated material flows for nano-TiO<sub>2</sub>, nano-ZnO, nano-Ag and CNTs for the system boundary of the USA are shown in t per year and as mode values of the simulation output distributions. Flows leaving the system describe the export of ENMs abroad. ENMs may be accumulated or eliminated (indicated as “dt”) within each compartment. For CNTs, the most prominent flows were from PMC to the waste incineration plant and to the landfill. For nano-ZnO, the flows from PMC to the sewage treatment plant and the application of sewage sludge to soil were the most important. The STP influent, the application of sewage sludge to soil, and the flow from PMC to the landfill were by far the predominant flows in the cases of nano-TiO<sub>2</sub> and nano-Ag. The most prominent flows for fullerenes (not shown) were from products to landfill and STP and from STP to WIP and surface waters; all flows, however, were less than 1 t/a.

### 3.3.2 Environmental concentrations

The main purpose of the model was to calculate the PEC for environmental compartments. Table 7 shows the predicted ENM concentrations for air, surface water, STP effluent and sewage sludge for each region and the increase of ENM concentration per year (base year 2008) for soil, sludge-treated soil and sediment. No concentrations in sludge-treated soil were calculated for Switzerland since, contrary to Europe and the USA, sewage sludge is not applied to soil, but is instead incinerated in waste incineration plants or used in cement plants as solid fuel. All results are shown as simulated mode (the most frequent value) and as range of the lower and upper quantiles, Q<sub>0.15</sub> and Q<sub>0.85</sub>. On average, the highest concentrations of ENM for Europe and USA were found in sludge-treated soil or in the sediment; for Switzerland in the sediment or in sewage treatment plants' effluent. Among the ENMs considered, nano-TiO<sub>2</sub> showed the highest concentrations in general for all regions.



Figure 11. Simulation results (mode values >0.0005 t/a) of the material flow for the ENMs TiO<sub>2</sub>, ZnO, Ag and CNT for the USA. The thickness of the arrows indicates the proportions of the ENM flows, the thickness of the horizontal line within the compartments the proportional magnitude of the removal or accumulation.

Table 7. Simulation results of the predicted environmental concentrations shown as mode (most frequent value) and as range of the lower and upper quantiles (Q(0.15) and Q(0.85)). For air, surface water and sewage treatment plant effluents, the results illustrate current (2008) ENM concentrations, for soil, sludge treated soil and sediments the annual increase of ENM concentration. The results for nano-Ag, CNT and nano-TiO<sub>2</sub> for Switzerland were taken from Gottschalk et al. (15).

	Europe			USA			Switzerland			
<b>nano-TiO<sub>2</sub></b>	<b>Mode</b>	<b>Q<sub>0.15</sub></b>	<b>-Q<sub>0.85</sub></b>	<b>Mode</b>	<b>Q<sub>0.15</sub></b>	<b>-Q<sub>0.85</sub></b>	<b>Mode</b>	<b>Q<sub>0.15</sub></b>	<b>-Q<sub>0.85</sub></b>	
Soil	1.28	1.01	-4.45	0.53	0.43	-2.13	0.28	0.21	-1.04	µg kg <sup>-1</sup> y <sup>-1</sup>
Sludge Treated Soil	89.2	70.6	-310	42.0	34.5	-170				µg kg <sup>-1</sup> y <sup>-1</sup>
Surface Water	0.015	0.012	-0.057	0.002	0.002	-0.010	0.021	0.016	-0.085	µg L <sup>-1</sup>
STP Effluent	3.47	2.50	-10.8	1.75	1.37	-6.70	4.28	3.50	-16.3	µg L <sup>-1</sup>
STP Sludge	136	100	-433	137	107	-523	211	172	-802	mg kg <sup>-1</sup>
Sediment	358	273	-1409	53	44	-251	499	426	-2382	µg kg <sup>-1</sup> y <sup>-1</sup>
Air	<0.0005			<0.0005			0.001	0.0007	-0.003	µg m <sup>-3</sup>
<b>nano-ZnO</b>										
Soil	0.093	0.085	-0.661	0.050	0.041	-0.274	0.032	0.026	0.127	µg kg <sup>-1</sup> y <sup>-1</sup>
Sludge Treated Soil	3.25	2.98	-23.1	1.99	1.62	-10.9				µg kg <sup>-1</sup> y <sup>-1</sup>
Surface Water	0.010	0.008	-0.055	0.001	0.001	-0.003	0.013	0.011	0.058	µg L <sup>-1</sup>
STP Effluent	0.432	0.340	-1.42	0.3	0.22	-0.74	0.441	0.343	1.32	µg L <sup>-1</sup>
STP Sludge	17.1	13.6	-57.0	23.2	17.4	-57.7	21.4	16.8	64.7	mg kg <sup>-1</sup>
Sediment	2.90	2.65	-51.7	0.51	0.49	-8.36	3.33	3.30	56.0	µg kg <sup>-1</sup> y <sup>-1</sup>
Air	<0.0005			<0.0005			<0.0005			µg m <sup>-3</sup>
<b>nano-Ag</b>										
Soil	22.7	17.4	-58.7	8.3	6.6	-29.8	11.2	8.7	-41.2	ng kg <sup>-1</sup> y <sup>-1</sup>
Sludge Treated Soil	1581	1209	-4091	662	526	-2380				ng kg <sup>-1</sup> y <sup>-1</sup>
Surface Water	0.764	0.588	-2.16	0.116	0.088	-0.428	0.717	0.555	-2.63	ng L <sup>-1</sup>
STP Effluent	42.5	32.9	-111	21.0	16.4	-74.7	38.7	29.8	-127	ng L <sup>-1</sup>
STP Sludge	1.68	1.31	-4.44	1.55	1.29	-5.86	1.88	1.46	-6.24	mg kg <sup>-1</sup>
Sediment	952	978	-8593	195	153	-1638	1203	965	-10184	ng kg <sup>-1</sup> y <sup>-1</sup>
Air	0.008	0.006	-0.02	0.002	0.0020	-0.0097	0.021	0.017	-0.074	ng m <sup>-3</sup>
<b>CNT</b>										
Soil	1.51	1.07	-3.22	0.56	0.43	-1.34	1.92	1.44	-3.83	ng kg <sup>-1</sup> y <sup>-1</sup>
Sludge Treated Soil	73.6	52.1	-157	31.4	23.9	-74.6				ng kg <sup>-1</sup> y <sup>-1</sup>
Surface Water	0.004	0.0035	-0.021	0.001	0.0006	-0.004	0.003	0.0028	-0.025	ng L <sup>-1</sup>
STP Effluent	14.8	11.4	-31.5	8.6	6.6	-18.4	11.8	7.6	-19.1	ng L <sup>-1</sup>
STP Sludge	0.062	0.047	-0.129	0.068	0.053	-0.147	0.069	0.051	-0.129	mg kg <sup>-1</sup>
Sediment	241	215	-1321	46	40	-229	229	176	-1557	ng kg <sup>-1</sup> y <sup>-1</sup>
Air	0.003	0.0025	-0.007	0.001	0.00096	-0.003	0.008	0.006	-0.017	ng m <sup>-3</sup>
<b>Fullerenes</b>										
Soil	0.058	0.057	-0.605	0.024	0.024	-0.292	0.026	0.019	-0.058	ng kg <sup>-1</sup> y <sup>-1</sup>
Sludge Treated Soil	2.2	2.1	-22.2	1.01	1.0	-12.2				ng kg <sup>-1</sup> y <sup>-1</sup>
Surface Water	0.017	0.015	-0.12	0.003	0.0024	-0.021	0.04	0.018	-0.19	ng L <sup>-1</sup>
STP Effluent	5.2	4.23	-26.4	4.6	4.49	-32.66	3.82	3.69	-25.1	ng L <sup>-1</sup>
STP Sludge	0.012	0.0088	-0.055	0.01	0.0093	-0.068	0.0107	0.0101	-0.068	mg kg <sup>-1</sup>
Sediment	17.1	6.22	-530	2.5	1.05	-91.3	20.2	8.2	-787	ng kg <sup>-1</sup> y <sup>-1</sup>
Air	<0.0005			<0.0005			<0.0005			ng m <sup>-3</sup>

For soils and sediments, the simulations provided the ENM amount deposited in these compartments in 2008. Using estimations of the worldwide market evolution for products containing ENMs for the period 2001–2012 (38, 39) and assuming zero concentrations in 2000 we scaled the deposition of ENM in 2008 to roughly estimate deposition amounts and ENM concentrations for each year of the period considered. (Fig. 12). The concentrations in sediments (USA) will presumably rise between 2008 and 2012 from 0.2 mg/kg to 0.6 mg/kg for nano-TiO<sub>2</sub>, from 1.8 µg/kg to 5.7 µg/kg for nano-ZnO, from 0.7 µg/kg to 2.2 µg/kg for nano-Ag, and from 0.2 µg/kg to 0.5 µg/kg for CNT. In the case of fullerene, the concentrations remain close to zero. The concentrations in sludge-treated soil increase from 0.1 mg/kg to 0.5 mg/kg for nano-TiO<sub>2</sub>, from 6.8 µg/kg to 22.3 µg/kg for nano-ZnO, from 2.3 µg/kg to 7.4 µg/kg for nano-Ag, and from 0.1 µg/kg to 0.4 µg/kg for CNT. In a manner similar to that of concentrations in sediments, no meaningful concentrations were observed in sludge-treated soil for fullerenes.

### 3.3.3 Risk estimation

Although several reports assessed toxic effects for different ENMs to organisms in environmental compartments (2, 3), difficulties in quantifying these effects still remain due to the lack of standardization in testing. However, toxicity data was available for some ENMs and environmental compartments (Table 19, Supporting Information), and risk quotients (RQ) could thus be calculated (Table 8). For the carbon based ENM fullerenes and CNTs, the RQs were below 1. For the inorganic ENMs (Ag, TiO<sub>2</sub>, ZnO), the RQs were greater than 1 for sewage treatment effluent, but below (TiO<sub>2</sub>, ZnO) this critical value for the other environmental compartments. However, with the exception of the USA, the RQs for nano-Ag in water bodies were around one. Unfortunately, due to the lack of available studies, it was not possible to calculate RQs for soil and sediment for some materials.

## 3.4 Discussion

Of all the ENMs considered, nano-TiO<sub>2</sub> generally showed the highest concentrations for all compartments, followed by nano-ZnO. This reflects the worldwide production volumes of the ENMs. Therefore, it seems obvious that production volumes of ENMs are crucial input factors. The uncertainty about ENM production volumes is very high and, hence, the range of the available data is very broad. Thus, reducing the great uncertainties in the quantification of the total production volumes and the allocation of these volumes to application quantities in relevant commercially available products is crucial for improving the model. However, apart from worldwide production and application volumes, comparable environmental concentrations of nano-TiO<sub>2</sub> and nano-ZnO also reflect a similar distribution of the main product categories (cosmetics and coatings & cleaning agents) that both result in significant release into water. Water concentrations of CNTs or fullerenes might possibly increase as well if those materials were applied in product categories with relevant ENM emissions to water bodies.

Comparing the modeled regions, it is noteworthy that the ENM concentrations for a particular environmental compartment are in a similar range for all three regions. This may be due to the fact that ENM production volumes were scaled according to the number of inhabitants of the particular region. Regional distinctions regarding ENM applications would be needed to better model region-specific ENM flows from the production, manufacturing and consumption processes to environmental and technical compartments. In order to incorporate these differences, it would

be useful to build regional databases on products containing ENM. In addition to enhancing region-specific modeling of ENM emissions, it will also be important to follow the development of new products containing engineered nanomaterial to further improve the model. Products with novel ENM emission properties, which are not currently relevant and thus not considered in the product categories, could lead to significantly higher ENM emission volumes that, combined with unexpectedly high ENM application and production volumes, could turn upside down the simulation results of ENM emissions from the PMC process to environmental and technical compartments.

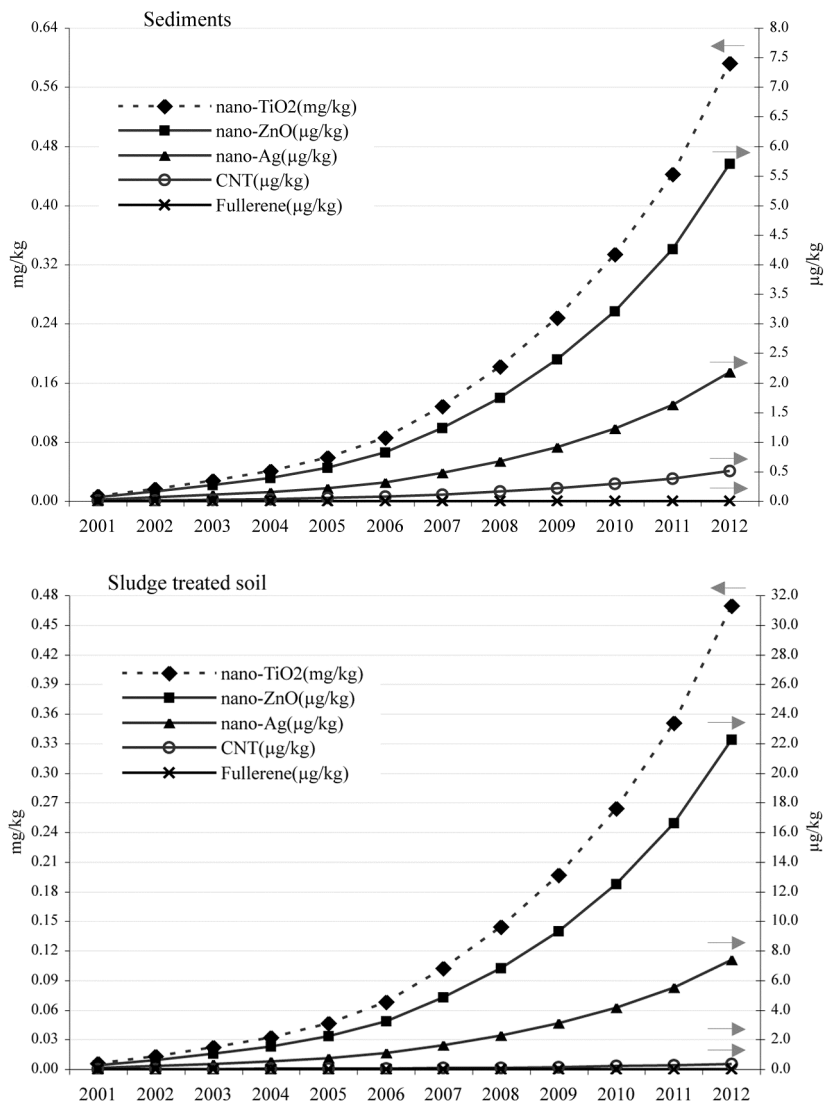


Figure 12. Predicted nanomaterial concentrations (USA) in sediment and sludge treated soil for nano-TiO<sub>2</sub> in mg/kg (left side axis ←) and for nano-ZnO, nano-Ag, CNTs and fullerene in µg/kg for the period 2001–2012.

Due to a lack of the mentioned regional information in the presented modeling, the input parameters differed only by the total ENM production volumes and material disposal pathways between the considered regions. Thus, the simulated flows and environmental concentrations of the corresponding ENMs do not vary significantly between the modeled systems. The main

difference between the regions is visible in the different approaches of handling sewage sludge. Countries with a high proportion of land-disposal will have to deal with increasing concentrations of ENMs in sludge-treated soil, while countries with complete incineration of sludge should not experience this problem.

*Table 8. Risk quotients (PEC/PNEC) for all ENM and regions. The quotients for soils and sediments reflect the current state of ENM accumulation as illustrated in Figure 12. The values for nano-Ag, CNT and nano-TiO<sub>2</sub> for Switzerland were taken from Gottschalk et al. (15).*

<b>Compartment</b>	<b>Europe</b>	<b>USA</b>	<b>CH</b>
	<b>nano TiO<sub>2</sub></b>		
Surface Water	0.015	0.002	0.021
STP Effluent	3.47	1.75	4.28
Air	<0.0005	<0.0005	<0.0005
Soil	0.004	0.002	0.001
Sludge Treated Soil	0.303	0.143	
	<b>nano-ZnO</b>		
Surface Water	0.247	0.019	0.316
STP Effluent	10.81	7.7	11.02
	<b>nano-Ag</b>		
Surface Water	1.098	0.166	1.031
STP Effluent	61.09	30.1	55.60
Air	<0.0005	<0.0005	<0.0005
	<b>CNT</b>		
Surface Water	<0.0005	<0.0005	<0.0005
STP Effluent	<0.0005	<0.0005	<0.0005
Sediment	<0.0005	<0.0005	<0.0005
Air	<0.0005	<0.0005	<0.0005
Soil	<0.0005	<0.0005	<0.0005
Sludge Treated Soil	<0.0005	<0.0005	
	<b>Fullerenes</b>		
Surface Water	<0.0005	<0.0005	<0.0005
STP Effluent	0.026	0.023	0.019
Soil	<0.0005	<0.0005	<0.0005
Sludge Treated Soil	<0.0005	<0.0005	

Our model assumes homogeneous and well-mixed compartments on a country or continent-wide scale (17). In order to cover local conditions such as e.g. those near ENM-producing factories, near sewage treatment outflows or for special release events such as accidents, further modeling has to be conducted which – once the data is available – will also be possible with the probabilistic approach.

For Europe and the USA, relatively high concentrations of ENMs were found on soil treated with sewage sludge. Due to the very low fraction of soil to which sewage sludge is applied, the relevant volume for this compartment is very low. Therefore, it seems reasonable that these particular concentrations are much higher than for the soil compartment as a whole. Our model also includes sedimentation of ENMs in surface waters. Although information on aggregation and

sedimentation of ENMs under natural conditions is sparse, we can expect that a relevant fraction of the ENMs will be removed from waters and settle into the sediment. The inclusion of this sedimentation process can explain the relatively large difference in the surface water concentrations of  $\text{TiO}_2$  and nano-Ag compared to the previous study of Mueller and Nowack (7). For all regions, air shows the lowest PEC compared to the other environmental compartments; this is mainly due to its high volume and the short residence time (10 days) of ultrafine particles. ENMs reach the atmosphere either during the usage of products or via emissions from waste incineration plants at low percentages. Additionally, they could agglomerate and/or be coated by organic and inorganic material on time scales shorter than 10 days.

In our modeling we did not distinguish between specific forms of ENMs, e.g. between single and multi-walled CNTs and the various forms of fullerenes (e.g. C60, C70). Due to the absence of data we also lumped together all the different modifications, functionalizations and surface-coatings of the ENMs. ENMs may be technically altered to fit the purpose of the end product such as e.g. being water soluble or insoluble. With the probabilistic modeling, we included this uncertainty in some processes (e.g. the sedimentation behavior) by using transfer factors that include the behavior of both pristine and modified ENMs, e.g., CNT and fullerenes. Derivatized fullerenes are assumed to stay dispersed in water, whereas almost complete sedimentation is assumed for non-derivatized fullerenes. In such cases, bimodal distributions have to be modeled. For the soluble ENMs (e.g. nano-Ag and nano-ZnO), the dissolution rate in water is difficult to quantify; further studies are needed to fully understand their behavior and fate in natural water bodies and to quantify their release during usage or washing of ENM containing products. Slightly soluble materials such as e.g. ZnO (at pH 7) may be protected from dissolution by a corrosion layer. Furthermore, ENMs may also be coated by other substances, such as silica, meaning that it is difficult to generalize the environmental fate of a particular ENM. Additional to such technically intended modifications in functionalization or coating characteristics, changes in the engineered nanomaterial properties induced by chemical and physical processes in the environment or by their reaction with natural compounds cannot be excluded. Besides this mentioned environmental fate and behavior, size and functionalization of ENMs could also influence the toxic effects of the particular ENM. However, due to a lack of data, a differentiation of toxicological data based on derivatization and functionalization of ENMs was not possible.

For nano-Ag, nano- $\text{TiO}_2$  and nano-ZnO, the RQ (PEC/PNEC) exceeded the critical value of one for sewage treatment plant effluents, meaning that further investigations are needed to evaluate the risk posed to aquatic organisms by these ENMs. This urgent need for further investigations is in addition emphasized by the fact that the RQ for nano-Ag in water is slightly above one (EU, Switzerland). For the other environmental compartments for which toxicological data was available, no risks to organisms are currently expected. However, it should also be emphasized here that the calculation of the RQ involves a safety factor of 1000. A RQ slightly above one does therefore not constitute an immediate risk but is an indication that further data are needed.

Although ENM concentrations in sediments and sludge-treated soil (USA) increase from 2008 to 2012, the RQs derived for CNTs in sediments and for nano- $\text{TiO}_2$ , CNTs and fullerenes in sludge-treated soil for 2012 are far below one. The only pronounced RQ (0.3) was calculated for nano- $\text{TiO}_2$  in sludge-treated soil. This parallels the modeled critical RQ for nano- $\text{TiO}_2$  in sewage treatment plant effluents and, given the implication that both nano-Ag and nano-ZnO show even

higher RQs for sewage treatment plant effluents, the ecotoxicological effects in sludge-treated soils of these two ENMs need further investigation as well.

In order to validate results of modeled environmental concentrations as presented in this study, a comparison between our data and measurement data is necessary. Kiser et al. (40) measured 5–15 µg/L nano-TiO<sub>2</sub> in STP effluents. This validates very well our calculations (mode values) of nano-TiO<sub>2</sub> in STP effluents: EU 3.47 µg/L, USA 1.75 µg/L, Switzerland 4.28 µg/L. However, it has to be noted that in their study Kiser et al. used filtration with 0.45 µm and their value may thus also include part of the bulk TiO<sub>2</sub> released into STP. Blaser et al. (9) calculated total Ag concentrations in surface waters which were by a factor 10–100 higher than our simulation results for nano-Ag and they also concluded that nano-Ag contributes only 1–15% to the total Ag into the environment. First measurements (40) of nano-TiO<sub>2</sub> in STP sludge indicated concentrations which ranged from 1 to 6 g/kg. Our simulations showed concentrations (mode values) of the same order of magnitude: EU and USA 0.14 g/kg, Switzerland 0.2 g/kg. These first measurements of ENM in the environment show concentrations in the same order of magnitude than our modeling results and thus allow a first validation of some aspects of our model.

### 3.5 Acknowledgments

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### 3.6 Supporting information available

Description of the system compartments. ENM production volumes and allocation of these volumes to product categories. Table with worldwide production volumes for ENM. Table with product categories for each ENM with the modeled input distribution. Table with parameters for release of ENM from products, Table with considered ecotox studies. This information is available free of charge via the Internet at <http://pubs.acs.org>.

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## 4. Possibilities and Limitations of Modeling Environmental Exposure to Engineered Nanomaterials by Probabilistic Material Flow Analysis

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### Abstract

Information on environmental concentrations is needed to assess the risks that engineered nanomaterials (ENM) may pose to the environment. In this study, predicted environmental concentrations (PEC) were modeled for nano-TiO<sub>2</sub>, carbon nanotubes (CNT) and nano-Ag for Switzerland. Based on a life-cycle perspective, the model considered as input parameters the production volumes of the ENMs, the manufacturing and consumption quantities of products containing those materials, and the fate and pathways of ENMs in natural and technical environments. Faced with a distinct scarcity of data, we used a probabilistic material flow analysis model, treating all parameters as probability distributions. The modeling included Monte Carlo and Markov Chain Monte Carlo simulations as well as a sensitivity and uncertainty analysis. The PEC values of the ENMs in the different environmental compartments vary widely due to different ENM production volumes and different life cycles of the nano-products. The use of ENM in products with high water relevance leads to higher water and sediment concentrations for nano-TiO<sub>2</sub> and nano-Ag, compared to CNTs, where smaller amounts of ENM reach the aquatic compartments. This study also presents a sensitivity analysis and a comprehensive discussion of the uncertainties of the simulation results and the limitations of the used approach. In order to estimate potential risks, the PEC values were compared to the predicted no effect concentrations (PNEC) derived from published data. The risk quotients (PEC/PNEC) for nano-TiO<sub>2</sub> and nano-Ag were larger than one for treated wastewater and much smaller for all other environmental compartments (e.g., water, sediments, soils). We conclude that probabilistic modeling is very useful for predicting environmental concentrations of ENMs given the current lack of substantiated data.

### Keywords

Probabilistic material flow analysis; Engineered nanomaterials; exposure assessment; Predicted environmental concentrations; Predicted no effect concentrations.

## 4.1 Introduction

An expected increase in the manufacture and usage of engineered nanomaterials (ENM) for research purposes, environmental applications and use in commercial products is likely to result in exposure of the natural environment to these materials [1–5]. Nanosized TiO<sub>2</sub> (nano-TiO<sub>2</sub>) and nanosized Ag (nano-Ag) are some of the ENMs most frequently used in consumer products [6; 7]: nano-TiO<sub>2</sub> are produced mainly for utilization in paints, coatings, cleaning agents, and cosmetics, nano-Ag for applications in consumer electronics, cosmetics, coatings, cleaning agents, and textiles ([8; 9], <http://www.nanotechproject.org/inventories>; <http://www.nanoroadmap.it/>). Carbon nanotubes promise to be suitable for applications primarily in the polymer and consumer electronics industries and the energy sector [10].

Release of ENMs into the environment may occur during the production of the ENMs, the manufacturing of ENM-containing products, and the use and reuse phases of these products [2; 11]. Risks from ENM emissions may emerge if both exposure (due to ENM presence in the environment) and hazards (in the form of toxic effects) are observed [4]. Thus, investigations on the environmental concentrations and on the toxicity of ENMs provide the basis for assessing the potential risks these compounds pose to the environment.

However, almost no analytical methods have been available so far to detect trace concentrations of such materials. Kaegi et al. [12] provided evidence of emissions of nano-TiO<sub>2</sub> from exterior facades into water and also detected engineered nano-TiO<sub>2</sub> in natural waters. Two other recent studies [13; 14] reported nano-Ag emissions into water from laundering nano-textiles. Due to the almost non-existent data basis concerning concentrations of manufactured ENMs in the environment, modeling of predicted environmental concentrations (PEC) is necessary. Only a few studies [6; 15–17] present quantitative estimations of PECs for engineered nanomaterials. Blaser et al. [15] have modeled Ag emissions from biocidal products which contained nanosized silver (nano-Ag). However, the emissions were modeled as the release of silver from ENMs; nano-Ag was seen exclusively as the source of Ag<sup>+</sup>. Thus, no particulate emission flows were considered. Boxall et al. [16] have presented a series of algorithms which were applied to predict concentrations of ENMs in air, soil and water. However, this is a simplistic modeling framework based on hypothetical usage scenarios for selected product types and applied to a limited range of products, environmental compartments and life cycle stages of ENMs. Mueller and Nowack [6] have presented the first investigations aimed at modeling quantities of engineered nanomaterials released into the environment from a complete life-cycle perspective. Three types of ENMs were studied: nano-Ag, nano-TiO<sub>2</sub>, and CNTs. The calculated PEC values for nano-TiO<sub>2</sub> in surface water ranged from 0.7 to 16.0 µg/L (realistic scenario to high emission scenario); for nano-Ag, they were 30 to 80 ng/L, and for CNT 0.5 to 0.8 ng/L.

For calculating risks, such PECs may be contrasted to predicted no effect concentrations (PNEC). Several studies have already reported toxic effects of ENMs on different organisms [2]. Predicted no effect concentrations may be derived, e.g. from NOECs (no observed effect concentrations), which are divided by extrapolation factors depending on the quality of available data (e.g., acute ecotoxicity, chronic ecotoxicity) [18]. Risk is then defined as the ratio PEC/PNEC, for which numbers equal to or greater than one indicate cause for concern. The calculated risk quotients (PEC/PNEC) for nano-Ag and CNT from Mueller and Nowack [6] did not indicate any expected negative effects. The risk quotient for nano-TiO<sub>2</sub>, however, was 0.7 to 16.0 for the water compartment. The study was not comprehensive, as the environmental

compartments sediment and groundwater as well as production, manufacturing, and recycling processes with all their associated ENM flows were not included. Furthermore, the incorporation of uncertainties and variability of the model input parameters were restricted to a two-scenario analysis.

A particular challenge in modeling environmental concentrations of ENMs is that risk estimation has to integrate the uncertainty about the accuracy of the calculated assessment parameters and the natural variability of these parameters. An extreme lack of empirical data cannot be resolved in a purely statistical manner because we often need predictions concerning parameter values that have not yet been measured. For many environmental contaminants, such data gaps are filled using assumptions, extrapolations or safety factors [19]. Estimating risks inherent in new compounds demands approaches to handling the inherent uncertainties and to simulating the compounds' environmental fate under various possible conditions. Because of the absence of data on the use, release and environmental fate and because of inconsistencies in the available information, the use of a probabilistic modeling approach [20–23] may be appropriate if one intends to take uncertainties about the magnitude and variability of the model input parameters into account. However, a Monte Carlo (MC) approach to build probability input distributions requires empirical data as well [24]; otherwise model input distributions have to be calculated only by means of assumptions. As an alternative Bayesian techniques [25] can provide model input distributions combining pure judgment also with very few available data. Gottschalk et al. [26] developed a probabilistic material flow analysis model (PMFA) based on a Monte Carlo and Markov Chain Monte Carlo (MCMC) approach, which is suitable to calculate PEC values for any chemical when faced with a lack of data or inconsistency in available data. This PMFA was recently used to model PECs for different ENM and regions [27]. However, methodological possibilities and limitations were not analyzed and discussed.

The goal of the present study is to discuss possibilities and limitations of the application of PMFA [26] in ENM exposure modeling based on a case study of nano-TiO<sub>2</sub>, CNTs and nano-Ag for Switzerland. The potential risks caused by these three ENMs were assessed by comparing the PEC values to available PNEC values. This study also extends the exposure modeling of Mueller and Nowack [6] by considering the environmental compartments sediment and groundwater as well as production, manufacturing and recycling processes.

## **4.2 Materials and methods**

### **4.2.1 System analysis**

The material flow model [26] consists of 11 boxes representing all ENM life-cycle stages. The model considers 35 internal, 11 accumulation, 1 ENM generation (within the first process), 11 elimination and 5 system leaving flows. The environmental compartments (lower atmosphere, soil, surface water, groundwater, and sediments) were regarded as homogeneous and equally mixed for estimating a regional PEC [18]. Accumulation in technical environments (production, manufacturing, and consumption processes (PMC), recycling process (R), sewage treatment plant (STP), waste incineration plant (WIP)) was not considered for steady state calculations. The geographical boundary of the model was Switzerland. All data and calculations refer to the base year 2008. No internal geographical differentiation was applied.

The PMC box was modeled as one unit subdivided into ENM production, manufacturing of ENM-containing products and consumption processes of such products, including the end of life phase of the ENM-containing products. Hence, the system input of ENM and the resulting particle release to the environment are presented by a three-layer modeling. However, there are no quantitative data available concerning emission quantities from such production and manufacturing processes. Zero to two (uniformly distributed) of the ENMs were thus assumed to enter the system from each of the two last-mentioned processes.

In Switzerland, all WIP are fitted with different types of filters ([28], <http://www.bafu.admin.ch/abfall/01495/01496/index.html?lang=en>). Electrostatic filters trap fly ash and dust, while gaseous pollutants are removed by means of gas scrubbers. Catalytic NOx/furan/dioxin removal equipment is also in operation at all facilities. Due to a landfilling ban, all non-recycled combustible waste must be incinerated.

Connection to STPs for wastewater is near 100% in Switzerland. The water volume of the STP effluent (treated water) was derived from a daily water consumption of 200 L [18] per inhabitant. The overflow discharge during heavy rainfall was uniformly distributed between 3 and 16% (P. Fischer, Federal Office for the Environment (FOEN), Bern, personal communication; R. Mueller, Kläranlage Hard, Winterthur, personal communication). The annual dry sewage sludge production in Switzerland was estimated to be 203,000 t [29] which was entirely burned in waste incineration plants. The application of sludge on landfills and soil is not permitted in Switzerland; all sludge is processed in the WIPs.

The surface water volume (rivers and lakes) of 5.2 km<sup>3</sup> was obtained considering a mixing depth of 3 m [18] which was then multiplied by 4.2% [18] of the total area (41,285 km<sup>2</sup>) of Switzerland. A water residence time of 40 d was considered [18]. The considered soil volume of 4.2 km<sup>3</sup> was calculated by multiplying areas of different soil types with their corresponding soil mixing depth [18], i.e., 0.2 m for agricultural soil and 0.05 m for natural and urban soil; the fraction of agricultural soil was 0.369 [30] and that of natural and urban ground was 0.631. A soil density of 1,500 kgm<sup>-3</sup> was used. The considered air volume was 41,285 km<sup>3</sup> and was obtained by multiplying the total area of Switzerland with the relevant air height for terrestrial ecosystems of 1 km [18]. The relevant sediment volume of 0.05 km<sup>3</sup> was calculated based on the area of the water surface, which was multiplied by a sediment depth of 0.03 m [18]. A dry sediment density of 260 kgm<sup>-3</sup> was taken. The density was calculated by subtracting the water content from the standardized value of 1,300 kgm<sup>-3</sup> recommended by the European Commission [18].

#### 4.2.2 Modeling and simulations

The simulations were conducted using a probabilistic material flow model presented in Gottschalk et al. [26], which is implemented in R [31] and allows one to treat all model parameters throughout the modeling process as probability distributions. The model output represents an ENM flow system, depicted by probability distributions. These distributions were derived from MC simulations. Bayesian inferences based on MCMC iterations were also modeled for parameters with available measurement data (e.g., sedimentation rate of nano-TiO<sub>2</sub> and CNT). In contrast to scenario analysis, this method provides insight into the probability of each modeled output value along with a higher quantity of outputs. The uncertainty and variability of the model input parameters as well as their impact on the modeled outputs were analyzed as well. Monte Carlo techniques were first used to compute probability distributions of all model input parameters and



then to repeatedly solve a linear equation system on which the proposed ENM flow chart system was mapped mathematically. For the computation of those model-input distributions as well as for the resolution of the equation system, 100,000 iteration steps were carried out. The robustness of this number of iterations is discussed and verified in Gottschalk et al. [26]. In a further step, both a sensitivity and an uncertainty analysis [26] were carried out by decreasing each input parameter by 10% in order to recalculate the ENM flows in every single case. This allowed us to identify the ENM flows that contribute most to the variances of the computed concentrations and to estimate the confidence degree of the exposure assessment. The latter might be considered higher when the most influential variables are based on comparably secure and more detailed input data.

*Table 9. Production quantities of ENMs in t per year for Switzerland<sup>a</sup>*

	Mode	Mean	SD	Sources
nano-TiO <sub>2</sub>	114	240	195	[7; 33; 68]
CNT <sup>b</sup>	1.9	2.6	1.2	[7; 11; 34; 69–71]
nano-Ag	1.1	2.3	1.7	[7; 15; 35]

<sup>a</sup>The values are based on the worldwide production volumes, scaled to production volumes for Switzerland (factor 139.91). The volumes for Switzerland describe mode, mean and standard deviation (SD) of lognormal distributions, which stem from Monte Carlo simulations (100,000 iterations), and which were modeled based on logarithmic means and standard deviations derived from the indicated data.

<sup>b</sup>Carbon nanotubes.

#### 4.2.3 Input parameters

The model input parameters were comprised by the annual ENM input into the system, the mass distribution of ENMs to product categories, and the transfer coefficients (TC) which determined the ENM flows between (emissions) and inside of the compartments (elimination and accumulation) as well as into (ENM generation) and out of the system (export). The number of model input parameters considered were 104, 69, and 106 for nano-TiO<sub>2</sub>, CNT, and nano-Ag, respectively. We chose triangular distributions for the input parameters when the most probable outcome was known (guessed or measured) and assumed this mode bounded between two parameter values, e.g., for some allocations of ENM production quantities to the amounts applied in different products categories or for coefficients of CNT flows in incineration plants. Uniform distributions were used for parameters that had not yet been well-studied, such as some TCs between the environmental compartments, and log normal distributions were applied where the input values ranged theoretically from 0 to an unlimited value, such as in the case of the amounts of the ENMs produced annually.

*ENM production.* Data found for ENM worldwide production quantities were allocated to Switzerland based on a comparison of the total population of high income countries [32] to the Swiss population. Information from Schmid and Riediker [7], the only empirical study which provided direct information to ENM production volumes for the studied region was used as well.

Lognormal distributions were modeled based on logarithmic means and standard deviations derived from these data. The most frequently assumed values (modes, rounded to two digits) of ENM production volumes for Switzerland (Table 9) were 114 t/a for nano-TiO<sub>2</sub>, 1.9 t/a for CNT and 1.1 t/a for nano-Ag. However, the relatively high standard deviations caused by the variance of the data are worth noting (Table 9). For the nano-TiO<sub>2</sub>, the literature search provided production volumes which, scaled to Switzerland, ranged from 5 t/a [33] to 435 t/a [7]. For CNT, the values ranged from 1 t/a [7] to 3.57 t/a [34]. For nano-Ag, the maximum found was 4.03 t/a [15], the minimum being 0.026 t/a [35]. On average 2% of the ENMs were considered to be released to the other system compartments during manufacturing of ENM containing products and ENM production. The remaining part of ENM was allocated to commercially available ENM-containing products.

*ENM products.* The ENM containing products were grouped into product categories (see Table 10). This categorization assumed equal ENM emission properties of the corresponding products. The categories were determined by means of an Internet-based ([8; 36], <http://www.nanotechproject.org/>; <http://www.ec21.com/>) qualitative analysis of commercially available ENM-containing products.

Table 10. Mass fractions of engineered nanomaterials allocated to product categories<sup>a</sup>

Product Category	nano-TiO <sub>2</sub>			CNT <sup>b</sup>			nano-Ag		
	Mean	Min	Max	Mean	Min	Max	Mean	Min	Max
Cosmetics	0.4218	0.0036	0.8190	-	-	-	0.008	0.004	0.019
Filter Aggregates	0.2724	0.0359	0.7221	-	-	-	0.048	0.012	0.106
Coatings and Cleaning Agents	0.1051	0.0006	0.4421	-	-	-	0.291	0.081	0.590
Plastics	0.1258	0.0004	0.5231	-	-	-	0.028	0.009	0.062
Composites	-	-	-	0.4862	0.0000	0.9758	-	-	-
Consumer Electronics	0.0397	0.0002	0.2397	0.4517	0.0000	0.9785	0.055	0.021	0.118
Paint	0.0198	0.0000	0.1648	-	-	-	0.201	0.000	0.528
Glass and Ceramics	0.0099	0.0000	0.0647	-	-	-	0.008	0.000	0.033
Light Bulbs	0.0020	0.0000	0.0153	-	-	-	-	-	-
Metals	0.0010	0.0000	0.0077	-	-	-	0.002	0.000	0.004
Batteries and Capacitors	0.0010	0.0000	0.0074	-	-	-	-	-	-
Textiles	0.0008	0.0000	0.0062	-	-	-	0.254	0.119	0.490
Ink	0.0007	0.0000	0.0045	-	-	-	-	-	-
Dietary Supplement	0.0000	0.0000	0.0000	-	-	-	0.106	0.034	0.283
Research and Development	-	-	-	0.0621	0.0000	0.8932	-	-	-

<sup>a</sup>The values (mean, minimum, maximum) describe the computed distributions of the input parameters extracted from Monte Carlo simulations (100,000 iterations).

<sup>b</sup>Carbon nanotubes.

The allocation of the considered ENM production mass to these product categories was calculated based on the ratio of the number of ENM-containing products in each category to the total number of ENM-containing products and the average mass of ENMs in each product. To count the commercially available ENM-containing products and assign them to the product categories, a four-fold web search was carried out. We used the international versions of Google (on 09/12/2008) and Yahoo (on 09/16/2008) search engines and the international inventories of EC21 ([36], <http://www.ec21.com/>) (on 09/15/2008) and the Woodrow Wilson Institute ([8], <http://www.nanotechproject.org/>) (on 09/15/2008; 10/6/2008). From the investigations based on the two search engines, the first 500 commercially available ENM-containing products were analyzed. Only products taken from the manufacturer's site were counted; those presented in general online sales were not considered. From the EC21 inventories (EC21, 2008), all results were counted with the exception of commercially unavailable products, e.g., masterbatch solutions and ENM powders. All results obtained from the Woodrow Wilson Institute's inventory of nanotechnology-based consumer products [8] were used. In addition, a report from National Industrial Chemicals Notification and Assessment Scheme (NICNAS) [33] was used for nano-TiO<sub>2</sub> applications, and Schmid and Riediker [7] was referred to for nano-TiO<sub>2</sub>, and nano-Ag ones. Based on the accuracy of the data, either a uniform or a triangular distribution of the fraction of products in each category was modeled. In most cases where the results from the four Internet search data basis showed identical or comparable values in at least three cases, triangular distributions were modeled. If the results did not show any trend, the lowest and the highest probable fraction of products per product category were considered when modeling uniform probability distributions. The average mass of ENMs per product in each category was estimated by means of the total mass of products containing ENM and the average fraction of ENMs per product in a corresponding product category. The ENM fraction was obtained from Boxall et al. [16], from manufacturer's specifications or from personal communications.

Table 11. Release of engineered nanomaterials (ENM) from products, manufacturing of ENM containing products and ENM production<sup>a</sup>

Product Category	STP <sup>b</sup>			WIP <sup>d</sup>			Atmosphere			Landfill			Soil			Water			Recycling			Elimination			Export				
	TiO <sub>2</sub>	Ag	CNT <sup>c</sup>	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT		
Nanomaterial	TiO <sub>2</sub>	Ag	CNT <sup>c</sup>	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT	TiO <sub>2</sub>	Ag	CNT		
Plastics				1.00	0.95	1.00																							
Cosmetics	0.90	0.73		0.05	0.04										0.05	0.04													
Coatings and Cleaning Agents	0.90	0.73		0.05	0.04		0.05	0.04																					
Batteries and Capacitors				0.28																							0.73		
Metals	0.05	0.05		0.05	0.05																					0.05	0.90	0.86	
Paint	0.20	0.16							0.50	0.41		0.25	0.20		0.05	0.04											0.18		
Light Bulbs				0.10																							0.91		
Glass and Ceramics				1.00	0.81																						0.19		
Filter Aggregates				0.28	0.22																						0.19	0.73	0.59
Consumer Electronics				0.28	0.26	0.28															0.73					0.05	0.73	0.69	
Textiles	0.50	0.20		0.25	0.14			0.05																		0.48	0.25	0.13	
Dietary Supplement	0.90	0.90		0.10	0.10																								
Research and Development			0.01			0.98					0.01																		
Ink	0.08			0.92																									
Manufacturing	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	0.33	
Production	0.75	0.75	0.75				0.25	0.25	0.25																				

<sup>a</sup>The values (averages that were enlarged and reduced by 20% to build uniform model input distributions) refer to the fraction of the total amount of ENM released, transferred or dissolved from a particular source.

<sup>b</sup>Sewage treatment plants.

<sup>c</sup>Carbon nanotubes.

<sup>d</sup>Waste incineration plants.

*ENM flows.* The acquisition of input data to model ENM flows was focused on the estimation of distributions for each TC. In cases where absolutely no data were found, e.g., for the TC of nano-TiO<sub>2</sub> from textiles to the STP, the TCs were uniformly distributed between 0 and 1. For some TCs, only a single deterministic value could be derived, and in such cases uniform distributions were built by increasing and decreasing the assumed mean value by 20%. Particles ending up in soil, landfill and sediments were assumed to accumulate within these compartments.

*PMC process.* Dissolution of nano-Ag was quantified based on information given in Blaser et al. [15] for the release of Ag from biocidal plastics and on Benn and Westerhoff [13] for release from textiles. No continuous dissolution was considered in natural waters, as relatively low dissolution was assumed during exposure [37] and little quantitative information was available on this reaction. It has been shown that nano-Ag dissolves by less than 1% in different natural waters [38] and in algal growth media [39]. For composites and sporting goods (plastics) complete waste disposal was assumed. Engineered nanomaterials from cosmetics, coating and cleaning agents, dietary supplements, or production processes were mainly emitted to sewage treatment plants. For textiles, emissions due to friction and especially laundering were considered, based on results obtained by Benn and Westerhoff [13]. Recycling was considered for consumer electronics (CNT), batteries and capacitors, textiles, cosmetics and filter aggregates (nano-Ag). There is no data basis to estimate ENM quantities leaving the *recycling* process. Engineered nanomaterials ending up in this process were assumed to be eliminated, as they are either combusted or incorporated into new materials, e.g., during metal smelting. Table 11 provides a complete overview of all TCs of the emission flows from PMC.

*Wastewater treatment.* For nano-Ag and nano-TiO<sub>2</sub>, a removal between 90.6 and 99.5% (uniform distribution) was used based on the only available study of ENM removal from wastewater [40]. A removal efficiency between 96.3 and 99.7% (uniform distribution) was estimated for CNT based on data about its aggregation in the presence of high concentrations of dissolved organic matter [41; 42].

*Waste incineration.* Engineered nanomaterials entered the environment in very small quantities via flue gas cleaning from WIPs. The removal efficiency of multistage flue gas cleaning filters for particles smaller than 100 nm was taken from Burtscher et al. [43] and was at least 99.9%. Eighty percent of the filter ash was exported [44], with the remaining being deposited in landfills. Carbon nanotubes are combustible and should, theoretically, burn fully. However, in the absence of oxygen (as in the case of batteries), these particles may reach the bottom ash [11; 45]. Based on standard carbon mass flows for incineration plants [46], a triangular probability distribution with a peak at 0.98 and boundaries between 0 and 1 for elimination of CNT was modeled. The fraction not eliminated was randomly allocated either to the slag or to the flue gas cleaning. The fraction ending up in slag was modeled as uniform distribution from 0 to 1. According to this distribution the remaining part was assumed to reach the flue gas cleaning installation. In the same way incombustible nano-Ag and nano-TiO<sub>2</sub> were allocated either to the flue gas cleaning installation or to the slag.

*Surface waters.* It was presumed that ENMs entering this compartment were either deposited to the sediment or transferred out of the system as part of the rivers' outflow. The sedimentation rate of nano-TiO<sub>2</sub> in water was modeled using results from Fang et al. [47] as measurement data to run MCMC iterations, which produced a highly right skewed lognormal posterior distribution for

the sedimented fraction with a minimum of 0.29 and a maximum of 1. The same applied to CNTs where results presented in Hyung et al. [41] and Kennedy et al. [42] were used to generate uniform distributions for the sedimented fraction with minimal and maximal values of 0.79 and 0.99. Due to an absence of information concerning the sedimentation of nano-Ag, a uniform distribution from 0 to 1 was assumed.

*Lower atmosphere.* Considering a retention time of 10 d for ultrafine particles [48], approximately one thirty-sixth of the ENM input into the air compartment constantly remains in the lower atmosphere. Dry and wet deposition from air to water and to soil occurs according to the ratio of the land areas covered by water and soil (0.042/0.958).

#### 4.2.4 Sensitivity analysis

The sensitivity analysis was performed as described in Gottschalk et al. [26]. First, the mean values of each simulated input parameter and output variable were calculated. Afterwards a differential value was computed for each output variable by decreasing in each case the mean of a particular input parameter by 10%. The proportional change in the output variable was then divided by the proportional change of the varied input. In order to calculate the “sensitivity” of a simulation output variable to the varied input considering also the uncertainty of the considered input, this ratio (proportional change of the input to the proportional change of the output) was multiplied by the standard deviation of the distribution of the changed input parameter. Lastly all single sensitivity values were summed (total sensitivity) to calculate each parameter’s contribution by percent to the total sensitivity of the studied simulation output variable.

#### 4.2.5 Toxicity assessment

The PNEC values for the studied ENMs were extracted or calculated from ecotoxicological literature. The given values (NOEC, median lethal effect concentration [LC50] and median effect concentration [EC50]) were, due to the low number of available studies, divided by an assessment factor of 1000 to obtain the PNEC [18]. The  $PNEC_{\text{nano-TiO}_2}$  (water) of 1  $\mu\text{g/L}$  for organisms in water was derived from NOEC values of 1 mg/L [49] for *Daphnia magna* and 0.98 mg/L [50] for *Pseudokirchneriella subcapitata*. The  $PNEC_{\text{nano-Ag}}$  (water) of 0.696 ng/L was derived from an LC50 of 0.696  $\mu\text{g/L}$  [38] for *Ceriodaphnia dubia*. In the case of CNTs for zebrafish embryos *Danio rerio* a NOEC of 40  $\mu\text{g/ml}$  [51] for multi-walled carbon nanotubes led to a  $PNEC_{\text{CNT}}$  (water) of 40  $\mu\text{g/L}$ . The only threshold concentrations found for sediments was an LC50 for *Leptocheirus plumulosus* of 68 g/kg [52], from which a  $PNEC_{\text{CNT}}$  (sediment) of 68 mg/kg was derived. For the air compartment, the  $PNEC_{\text{nano-TiO}_2}$  (air) of 10  $\mu\text{g/m}^3$  is based on a lowest observed effect concentration of 10 mg/m<sup>3</sup> derived from different inhalation studies [53]. The  $PNEC_{\text{CNT}}$  (air) of 0.1 mg/m<sup>3</sup> [54] was derived from a threshold providing a CNT occupational exposure limit. The  $PNEC_{\text{nano-Ag}}$  (air) of 0.1  $\mu\text{g/m}^3$  is based on a NOEC of 100  $\mu\text{g/m}^3$  [55]. Concentrations of 10 to 1000  $\mu\text{g}$  [56] TiO<sub>2</sub>/g dry food were identified as safe for terrestrial isopods *P. scaber* Latreille, 1804. Based on these thresholds a  $PNEC_{\text{nano-TiO}_2}$  (soil) >1000  $\mu\text{g/kg}$  was used. Furthermore, a  $PNEC_{\text{CNT}}$  (soil) for *Eisenia Veneta* of 176  $\mu\text{g/kg}$  was derived from an EC50 of 176 mg/kg [57].

## 4.3 Results

### 4.3.1 Intermediate outputs of the MC simulations

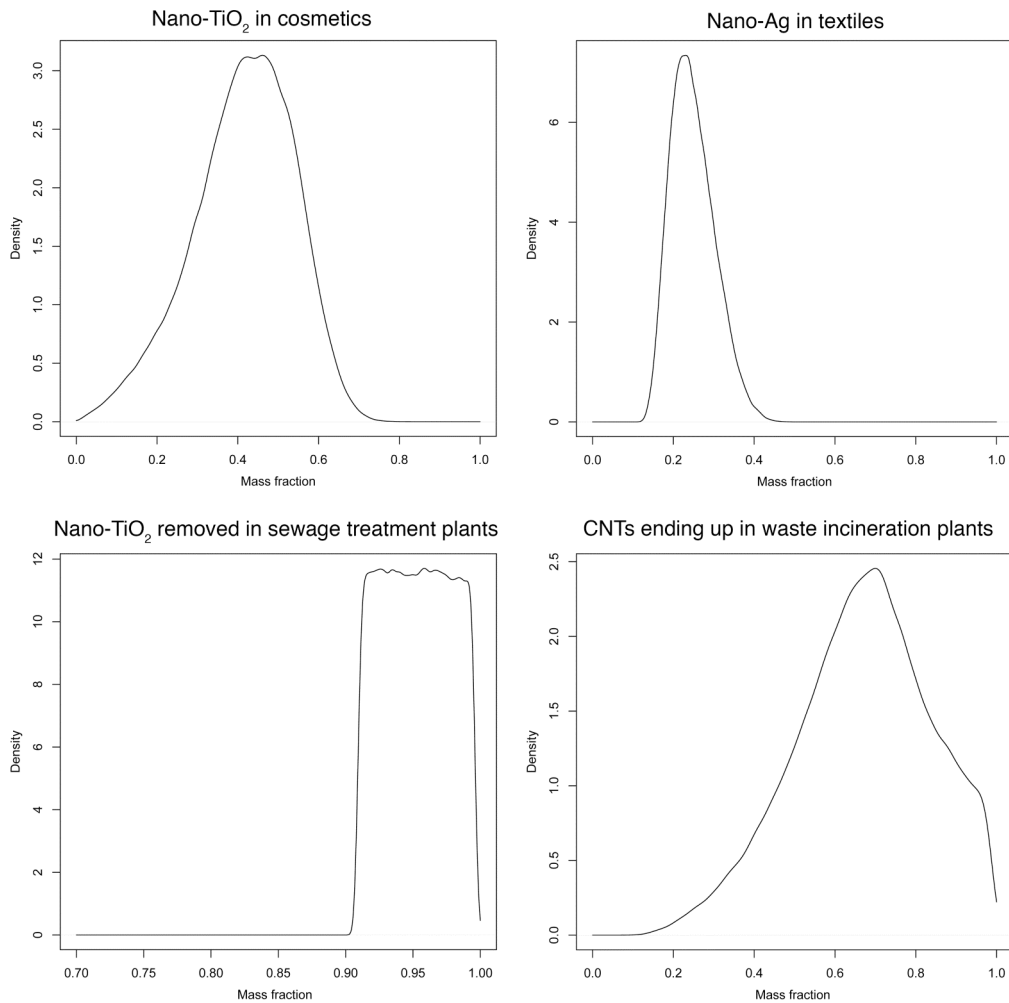
*Distribution of the ENM to Product Categories.* The mass fractions of ENMs in product categories were modeled based on the categorization of products explained above. The simulation results, given as means (Table 10), showed that the proportions of the cosmetics (0.42), filter aggregates (0.27), plastics (0.13) and coating and cleaning agents (0.11) had covered the majority of the application field of nano-TiO<sub>2</sub>. For CNT, the results indicated that almost all the ENMs had been allocated nearly equally to the categories composites and consumer electronics. However, the estimation of the ENMs mass distribution within these three categories was difficult due to the particularly distinct lack of information concerning CNT-containing and commercially available products. In the case of nano-Ag, the proportions of the categories coating and cleaning agents (0.29), textiles (0.25), and paints (0.2) represented more than two thirds of the mass of ENMs incorporated in commercially available products. Figure 13 exemplarily illustrates the simulated mass proportions of nano-TiO<sub>2</sub> in cosmetics (top left) and the proportion of nano-Ag in textiles (top right).

### 4.3.2 Transfer coefficients

The amounts of ENMs emitted to the environment or ending up in technical compartments were derived from the simulated ENM flows, quantified by transfer coefficients determined by the life cycle and lifetime of the products and on the strength of the fixation of the ENMs within the products in each product category. However, after the MC iterations were run, the modeled TCs that describe the total fraction of ENMs transferred from the PMC process to each other compartment were extracted from the simulation output. Such total TCs brought together all the single TCs from each product category into a unique TC. The most prominent TCs determining direct emissions of nano-TiO<sub>2</sub> during product usage displayed the following means: emission as part of wastewater from PMC to STP was 0.48, transfer from PMC to WIP was 0.25, and transfer out of the system as part of exported products was 0.23. In the case of CNTs, the two relevant transfers were waste from PMC to WIP (0.66) and the transfer from PMC to the recycling process (0.3). Carbon nanotubes were almost exclusively incorporated in polymer matrices or in batteries and consumer electronics. Thus, except from CNTs in textiles, release during product usage was not observed [11]. Nano-Ag was mainly emitted from the PMC to the STP as part of the wastewater flow (0.39) or as part of the waste from PMC to the WIP (0.12). A third relevant part was eliminated as release of Ag from nanoparticles in ionic form (0.22). This release of Ag in ionic form has to be regarded as a major emission process from textiles and plastics [15].

The most relevant simulated TCs that define the ENMs' behavior after being emitted from the PMC process described the fate of ENMs in STP and WIP. For nano-TiO<sub>2</sub> and nano-Ag, the mean simulated TCs showed the following results: from STP to WIP in the form of STP sludge accounted 0.86; from the WIP to the air compartment there was an equal-to-zero emission of 0.002, and the remaining part was exported or transferred to landfills within slag or filter ash. In the case of CNTs, the greater part (mode) of the particles were burned during the waste incineration process (0.94). Most of the remaining fraction ended up in filter ash and slag (0.038). Figure 13 illustrates the simulation output of the removal efficiency of sewage treatment plants for nano-TiO<sub>2</sub> (bottom left) and of the total mass fraction of CNTs ending up in waste incineration

plants (bottom right). The simulation results showed that 90.8 to 99.6 % of the nano-TiO<sub>2</sub> mass had been removed in STPs and that 68.7 % (mode) of the CNTs had ended up in WIPs.



*Figure 13. Probability distributions of Monte Carlo simulation outputs (100,000 iterations) describing exemplarily input parameters such as the mass fraction of nano-TiO<sub>2</sub> ending up in cosmetics (top left) and nano-Ag ending up in textiles (top right) and the mass fraction of the removed nano-TiO<sub>2</sub> in sewage treatment plants (bottom left) and carbon nanotubes (CNTs) reaching e.g. waste incineration plants (bottom right).*



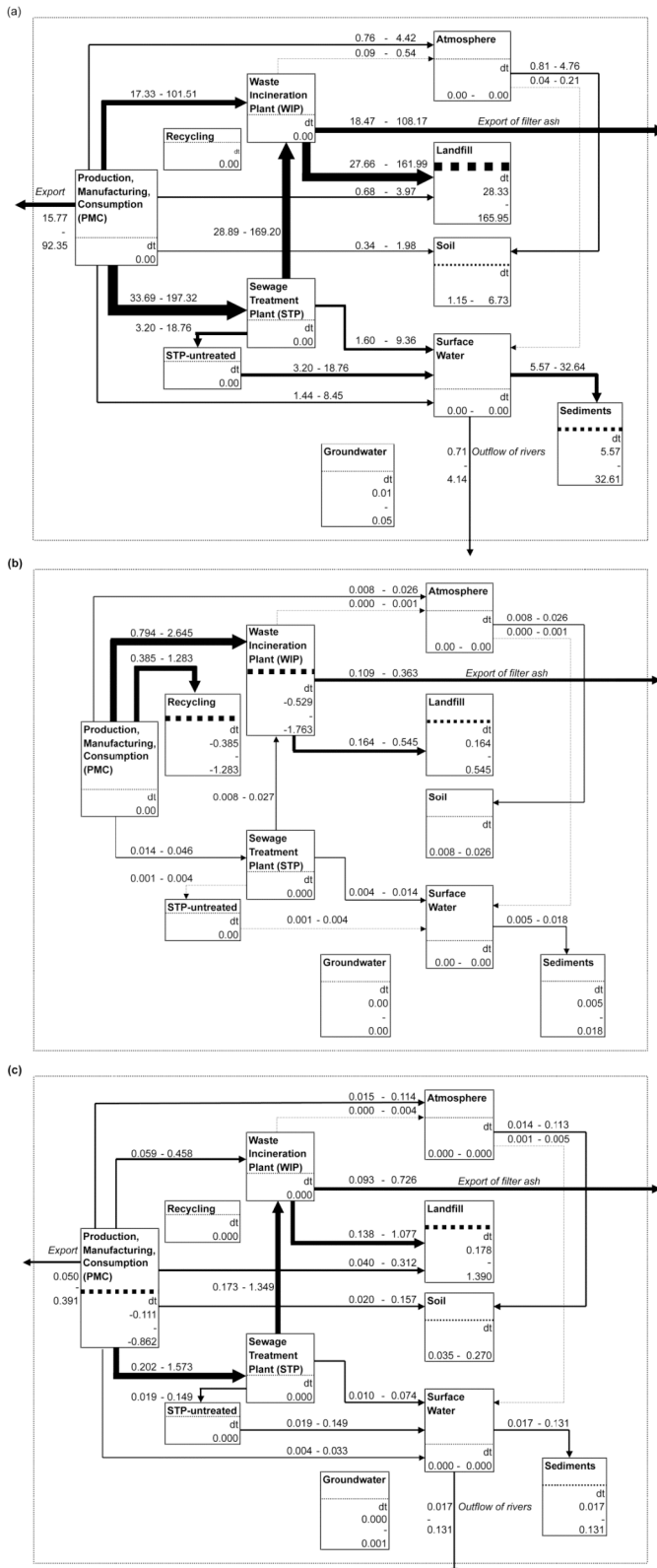


Figure 14. (a) nano-TiO<sub>2</sub> (>0.005 t/a), (b) carbon nanotubes (>0.0005 t/a), and (c) nano-Ag flows (>0.0005 t/a), accumulation and elimination rates shown as range of the lower and upper quantiles (Q(0.15) and Q(0.85)). The thickness of the arrows indicates the proportions of the engineered nanomaterial flows. The thickness of the horizontal line in the boxes indicates the proportion of the yearly accumulation or elimination.

### 4.3.3 Main MC simulation results

*Material flow charts.* Figure 14 shows the relevant flows of nano-TiO<sub>2</sub> (>0.005t/a) and of CNTs and nano-Ag, the latter two of which were higher than 0.0005t/a. The most prominent emission flows of nano-TiO<sub>2</sub>, shown as the range of the lower and upper quantiles Q(0.15) and Q(0.85), were wastewater (33.7–197.3 t/a), sludge from STP to WIP (29.9–169.2 t/a), filter ash from WIP to landfill (27.7–162 t/a), export of filter ash from WIP outside the system boundary (18.5 – 108.2 t/a), waste from PMC to WIP (17.3–101.6 t/a) and export in products from PMC outside the system boundary (15.8–92.4 t/a). The relevant CNT flows were waste from PMC to WIP (0.8–2.7 t/a), elimination in WIP (0.5–1.8 t/a) and the transfer to and elimination within the recycling process (0.4–1.3 t/a). Due to a small periodic input of nano-Ag into the system, relative small amounts of nano-Ag were transferred to and within the studied compartments. The most noteworthy of these (albeit small) flows were those from PMC to STP (wastewater) (0.2–1.6 t/a), sludge from STP to WIP (0.2–1.4 t/a), filter ash from WIP to landfill (0.1–1.1 t/a) and filter ash export from WIP outside the system boundary (0.1–0.7 t/a).

*Table 12. Predicted environmental concentrations of nano-TiO<sub>2</sub>, carbon nanotubes and nano-Ag shown as mode and as range of the lower and upper quantiles (Q(0.15) and Q(0.85))<sup>a</sup>*

NP	PEC			Unit
nano-TiO <sub>2</sub>	Mode	Q <sub>0.15</sub>	-	Q <sub>0.85</sub>
Air	0.001	0.0007	-	0.003
Surface				µg m <sup>-3</sup>
Water	0.021	0.016	-	0.085
STP <sup>b</sup> Effluent	4.3	3.5	-	16.3
STP Sludge	211	172	-	802
Sediment	499	426	-	2382
Soil	0.28	0.21	-	1.04
				Δµg kg <sup>-1</sup> y <sup>-1</sup>
CNT <sup>c</sup>				
Air	0.008	0.006	-	0.017
Surface				ng m <sup>-3</sup>
Water	0.0033	0.0028	-	0.025
STP Effluent	11.8	7.6	-	19.1
STP Sludge	0.069	0.051	-	0.129
Sediment	229	176	-	1557
Soil	1.92	1.44	-	3.83
				Δng kg <sup>-1</sup> y <sup>-1</sup>
nano-Ag				
Air	0.021	0.017	-	0.074
Surface				ng m <sup>-3</sup>
Water	0.72	0.56	-	2.63
STP Effluent	38.7	29.8	-	127
STP Sludge	1.88	1.46	-	6.24
Sediment	1203	965	-	10184
Soil	11.2	8.7	-	41.2
				Δng kg <sup>-1</sup> y <sup>-1</sup>

<sup>a</sup>For air, surface water and sewage treatment plants effluent the concentrations are given, for soil and sediments the annual augmentation of the concentration is shown.

<sup>b</sup>Sewage treatment plants.

<sup>c</sup>Carbon nanotubes.

#### 4.3.4 Concentration and accumulation of ENMs

Figure 15 illustrates simulation results of the predicted concentrations in surface water, STP effluent and STP sludge and of the annual increase in soil for nano-TiO<sub>2</sub>, CNTs, and nano-Ag. It is worth mentioning that there was a very high probability of extremely small amounts of CNT ending up in surface water. All the other distributions showed typical skewed log-normal shapes as often observed for the distribution of chemicals in the environment and which are particularly common if the observed values are not negative, the mean values relative low and variances relative large [58]. Density distributions modes and quantile ranges were derived thereof.

Table 12 shows the PEC values as modes within the range of lower and upper quantiles (Q(0.15) and Q(0.85)). The predicted values of ENMs' concentration for air, surface water, STP effluent (treated water) and STP sludge as well as the predicted annual deposition of ENM concentrations in sediment and soil are illustrated. Noteworthy were the relatively small concentrations (modes) in surface water (nano-TiO<sub>2</sub>, 0.02 µg/L; CNT, 0.003 ng/L; and nano-Ag, 0.72 ng/L compared to the concentrations in the STP effluent (nano-TiO<sub>2</sub>, 4.3 µg/L; CNT, 11.8 ng/L; and nano-Ag, 38.7 ng/L). High rates of sedimentation led to remarkable annual deposition in sediment: nano-TiO<sub>2</sub>, 499 µg/kg; CNT, 0.229 µg/kg; and nano-Ag, 1.2 µg/kg. Although sludge application on landfills and soils was not considered (prohibited in Switzerland) and the sludge incinerated in WIP or used in cement plants, the concentrations in STP sludge were calculated nonetheless. High ENM concentrations were predicted for STP sludge: 211 mg/kg for nano-TiO<sub>2</sub>, 0.069 mg/kg for CNT, and 1.88 mg/kg for nano-Ag.

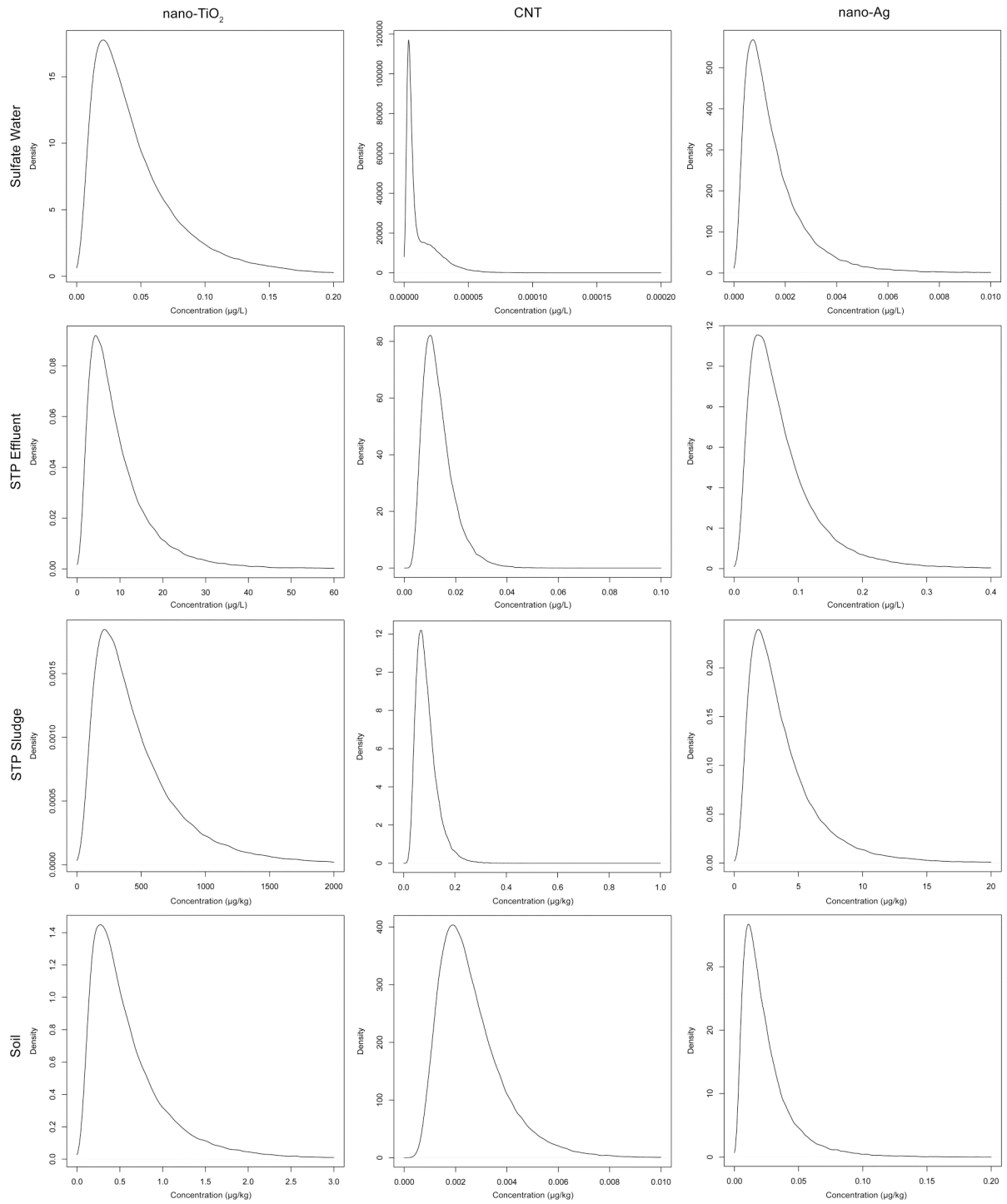


Figure 15. Probability densities of the predicted concentrations in water and cleaned water (sewage treatment plants (STP) effluent), STP sludge and of the annual increase in soil for nano-TiO<sub>2</sub>, carbon nanotubes (CNT) and nano-Ag.

#### 4.3.5 Sensitivity and uncertainty analysis

The 8 most influential parameters determining concentrations in water and soil are shown in Table 13. For nano-TiO<sub>2</sub> and nano-Ag changes in the parameters STP inflow, STP overflow, and STP removal efficiency covered at least 98% of the source of variation of the ENM concentrations in water. The variation of the parameters STP overflow and STP removal efficiency showed an 88% probability that CNT concentrations in water responded to changes in input parameters. Thus, the sensitivity results confirmed that CNTs ended up in water almost only via STP, and that CNT did not reach water environments in relevant amounts. Changes in waste and particle emissions from WIP to air explained 84% of the caused variation of CNT concentrations in soils. However, the sensitivity of CNT water concentrations to variation in the STP inflow was very marginal. For nano-TiO<sub>2</sub> and nano-Ag the influence of the input parameter variation to the ENM concentrations in soils was distributed more evenly to various parameters. Due to the high uncertainties associated with the sedimentation process and the fate and behavior of ENMs in the air the sensitivity of ENM concentrations in air and sediments to variations of the input parameters was not evaluated.

*Table 13. Results of the sensitivity analysis indicating the most influential model input parameters to the calculated environmental concentrations of nano-TiO<sub>2</sub>, carbon nanotubes and nano-Ag in water and soil.*

	Water		Soil			
	nano-TiO <sub>2</sub>	CNT <sup>a</sup>	nano-Ag	nano-TiO <sub>2</sub>	CNT	nano-Ag
STP <sup>b</sup> Inflow	74%	1%	64%	32%		5%
STP Overflow	18%	41%	33%			
STP Removal Efficiency	6%	47%	2%			
Waste Incineration Emissions from WIP <sup>c</sup> to Atmosphere		4%		13%	42%	
Dry/Wet deposition to Soil		4%			42%	
Direct Emissions to Atmosphere				22%	12%	38%
Sedimentation				10%	3%	35%

<sup>a</sup>Carbon nanotubes.

<sup>b</sup>Sewage treatment plants.

<sup>c</sup>Waste incineration plants.

#### 4.3.6 Risk quantification

The comparison of the PNECs to the modeled PECs provided the risk quotients (risk quotient = PEC/PNEC). A risk quotient (RQ) greater than or equal to one indicates a potential risk. The PECs were modeled within these risk assessments as mode and median values of the corresponding output distributions. The results based on the modes indicate the greatest observed frequency of RQ-values. Because of the positive skewed lognormal-shaped output

distributions (Fig. 15), the medians provided RQs higher than the mode-based results. The median was preferred to the mean, because in a skewed distribution, the mean is farther out in the long tail with low densities than is the median.

The RQs (Table 14) suggest that CNTs currently do not pose a risk to organisms in air, surface waters, soils, and sediments. All  $RQ_{CNT}$  were smaller than 0.0005. For the other two ENMs, ecotoxicological data on sediment organisms are still scarce, and evaluation was therefore not yet possible for this compartment. Risk was observed for organisms in the STP effluent exposed to nano-TiO<sub>2</sub> and nano-Ag and for organisms in waters exposed to nano-Ag. The  $RQ_{nano-TiO_2}$  for the STP effluent was 4.28 (quotient based on the mode) or 7.58 (quotient based on the median), and the  $RQ_{nano-Ag}$  for the STP effluent are 55.6 and 88.41, respectively. Nano-Ag in water showed RQs of 1.03 and 1.74.

*Table 14. Risk quotients (predicted environmental concentrations/predicted no effect concentrations) of nano-TiO<sub>2</sub>, carbon nanotubes and nano-Ag for air, surface water, cleaned water (sewage treatment plants effluent), sediments and soils (rounded to three digits).*

	Nano-TiO <sub>2</sub>		CNT <sup>a</sup>		Nano-Ag	
	mode	median	mode	median	mode	median
Air	<0.0005	<0.0005	<0.0005	<0.0005	<0.0005	<0.0005
Surface Water	0.02	0.04	<0.0005	<0.0005	1.03	1.74
STP <sup>b</sup> Effluent	4.28	7.58	<0.0005	<0.0005	55.60	88.41
Sediment	NA	NA	<0.0005	<0.0005	NA	NA
Soil	0.001	0.003	<0.0005	<0.0005	NA	NA

<sup>a</sup>Carbon nanotubes.

<sup>b</sup>Sewage treatment plants. NA = ecotox studies not available.

#### 4.4 Discussion

The flow charts of nano-TiO<sub>2</sub> and nano-Ag show that for these materials the most dominant ENM transfers are from products to STP and WIP, STP to WIP and from there to landfills. In the case of CNTs, the majority of the nanotubes ended up in the WIP. These results are in agreement with the flow analysis of Mueller and Nowack [6]. However, the comparison of the single ENM flows computed in this work to the flows presented in the preceding study [6] is difficult given an enlargement of the system to more compartments and ENM flows associated to these compartments, newly available model input data and a different categorization of the products and allocation of the ENMs' mass to the product categories. For CNTs, the values of the predominant flow PMC to WIP found in the "realistic" as well as in the "high exposure" scenarios in Mueller and Nowack [6] are covered by the range of the 0.15 and 0.85 quantiles presented in the present study. The predominant flows from production/manufacturing/consumption to STP and STP to WIP of the realistic scenario are, in the case of nano-Ag, also covered by the same range; in the case of nano-TiO<sub>2</sub>, they are smaller than the values of the 0.15 quantiles by about a factor of 1.5. The corresponding nano-TiO<sub>2</sub> and nano-Ag flows of the high exposure scenario in

Mueller and Nowack [6] are approximately identical to or up to a factor of 2 higher than the results of the 0.85 quantiles calculated in this work. However, the most useful aspects of such comparisons are to test roughly the model's consistency. Results of a two-scenario analysis evidently do not cover the whole range of output distributions of a MC or MCMC analysis.

The lowest PEC values generated from the ENM flows to the environment were observed for CNTs. However, it would be a fallacy to conclude that the currently observed small ENM production volumes implicate a guarantee of small CNT environmental concentrations in the future. If the price of CNTs falls and CNT application becomes more widespread, the CNT concentration in the environment could increase considerably. For nano-TiO<sub>2</sub> and nano-Ag, air shows the lowest PEC values. Particularly striking are the high PEC values for all materials in STP sludge. As mentioned, however, STP sludge is incinerated in WIP, exported or used for cement production in Switzerland. Nevertheless, one needs to take a closer look at such concentrations within a risk assessment, because STP sludge is applied to soil in other regions (United States, European Union). The highest ENM concentrations relevant for the studied region were found for all materials in the STP effluent, even though a high treatment efficiency of the STP was assumed. Due to the relative high volume, the air compartment showed the lowest PECs. This can be explained by the very small quantities of ENMs emitted to the air during the usage phase of the products and during the treatment of ENMs in the WIP.

The sensitivity analysis allowed us to identify the key parameters that needed to be studied more precisely. From these results, we may conclude that a closer look is needed at the parameters covering the release of ENMs from the products to the STP, the STP removal efficiency and overflow and the sludge from this compartment ending up in the WIP, where it is incinerated, exported or deposited in landfills. Changes in the parameters STP inflow, STP overflow, and STP removal efficiency explain for nano-TiO<sub>2</sub> and nano-Ag almost the whole variation of the ENM concentrations in water. The reason for the dominance of that factor is that the major application volumes of these ENMs are within the product categories cosmetics and coatings for nano-TiO<sub>2</sub>, and coatings, cosmetics, paints and textiles for nano-Ag. Releases from such applications mostly result in emissions into STP inflow. Even though CNTs end up in very small amounts in the STP inflow, the parameters STP overflow and STP removal efficiency influence most of all the CNT concentrations in water. The interpretation of these results is further complicated by the fact that very small amounts of ENMs actually reach this compartment. However, the sensitivity analysis shows that to improve the prediction of the final location of the ENMs, the most critical information is not only related to fate and behavior in technical systems or in the environment but also to the usage of ENMs in products and their release during the use phase.

Except for nano-TiO<sub>2</sub> and nano-Ag in STP effluent and nano-Ag in water, all the PNEC values derived were smaller than the corresponding modeled PEC values in the environment. However, although most of the modeled PECs were much smaller than the corresponding PNECs, toxicological effects of ENMs, even at such low concentrations, cannot be excluded when present in complex mixtures. In our modeling we lumped together all modifications of the ENMs, e.g., the different modifications of TiO<sub>2</sub> or surface functionalizations, mainly due to the absence of data. However, the size and functionalization of ENMs might have an influence on their toxic effects [59; 60]. Further ecotoxicological studies should be carried out to elucidate whether the modeling has to take this into account, and the environmental behavior of the different functionalized ENMs also needs to be studied.

The risk estimation results provided by the present study suggest that, except for organisms exposed to nano-TiO<sub>2</sub> and nano-Ag in STP effluent and STP sludge and especially nano-Ag in water, the ENMs studied currently (2008) pose no risks to organisms in the environment. Hence, further investigations are needed to evaluate the risks posed to aquatic organisms by nano-TiO<sub>2</sub> and nano-Ag. In addition an urgent need for further studies concerning silver concentrations in water is evidenced by the fact that silver ion release and emissions of microsized silver were not covered by our risk calculations. Ecotoxicological data on soils and sediments are very scarce, if available at all. Thus, this lack of data should be filled.

Although a comparison of the present study to a previous study [6] and a first validation of modeled concentrations [27] has been done, the discussion of the limitations of such a probabilistic/stochastic modeling is essential to guarantee good scientific and practical use of the outputs and to illustrate simultaneously the requirements for reducing the uncertainties in the simulations. Summing up the key limitations of the results may be seen in the general lack of input data, the focus on one unique region (Switzerland) and the steady state calculations for only one time period (2008).

First, the data found in the literature for the annual production volumes of ENMs vary widely, sometimes by a factor of 100. Hence, relatively large ranges of input distribution had to be modeled. In accordance with the deterministic study of Mueller and Nowack [6], the production quantities of ENMs was the key parameter in our modeling. In the meantime more data concerning the production volumes of ENMs had become available. However, estimating ENM production volumes was still difficult. Producers do not necessarily advertise nanosized ingredients, and whenever data from companies are available, such information should be trusted only sparingly. Furthermore, there are no complete inventories listing all products containing ENMs. Schmid and Riediker [7] provide the only quantitative overview containing product categories allocated to incorporated ENM volumes. More data on the production and use of ENMs in commercially available products will hopefully become available in the next few years when ongoing governmental investigations on nanosized materials are concluded. One critical point of the steady state approach is that storage of ENMs and ENM-containing products within the PMC was not considered. Data concerning such storage are missing entirely. Furthermore, production quantities of ENMs and ENM-containing products were only calculated for current (base year 2008) quantities of materials and products. Hence, modeling time-dependent ENM production quantities and consideration of storage processes would be crucial for improving the simulations. However, the available data do not show any correlation between the estimated nanomaterial production amounts and the year of estimation. Thus, no trend is obtainable from such estimations that would afford dynamic modeling of ENM production amounts.

Furthermore, no quantitative data on ENM emissions during the manufacturing of ENM-containing products and during the production of ENMs are available yet. Experimental data are restricted almost exclusively to emissions from textiles [13; 14] or paints [12]. The same absence of data is observed for the ENM release during the production of ENM and manufacturing of ENM-containing products although first measurements at companies producing ENM showed that worker exposure to these materials occurs [61–65]. Thus, there is a release, but it cannot be quantified for modeling purposes and an allocation has to be made based on assumptions. In addition, the assignment of the average mass of ENMs in products is also associated with great uncertainties. However, the estimation of the average weight of a prototypical product of each



category and modeling the average proportion of ENM in these products by means of probability distributions allowed us to cope with the uncertainty and variability of these model parameters. Nevertheless, measurement data related to such model parameters are urgently needed. The allocation of ENMs to product categories also depends on the number of products sold, information that is even more lacking than the concentrations in products.

Additional key limitations are represented by the lack of data on the fate of engineered nanomaterials in nature. In particular the exchange between water and sediment through re-suspension and burial processes were not considered. Accumulation in sediments was equated to sedimentation/aggregation. The impact of streambed roughness, flow velocity, and streambed depth on ENM transport distances and accumulation in sediments were neglected, although they may influence considerably, e.g., ENM exposure of plankton and adsorbed microorganisms [66]. Carbon nanotubes and other ENMs may be functionalized to achieve water solubility or solubility of the products containing them [11]. Obviously, different behaviors in environmental and in technical compartments may result from such different material properties. While the aggregation behavior of ENMs has been extensively investigated in laboratory systems, almost nothing has been done under environmentally realistic conditions thus far. The extrapolation of laboratory aggregation studies to sedimentation in natural systems is difficult. We have based our modeling on the few studies that report quantitative data on the stability of ENM suspensions under natural conditions that can be used to obtain transfer coefficients. More research is clearly needed to investigate the conditions under which single suspended ENMs can be formed in the environment and how quickly ENMs sediment in the water column. The same applies to biotransformation and accumulation, or dissolution of ENMs. Furthermore, the modeling of aerodynamics was restricted to rough calculations on atmospheric deposition based only on data for ultrafine particles [48]. A distinction of dry and wet deposition, as well as insights into the tendency of suspended nanoparticles to agglomerate, are required.

We should emphasize once again that this study was focused exclusively on Switzerland and that we assumed environmental compartments were mixed well. In Switzerland it is prohibited to apply sludge to landfills and soil, and almost 100% of all buildings are connected to STPs for wastewater and to WIPs for flows of waste. Hence, in order to understand system behavior in other countries and under different conditions, further investigations should be focused on more than one single region, as done for following the example of Gottschalk et al. [27]. Much higher concentrations could also occur locally, such as on sludge-treated soils or in industrial areas near ENM production plants. In addition, leachate from landfills, e.g., cannot be excluded, given that the standard of landfills most likely varies between regions. Thus, a further differentiation is necessary in the form of a spatial analysis of ENM flows inside environmental compartments.

Finally, the risk assessment for ENM based on a PEC/PNEC comparison suffers also from the PNEC estimation uncertainties. The derivation of PNECs is difficult due to the limited number of studies that are mainly focused on acute toxicity and cover only a few numbers of test species and toxicity endpoints. Engineered nanomaterial toxicity is mostly studied on model organisms (bacteria and algae, daphnids, etc.) and using ENM concentrations several orders of magnitude higher than available PECs [66]. Long-term low exposure studies to obtain chronic endpoints are missing to a great extent [67]. In addition, adverse effects are not necessarily caused exclusively by individual nanoparticles but also by agglomerated particles as observed for nano-TiO<sub>2</sub> [66]. Considering such limitations it is difficult to discuss conclusively to what extent the use of a safety

factor of 1000 covers all these limitations in ecotoxicological research. It is furthermore also difficult to compare a deterministic PNEC to PEC values from density distributions. In the present study we used mode and median values for this comparison. Mode and median were preferred to the mean and the 15 and 85% quantiles were used to avoid an overemphasis of very uncertain results on the long tail of lognormally shaped simulation outputs. However, in risk assessment such arbitrary choices are justified rather by practical applicability than by scientific legitimation. Thus, simply concluding, e.g., that for carbon based ENM no risks for nature may be expected because all PNECs were smaller than the corresponding PECs (Table 14) would be irresponsible. Our risk quotients refer only to the base year of the simulations 2008 and only to a few ecotoxicological studies that in turn consider only single types of CNTs. Thus, especially for CNTs, where low current production amounts and use in water-irrelevant products were observed, a future breakthrough in the commercialization and the development of novel products containing new functionalized CNTs could make an immediate re-assessment necessary.

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## 5. Engineered nanomaterials in rivers – an exposure assessment for Switzerland at high spatial resolution for nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag

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### Abstract

Two models, one based on probabilistic material flow analysis and one based on graph theory, were combined to calculate predicted environmental concentrations (PEC) of engineered nanomaterials (ENMs) in Swiss rivers at high spatial resolution. PECs for nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag were calculated for 742 river sections downstream from 742 sewage treatment plants at base flow conditions  $Q_{95\%}$  (flow reached or exceeded annually in 95% of the time, averaged in Switzerland over a ten-year period). Additionally, flow measurements for 20 selected locations over a 20-year period (1988–2007) were used to assess temporal variations. At base flow the highest PECs (modal values) were found for nano-TiO<sub>2</sub> where the PECs at  $Q_{95\%}$  ranged from 0.1 ng/L to 7,800 ng/L, followed by nano-ZnO (0.004 ng/L to 500 ng/L) and nano-Ag (0.3 pg/L to 32,500 pg/L). Comparing PECs with PNEC values (predicted no effect concentrations) revealed that based on the used hydrological data and averaged for all 20 stations and scenarios (scenario with and scenario without sedimentation) the PNEC was exceeded for nano-Ag using modal concentrations at 234 days annually. The equivalent results for nano-ZnO and nano-TiO<sub>2</sub> were 150 and 109. This study shows that linking a probabilistic material flow analysis to a geo-referenced model fills two gaps: the PEC calculations for rivers were improved compared to calculations at regional level by considering geographical distribution of the ENM emissions and a clear distinction between input uncertainty and natural water flow variations could be achieved. Variability in the stream flow variation influenced the ENM concentrations up to a factor of 5, the uncertainty in the ENM loads caused a difference in the PEC calculations up to a factor 10.

## 5.1 Introduction

Production and application quantities of engineered nanomaterials (ENMs) are growing and it has to be expected that ecosystems will be exposed to significant levels of such materials (1–5). Unfortunately, the quantitative detection of ENMs in the environment is currently extremely limited, the distinction between engineered and naturally occurring nanomaterial is almost impossible (6). Thus, modeling the ENM release to and fate in the environment is crucial to predict environmental exposure. However, in the case of ENM, modeling the exposure is difficult as it has to cover diffuse emissions from a large number of relevant ENM-containing products and life cycle stages. These include but are not limited to ENM release into the environment from ENM production, ENM incorporation into products and storage, use, waste generation and disposal of such products. Once released into the environment, ENMs will to some extent agglomerate, associate with suspended solids or sediments, and accumulate in organisms, entering into the food chain or drinking water sources (7).

Recently, scientific awareness was emphasized particularly on aquatic pollution derived from the release of ENMs into surface waters (5, 7–9). Battin et al. (5) presented first evidence that nano-TiO<sub>2</sub> at ambient UV radiation levels and realistic nano-TiO<sub>2</sub> concentrations have significant impacts on natural microbial aquatic communities. Basically, industrial and domestic products and wastes containing ENMs tend to end up in water: either they are released directly into rivers and lakes, e.g. from outdoor use of sunscreens, or indirectly via surface run-off, domestic or industrial wastewater (10). In addition, ENMs are also envisaged for applications in environmental remediation techniques (11, 12) that may lead to direct injection of such materials into aquifers (13).

Mass balance partitioning models (14–18) have already been used to predict environmental concentrations of ENM. Boxall et al. (14) used a series of algorithms to predict concentrations of ENMs in water, soil, and air by means of a specified but non-comprehensive range of ENM applications. Blaser et al. (15) modeled the flow of silver in the environment including dissolved silver released from nano-Ag in textiles and biocidal plastics. Water and sediment concentrations were estimated based on a river box model developed by Scheringer et al. (19) where each box had been subdivided into a compartment of moving water, a compartment of stagnant water and a sediment compartment. However, biocidal plastics and textiles were predicted to account only for up to 15% of the total silver release into water. Mueller and Nowack (16) modeled ENM emissions to the environment based on analyzing the complete life cycle of ENM and ENM containing products concluding that in particular PECs (predicted environmental concentrations) for nano-TiO<sub>2</sub> were close to or higher than the used PNEC<sub>water</sub> (predicted no effect concentrations) (<1 µg/L). Recently, ENM exposure studies (17, 18) were carried out by means of probabilistic mass balance multi-compartment modeling (20). Simulated PECs and risk quotients (PEC/PNEC) at regional (national) level indicated that risks to aquatic organisms may emanate from nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag in sewage treatment effluents and for nano-Ag in surface waters (17). The latter modeled ENM concentrations could be validated roughly based on sewage treatment plant (STP) effluent and STP sludge specific measurements (nano-TiO<sub>2</sub> (21)).

To overcome one of the main limitations of PEC calculations at regional scale – the assumption of homogeneous material distribution within aggregated environmental compartments – the modeling of concentrations at higher spatial and temporal resolution at a local level (22) is

required. As a consequence, for studying ENM concentrations in rivers the following refinements are necessary: 1) The total (national) ENM input into rivers should be distributed to individual river sections according to population density. 2) Transport and fate of ENMs within the system – i.e. the real river network – need to be studied in more detail. 3) Geographical differentiation and temporal variations of relevant flow rates should be considered.

Ort et al. (23) developed a model to predict realistic pollutant loads originating from STPs throughout complex river networks. With site-specific measurements in rivers the model was validated for several recalcitrant micropollutants. Only a minimum of input data is required to screen for hotspot concentrations in individual river stretches across catchments in Switzerland (existing structure of digital river network, location of STP discharge points, annual sales data for compounds of interest, transformation of compounds during application and average elimination in STPs). Conceptually, this model is not restricted to the simulation of micropollutant loads in rivers and can basically also be applied to study the distribution and concentrations of nanopollutants. First, the only catchment-related input, the population each STP serves, does not vary significantly among chemicals or size of pollutants. Second, as shown in Gottschalk et al. (20), estimates for the required substance-specific inputs such as e.g. consumption and STP removal rates are also available for ENMs.

The innovation of the modeling framework presented in this study is that a probabilistic material flow analysis (PMFA) (20) covering the uncertainties related to the total ENM input into rivers was linked to a geo-referenced model (23). This approach fills two gaps: 1) The PEC calculations for rivers were improved compared to calculations at regional level by considering geographical distribution of the ENM emissions and 2) a clear distinction between input uncertainty and natural water flow variations could be achieved.

Previous regional studies (17, 18) predicted the highest concentrations and risk coefficients in surface water for nano-TiO<sub>2</sub>, nano-Ag, and nano-ZnO. Thus, the goal of our study was to calculate local concentrations for these ENMs along all rivers in Switzerland at baseflow ( $Q_{95\%}$ ). This is the flow reached or exceeded annually in 95% of the time, averaged in Switzerland over a ten-year period. This will allow identifying river sections where PECs are expected to exceed PNECs at minimum dilution at least during 5% of the year. Additionally, PECs and duration of exceedance should be calculated as a more detailed estimate of potential risks for aquatic organisms exposed to ENMs is possible for selected river sections with complete hydrological information.

## 5.2 Material and methods

### 5.2.1 Input data and model setup

#### 5.2.1.1 ENM input into rivers

The total annual ENM input for nano-ZnO and nano-Ag into surface waters was taken from Monte Carlo (MC) simulation results by Gottschalk et al. (17). The total annual input of nano-TiO<sub>2</sub> was recomputed considering also new data on production volumes (24). Annual ENM emissions into rivers were modeled as probability distributions that consider release from the ENM production process and the incorporation of ENM in consumer products (manufacturing), emissions during

the ENM containing products' life cycle and immissions of these materials from STPs and natural compartments (atmosphere, soils, sediments). The distribution of the consumption and use of ENM-containing products and consequently the release of ENMs to the environment was assumed to be proportional to the population in the catchment of a particular STP. High short-term emissions (STP overflow) leading mostly to short-term (<24 h) release of pollutants into rivers were not modeled in this work.

In addition, direct ENM release during the consumption and disposal phase of ENM containing products into surface waters and the marginal amounts of material emitted from natural compartments into rivers were also weighted according to the population connected to the corresponding STPs. Such direct emissions from technical compartments depend strongly on the ENM containing products' life cycle that is determined by the geographical distribution of the consuming population.

#### 5.2.1.2 ENM loads in rivers

An elementary modeling approach based on graph theory was used to calculate ENM loads throughout all rivers in Switzerland. The model by Ort et al. is described in detail in (23). It comprises 742 STPs, each with a design capacity of more than 500 population equivalents (PE), covering over 97% of the population of Switzerland. The large number of STPs represent the distribution of the population density and provides geographic information of ENM discharge locations at high spatial resolution. The study of fate and behavior of ENM in river water was reduced to sedimentation. Due to the ambiguity of the available data on sedimentation rates and due to the fairly short residence time (<24 h) (23) of the Swiss rivers between reservoirs (lakes) two scenarios were considered to cover the possible spectrum: 1) No sedimentation in the whole surface water system – the effluent loads of all STPs were assumed to remain in the water phase and added up along the flow path. 2) Complete sedimentation between two STPs – in this scenario all ENM loads from upstream STPs are assumed to accumulate in the sediments and do not reach the discharge point of the next STP downstream (no resuspension). Therefore, total degradation or sedimentation was assumed to take place before water from a particular STP effluent reached a subsequent treatment plant. Dissolution of nano-Ag and nano-ZnO was not considered in the no-sedimentation scenario as currently no kinetic data are available to model dissolution of these ENM under natural conditions. However, for nano-Ag and nano-ZnO the complete sedimentation scenario would be equivalent to a complete dissolution scenario.

#### 5.2.1.3 Procedure to link the two models

For the application of the model of Ort et al. (23) to ENM, removal rates for STPs were taken from Gottschalk et al. (17). To calculate the geographical referenced release of ENMs via STP, the STP box in Gottschalk et al. (17) was segmented into single STPs. The ENM input into rivers was assigned to all river sections according to the number of inhabitants (25) connected to each corresponding STP assuming a homogeneous per capita consumption over the population and throughout the year. Because the ENM input, the allocation of ENM emission volume to STPs as well as variations in the water flows were coded in the programming language for statistical computing R (26), the two models could be linked and the simulations run without the need of data transformation. Five thousand MC iterations were found to be sufficient to account for the variable input into rivers.

#### 5.2.1.4 Flow conditions and risk evaluation

To calculate local PECs the expected ENM loads were divided by the corresponding water flow. Base flow conditions ( $Q_{95\%}$ ) were used to account for minimum dilution (worst-case scenario). A method was developed to estimate this flow rate also for locations without measurements (25). Measured  $Q_{95\%}$ -values were taken from Aschwanden et al. (26). River sections without an estimate for the  $Q_{95\%}$  only receive treated wastewater from small STPs, overall from approximately 5% of the total population. However, their ENM loads, as well as STPs discharging directly to lakes, were included in the simulations, but no concentrations could be calculated directly downstream from these STPs. This evaluation will identify river sections, where high ENM concentrations must be expected at base flow. The outcome is expected to mainly depend on the scenario for transportation and the variable ENM input into rivers because only one flow condition is considered.

Additionally, 20 river sections where long-term discharge information was available – measured daily flow rates over a 20-year period (1988–2007) – were used to assess the exposure concentrations in more detail. This evaluation is thought to provide more insight into the question which of the three factors 1) the uncertain ENM input into rivers, 2) the transport scenario (with or without sedimentation) or 3) the natural flow variation is the most sensitive parameter in the prediction of environmental concentrations. This time period from (1988–2007) was not used to calculate ENM-concentrations during that time but was considered to be representative also for the changes in flow conditions in the near future.

### 5.3 Results

#### 5.3.1 Concentrations at base flow ( $Q_{95\%}$ )

The highest PECs (modal values) for the scenario without sedimentation were found for nano-TiO<sub>2</sub> where the results for all river sections ranged from 0.3 ng/L to 7,800 ng/L, followed by nano-ZnO (0.02 ng/L to 500 ng/L) and nano-Ag (0.001 ng/L to 32 ng/L). The ranges for the scenario with sedimentation were 0.1 ng/L and 6,600 ng/L for nano-TiO<sub>2</sub>, for nano-ZnO 0.004 ng/L and 500 ng/L and for nano-Ag 0.3 pg/L and 27,700 pg/L.

Based on the PEC simulation results, PNEC-exceedances for all river sections (scenario with and scenario without sedimentation) considering base flow ( $Q_{95\%}$ ) conditions were calculated. For nano-Ag (scenario without sedimentation) the 0.7 ng/L (PNEC) (17) was exceeded in 5000 simulations at least once in 539 (99%) river sections directly downstream from 543 STPs and in 443 (82%) river sections in at least 50% of the time. Considering the scenario with sedimentation the equivalent results were 448 (83%) and 298 (55%). In the case of nano-ZnO (scenario without sedimentation) 40 ng/L (PNEC) (17) were exceeded at least once in 525 (97%) river sections and in at least 50% of the time in 325 (60%) cases. For the scenario with sedimentation these values were 398 (73%) and 207 (38%). For nano-TiO<sub>2</sub> (scenario without sedimentation) the PNEC of 1 µg/L (17) was exceeded at least once in 505 (93%) river sections and in at least 50% of the time in 241 (44%) cases. Considering sedimentation the equivalent results were 362 (67%) and 162 (30%).

The modal values (most frequent modeled values) of the simulated density distributions for the PECs of the  $Q_{95\%}$  calculations (scenario with and scenario without sedimentation) were categorized into different concentration ranges. The spatial distribution of the concentrations for nano-Ag is shown in Figure 16. For all ENMs, scenarios and water level conditions, the highest concentrations were found in the midland or near urban centers. The calculated concentrations in rural, alpine and pre-alpine areas were even at low water for all three nanomaterials negligible small. One exception, however, were river sections in the area of large tourist destinations in the Alps, where the PECs were high compared to the values of rural areas. Roughly speaking, the concentrations are generally significantly higher for the scenario without sedimentation compared to the modeled concentrations for the scenario with sedimentation. However, there is no general factor that would predict such differences. For river sections at the beginning of a flow sequence the differences are marginal, for river sections near confluences to lakes however differences up to a factor of 10 and more were observed.

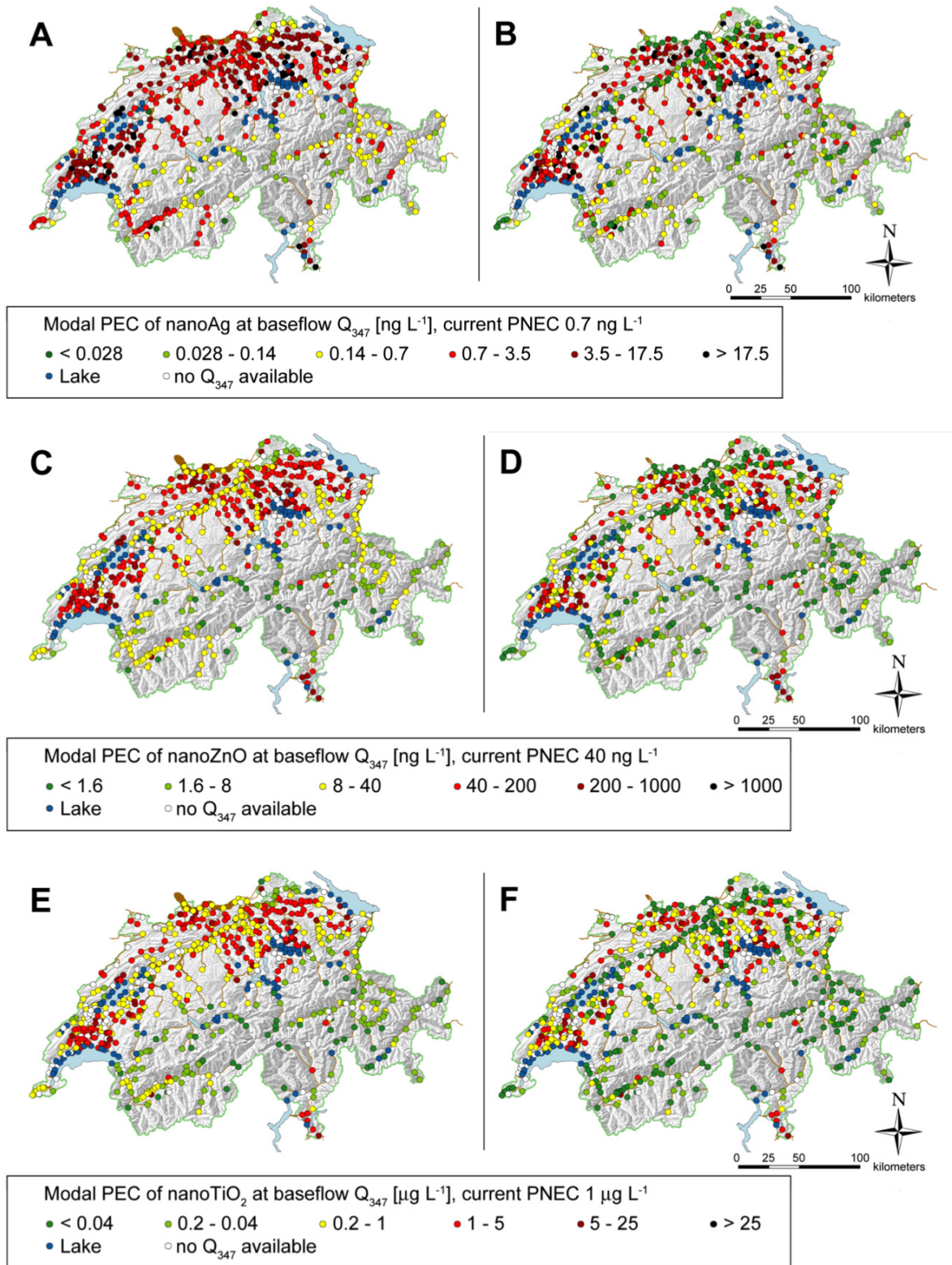


Figure 16. Predicted environmental concentrations (PECs) (mode values) of nano-Ag (A,B), nano-ZnO (C,D) and nano-TiO<sub>2</sub> (E,F) in Swiss rivers derived at base flow conditions  $Q_{95\%}$  (water level reached or exceeded in 95% of the time) and categorized in different ranges of magnitude (scenario without sedimentation (left side) and scenario with sedimentation). Red dots indicate river sections downstream from sewage treatment plants in which the corresponding PNEC is exceeded.

### 5.3.2 Concentrations modeled based on measured stream flows

Additionally, stream flow measurements for 20 selected locations over a 20-year period (1988–2007) were used to assess temporal PEC variation. The alpine river stretch named Vorderrhein (Ilanz) showed the smallest concentrations. The modal PECs for nano-Ag ranged from 0.04 ng/L to 0.07 ng/L (scenario without sedimentation). However, they were almost zero for the sedimentation scenario and for the whole considered time period. The highest concentrations were observed within the lowland river section Ergolz (Liestal). The modal PECs ranged from 5 ng/L to 12 ng/L (scenario without sedimentation). The sedimentation scenario values were approximately by a factor 3 smaller. The PECs (no sedimentation scenario) for nano-ZnO were approximately by a factor 17 higher and the same values for nano-TiO<sub>2</sub> by a factor 250 higher than the nano-Ag simulation outputs. However, also for these two materials the PECs for the Vorderrhein river (sedimentation scenario) were innumerable small.

The comparison PECs with PNEC values revealed that based on the used hydrological data and averaged for all 20 stations and scenarios (scenario with and scenario without sedimentation) the PNEC was exceeded for nano-Ag using modal concentrations at 234 days annually. The equivalent results for nano-ZnO and nano-TiO<sub>2</sub> were 150 and 109.

A detailed evaluation of simulated concentrations was conducted for two typical but different river sections (Fig. 17, left side): Birse-Soyhières after STP Courroux (initial part of the whole flow sequence) and Seyon-Valangin after STP Valangin (end of the flow sequence before flowing into a lake). For nano-Ag the most frequent simulated PECs for the scenario without sedimentation (modal values derived from the most frequent ENM load and water level data) ranged for the Birse-Soyhières river section (named Birse) from 0.7 ng/L (rain-packed year 1999) to 2 ng/L (dry year 1989), for the Seyon-Valangin river (named Seyon) from 3 ng/L to 8 ng/L. For the scenario with sedimentation in the Birse the equivalent PECs were all about half as large as for the scenario without sedimentation. For Seyon, those PECs for the scenario with sedimentation were immeasurably small. The reason is the small catchment area of this river section and that it is located after the last treatment plant before flowing (ca. 5 km) into Lake Neuchâtel. Thus, leaving out the ENM release from several other STPs has in such a case a higher impact on the ENM load than for river sections at the beginning of a flow sequence as the case e.g. for the Birse. For nano-TiO<sub>2</sub> the PEC values were again about a factor 250 higher for both river sections, in the case of nano-ZnO approximately 17 times higher.

The risk evaluation using water level data for the two prototypical river sections (Fig. 17, right side) showed (Birse, nano-Ag) for both scenarios (with and without sedimentation) and for most of the years annually approximately 200 and 350 days of exceedance at modal concentrations. In contrast, for Seyon a significant difference between the two scenarios was observed. For the case without sedimentation all the exceedances were higher than 340. However, considering full sedimentation between single STPs, only up to 50 days of PNEC-exceedance were observed. For nano-ZnO the simulations showed (Birse) for most of the years between 100 and 200 exceedances (with sedimentation) and only up to 80 days for the scenario without sedimentation. For Seyon the same divergence as for nano-Ag was observed. Considering sedimentation almost no exceedances were seen. However, for the scenario without sedimentation in most of the years more than 250 days of exceedance have been identified. In the case of nano-TiO<sub>2</sub> the number of exceedances was marginal for both scenarios (Birse), almost no exceedances for the scenario



with sedimentation and only between 10 and 100 days for the scenario where sedimentation was not considered. For Seyon the same divergence as for nano-Ag was observed. Almost no exceedances were observed for the sedimentation scenario, in contrast however, neglecting sedimentation about 200 to 300 exceedances.

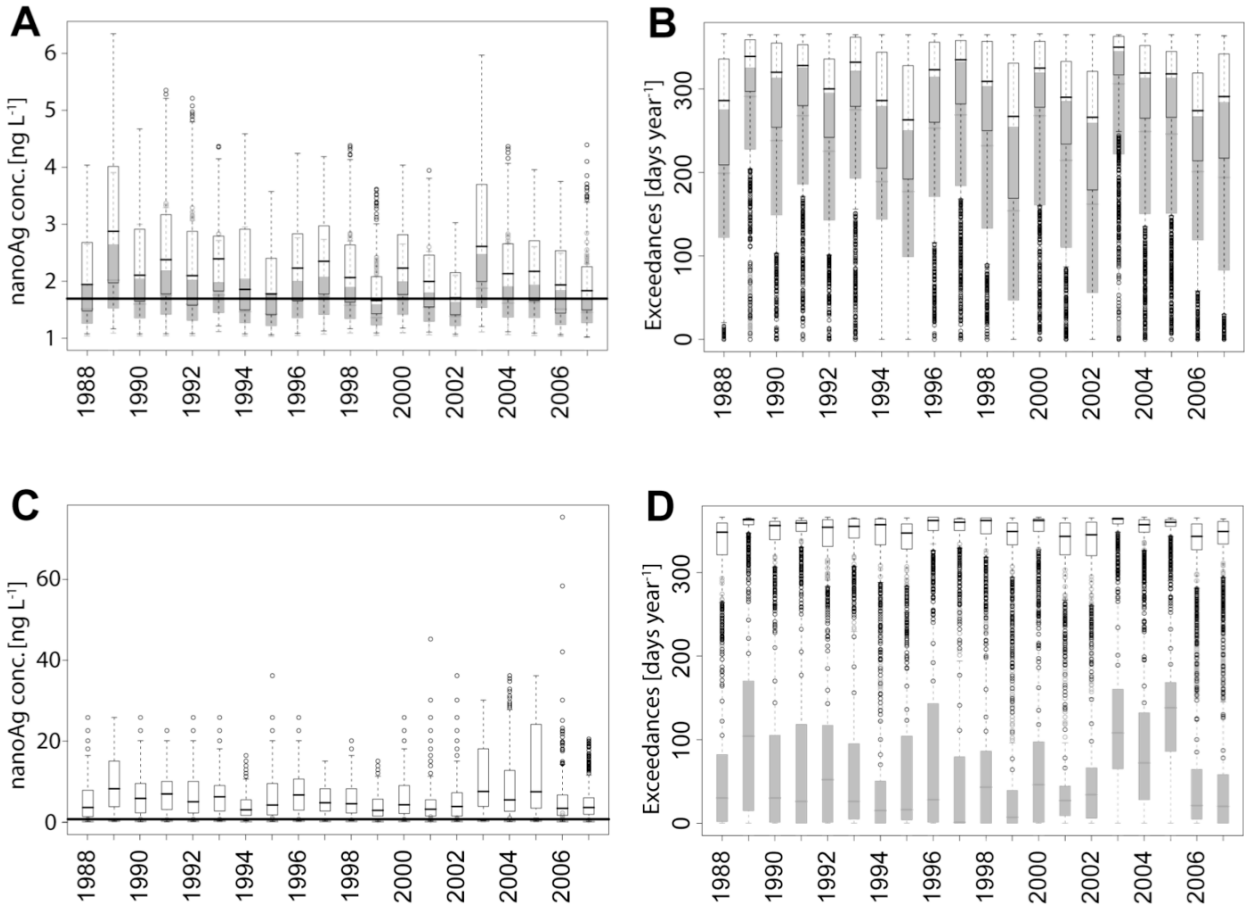


Figure 17. Predicted environmental concentrations (PECs) and exceedances (right side) of PECs above predicted no effect concentrations (PNECs) for nano-Ag ( $0.7 \text{ ng L}^{-1}$ ) in two river sections (Birse-Soyhières after STP Courroux (Délemont) (A,B) and Seyon-Valangin after STP Valangin (Valangin) (C,D) derived based on modal ENM loads and by means of water level measurement data (scenario without sedimentation (gray box-and-whisker diagram) and scenario with sedimentation).

Summing up, the diverging results – high correlation between the number of exceedances for the scenario with sedimentation and the scenario without sedimentation for the river Birse and conflicting results for the Seyon river (very high number of exceedances for the no sedimentation scenario and very low number of exceedances for the sedimentation scenario) – illustrate that the model parameter sedimentation influences considerably the ENM concentrations in river water (Fig. 17). The results showed in particular that the impact of sedimentation increases with increasing distance from the river source. However, the fact that such a crucial parameter had to be calculated based on hypothetical scenarios rather than based on a robust empirical data basis also shows the urgency of refining the sedimentation modeling.

## 5.4 Discussion

Modeling concentrations of pollutants in natural waters is influenced by two main parameters, the amount discharged into water and the water volume the compound is diluted in. Concerning the discharge there are some critical points. First, the total ENM input into rivers was distributed to each single river section exclusively based on the population each STP serves. This is reasonable so far as the studied metallic nanomaterials are used mostly in household products like cosmetics, coatings and cleaning agents (or for nano-Ag also textiles) (18). However, such a geographical allocation should be reconsidered e.g. if the industrial ENM use predominates in terms of volume the amount of household applications. Second, emissions from industry as e.g. direct release into rivers from ENM production and manufacturing facilities or ENM transport processes may undoubtedly occur as well. This applies at least for nano-Ag that is produced also in Switzerland (16) and thus not only imported from outside of the analyzed system. However, a nearly complete lack of data to such direct emissions makes these ENM release calculations very difficult. For improving this part of the model a distinction between produced, imported and exported ENM would be necessary. Unfortunately, doing this is almost impossible without trustable information from industry.

Regarding the ENM dilution this study represents an important improvement of the ENM PEC modeling for rivers since it considers real stream flows, avoiding to simply assume a one year retention time of ENM within a homogenous water cube as it is done for PEC calculations at regional level (national, continental resolution) (e.g. (20)).

The local PECs for ENM modeled at high spatial resolution in this work can however be compared to regional PECs obtained in previous modeling studies (16–18). The modal PECs calculated at base flow ( $Q_{95\%}$ ) conditions as well as the modal PECs calculated for the 20 river stretches based on historical water level measurement data are all covered by the range of the regional PECs (17) for surface water and for sewage treatment plant effluents (Table 15). However, Table 15 shows how challenging an improvement of the sedimentation modeling is and how difficult it is to compare results derived from different modeling approaches. PECs calculated in this study e.g. at base flow conditions ( $Q_{95\%}$ ) assuming complete sedimentation between two STPs are only about a factor 1.3 smaller than the equivalent values calculated considering the effluent loads of all STPs to remain in the water phase along the whole flow path. In contrast, the highest no-sedimentation PEC values in Mueller and Nowack (16) are approximately by a factor 7 higher than the highest no-sedimentation and  $Q_{95\%}$  (minimum dilution) PECs in this study. This shows again that results of a two-scenario analysis do not necessarily cover the whole range of relevant modeled output distributions of a MC analysis (18), in this study e.g. the range of the  $Q_{0.15}$  and  $Q_{0.85}$  quantiles.

Table 15. Predicted engineered nanomaterial (ENM) concentrations (PECs) in rivers, surface waters and sewage treatment effluents (STP) in Switzerland.

nano-TiO <sub>2</sub>	with sedimentation		without sedimentation		µg L <sup>-1</sup>	sources
STP Effluent (PEC <sub>regional-probabilistic analysis</sub> ) <sup>a</sup>					4.28 (3.5–16.3)	(17)
Surface Water (PEC <sub>regional-probabilistic analysis</sub> ) <sup>a</sup>	0.021 (0.02–0.09)					(17)
Surface Water (PEC <sub>regional-scenario analysis</sub> ) <sup>b</sup>			0.7–16			(16)
River Water PEC <sub>local</sub> ((Q95%) flows) <sup>c</sup>	0.01–2		0.09–2.5			(this study)
River Water PEC <sub>local</sub> (Birse-Soyhières) <sup>d</sup>	0.21	1.10	0.39	2.03	µg L <sup>-1</sup>	(this study)
	0.04	0.22	0.08	0.40	µg L <sup>-1</sup>	(this study)
River Water PEC <sub>local</sub> (Seyon) <sup>d</sup>	0.07	0.35609	2.31	12.11	µg L <sup>-1</sup>	(this study)
	0.68	0.03561	0.23	1.21	µg L <sup>-1</sup>	(this study)
<b>nano-ZnO</b>						
STP Effluent (PEC <sub>regional-probabilistic analysis</sub> ) <sup>a</sup>					0.44 (0.3–1.3)	(17)
Surface Water (PEC <sub>regional-probabilistic analysis</sub> ) <sup>a</sup>	0.013 (0.01–0.06)					(17)
River Water PEC <sub>local</sub> ((Q95%) flows) <sup>c</sup>	0.00–0.14		0.01–0.2			(this study)
River Water PEC <sub>local</sub> (Birse-Soyhières) <sup>d</sup>	0.02	0.07	0.03	0.14	µg L <sup>-1</sup>	(this study)
	0.07	0.01	0.01	0.03	µg L <sup>-1</sup>	(this study)
River Water PEC <sub>local</sub> (Seyon) <sup>d</sup>	0.01	0.02	0.17	0.81	µg L <sup>-1</sup>	(this study)
	0.00	0.00	0.02	0.08	µg L <sup>-1</sup>	(this study)
<b>Nano-Ag</b>						
STP Effluent (PEC <sub>regional-probabilistic analysis</sub> ) <sup>a</sup>					38.7 (30–127)	ng L <sup>-1</sup> (17)
Surface Water (PEC <sub>regional-probabilistic analysis</sub> ) <sup>a</sup>	0.72 (0.6–2.6)					ng L <sup>-1</sup> (17)
Surface Water (PEC <sub>regional-scenario analysis</sub> ) <sup>b</sup>			30–80			ng L <sup>-1</sup> (16)
River Water PEC <sub>local</sub> ((Q95%) flows) <sup>c</sup>	0.02–8.3		0.4–10.4			ng L <sup>-1</sup> (this study)
River Water PEC <sub>local</sub> (Birse-Soyhières) <sup>d</sup>	0.84	4.20	1.55	7.72	ng L <sup>-1</sup>	(this study)
	0.16	0.82	0.30	1.51	ng L <sup>-1</sup>	(this study)
River Water PEC <sub>local</sub> (Seyon) <sup>d</sup>	0.27	1.36	9.26	46.08	ng L <sup>-1</sup>	(this study)
	0.03	0.14	0.93	4.61	ng L <sup>-1</sup>	(this study)

<sup>a</sup> Predicted environmental concentrations (PEC) modal values (lower and upper quantiles Q<sub>0.15</sub> and Q<sub>0.85</sub>) taken from Gottschalk et al. (17).

<sup>b</sup> PEC range derived from the realistic scenario and high emission scenario in Mueller and Nowack (16).

<sup>c</sup> PECs derived from modal ENM loads (range of the lower and upper quantiles (Q<sub>0.15</sub> and Q<sub>0.85</sub> of the ENM load distribution of all river sections) at water level conditions Q<sub>95%</sub> (water level reached or exceeded in 95% of the time).

<sup>d</sup> PECs derived from lower (left side) and upper quantiles (Q<sub>0.15</sub> and Q<sub>0.85</sub>) of ENM loads and lower (above) and upper quantiles (Q<sub>0.15</sub> and Q<sub>0.85</sub>) of flow rates.

Thus, the results in Table 15 reflect very well the different approaches used to cope with the difficulties to model such water-sediment partitioning of ENM. In Mueller and Nowack (16) secondary compartments (sediment and groundwater) had not been considered due to a total lack of data. Gottschalk et al. (17) later reduced the analysis of ENM fate in rivers to the modeling of probability distributions for sedimentation rates based on first available data. Due to the consideration of the sedimentation of the ENM in surface water the simulated PECs are significantly smaller compared to the results in Mueller and Nowack (16).

Finally, the results in Table 15 show also that different water flow conditions (15% and 85% quantiles of the water level distributions) may influence the concentrations up to a factor of 5. The comparison of concentrations based on different ENM loads (15% and 85% quantiles of ENM emission distribution) show a difference of about a factor 5 for the river section Birse and about a factor of 10 for the river section Seyon. This makes answering the question difficult whether the uncertainty in the input of ENM into rivers influences more or less the concentrations than the time dependent variability of the water level. In the case of the Birse the ENM input into rivers equals the uncertainty in the PECs caused by the uncertainties in the estimation of the natural variability of the water levels. However, the river section Seyon shows that the variability in the water levels influences much more (up to a factor 2) the ENM PECs than the computed variation in the ENM input. This underlines first that considering dilution caused by variability in water levels is significant in the ENM PEC modeling for rivers and second that the influence of such variability differs considerably between single river stretches. This illustrates however also the necessity to integrate in the calculations a dynamic (time dependent) modeling of the ENM input into the environment to improve the PEC calculations. Such a time based differentiation in the ENM input simulations would in combination with the consideration of water level dynamics lead for the first time to a real and high temporal resolution of the ENM PEC modeling for rivers.

In addition, the results also showed that the geographical location between river head and estuary in the river sequence has a significant impact on the concentrations. Locations near the river head do normally not suffer from too high anthropogenic ENM input into river water and consequently show in general only marginal concentrations (see also Fig. 16). However, the stream flow variability, which was shown to be a crucial model parameter, may depend on the geographical position as well. River sections at the end of the river course near the river mouth show e.g. a different seasonal variation in the water flows than for instance alpine river sections near the river source with relatively small water catchments and e.g. small dependence of rainwater.

Nevertheless, due to a revised modeling of ENM release to and water contents in rivers, such a model should primarily be improved by including the modeling of fate and behavior of the considered material in river water. Thus, studying in more detail the extent of solubility, agglomeration, aggregation, adsorption, deposition behavior and interaction of ENM with organisms in rivers has high priority in the improvement of such ENM load modeling. However, in this work we were still faced with similar uncertainties in the available data to ENM aggregation/deposition behavior in river water. Rapid deposition rates leading to almost full sedimentation after 24 h was shown in Boncagni et al. (27) e.g. for commercially available aerioxide P25 TiO<sub>2</sub>. In contrast, for sol-gel synthesized porous anatase TiO<sub>2</sub> almost no

sedimentation was observed. Since the two nano-TiO<sub>2</sub> types showed totally different deposition/aggregation behaviors the authors state that examining more types of nano-TiO<sub>2</sub> to draw generic conclusions for modeling sedimentation of nano-TiO<sub>2</sub> was necessary (27). Battin et al. (5) complemented the results of Boncagni et al. (27) by studying effects of benthic biofilms on ENM exchange between water and streambed. The authors demonstrated that biofilms strongly effect the travel distance of two types of nano-TiO<sub>2</sub>. Hombikat UV-100 and P25 nano-TiO<sub>2</sub> traveled in a control flume without biofilm 10 and 12 km downstream before being removed from the water. However the results also showed that biofilms had reduced the travel length 2.3 times for Hombikat UV-100 and 2.7 times for P25. In addition, the authors anticipated that in natural streams, streambed roughness and hydrodynamic exchange could shorten the transport distance of ENM. However, they also stated that different ratios of flow velocity to streambed depth may in contrary contribute to longer transport distances and that size fractionation during longitudinal transport leads to exposure to different particle sizes of the same material. Being far away from a comprehensive understanding of sedimentation our scenarios of no sedimentation as well as full sedimentation represented thus only a rough approximation to uncertainties and ambiguities on the ENM deposition behavior.

So far, an improvement of dispersion and stability modeling of such compounds in river water requires a distinction between the different modifications of the analyzed compound. Efforts to improve the environmental fate analysis should e.g. focus on the impact of coatings and surface treatments that may affect considerably ENM aggregation and agglomeration behavior. However, besides intended surface functionalization of the ENM by chemical or biological processes, such an improved model should furthermore consider that nanomaterial may be modified on their surface also by environmental factors such as coatings of organic matter (3).

A further way to overcome limitations of our approach would be to integrate also storm water runoffs (STP overflow) that cause short-time pollutant loads in rivers but at the same time also lead to very high water flows and thus dilution. However, in this study the mostly small and regulated Swiss rivers were estimated to have a residence time from their formation until they reach a reservoir (e.g. lake) or leave the national border of less than one day (23). Thus, STP overflows leading mostly to short-term (<24 h) release of pollutants into rivers were not relevant for such a small systems.

Gottschalk et al. (17) calculated the following modal risk quotients for organisms in surface water based on available ecotoxicological literature and a safety factor of 1000: nano-Ag (1.03), nano-ZnO (0.32), and nano-TiO<sub>2</sub> (0.02). Our calculations for rivers confirmed these results reflecting the same order of PNEC exceedances for these three substances. At base flow conditions for nano-Ag the PNEC was exceeded in more than 90% of the simulations in 339 river sections out of 539, in the case of nano-ZnO in 210 river sections and for nano-TiO<sub>2</sub> in 126 sections. Considering water level measurement data the PNEC was exceeded e.g. for the Birse-Soyhières river (scenario with sedimentation) in average at 314 days per year for nano-Ag, at 144 days for nano-ZnO and in the case of nano-TiO<sub>2</sub> in 22 days. Also these latter results reflect the same order of concentrations and demonstrate in accordance to the previous works (16–18) especially the need for further studies on aquatic exposure to nano-Ag. Lastly, we should also keep in mind that although the simulations were carried out at high spatial and time resolution at local scale, in some river sections e.g. near ENM production sites much higher ENM concentrations could be

observed. Also accidents with ENM or e.g. new ENM products on the market with novel emission properties could lead to significant higher ENM loads.

The results presented in our work provide ecotoxicologists with concentration ranges for ENM that can be used to design acute and chronic toxicity tests. The data also provide hints in which river stretches currently high concentrations and frequent PNEC-exceedances of ENM can be expected and thus effects on aquatic and benthic communities might be expected first. These results may thus provide ecologists with background information where to look for possible effects of ENM. Our modeled concentrations will also help analytical chemists to develop trace methods for ENM analysis in waters as they provide a guidance which concentration level needs to be reached and where the highest concentrations can be found. An experimental validation of the modeled concentrations would be highly desirable but currently no methods sensitive enough for trace analysis in the environment are available (28).

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## 6. Concluding remarks

Currently there is a lot of attention paid to potential life cycle impacts and toxicity of engineered nanomaterials (Alvarez et al. 2009; Andreev et al. 2009; Borm et al. 2006; Chaudhry et al. 2008; Handy et al. 2008; Helland et al. 2006; Hund-Rinke and Simon 2006; Klaine et al. 2008; Nowack 2007; 2008; 2009; Oberdorster et al. 2007; Scheringer 2008; Som et al. 2010; Wiesner et al. 2006; Wiesner et al. 2009). Unfortunately, there is still very limited data available on the environmental fate and effects of such material, and consequently a lot of questions arise concerning the possible risks caused to the environment and human health. In addition, ENM specific regulations lag behind the technological development of products containing nanomaterial and probably also behind first available scientific insights into the potential risks caused by ENM. Furthermore, voluntary industrial risk study initiatives are considered vital to questions on the effects of ENM on environmental health and safety (Helland 2007). However, availability and quality of such engagement from industry are difficult to monitor. Because hardly any analytical methods are available for ENM, the discussion of ENM and the environment differs completely from that on e.g. organic micropollutants, where advances in analytical detection of the compounds in the environment have been the starting point for scientific and public discussions (Nowack and Bucheli 2007). Thus, compared to conventional contaminants (chemicals) for ENM the discussion clearly anticipates the possibility of their quantitative detection in the environment. As a consequence, predictions of the concentrations to be found in the environment and studies on potential exposure pathways based on mathematical modeling are needed and, as shown in this thesis, would be a valuable first tool to evaluate and predict risks posed by ENM to the environment. In doing so, life cycle concepts should be considered to provide a comprehensive identification of priorities of the analysis of ENM release and assess the potential of organisms in the environment being exposed to such materials (Som et al. 2010). Since only a few studies are available on ENM release from products and almost no data on ENM emissions from ENM production and nanoproducts' manufacture processes, and the existence of main or strong dominant single ENM polluter are not expected, covering all life stages of the contaminants will also in the future have a high priority in the ENM exposure modeling. However, such life cycle thinking is difficult, communication between the actors of the value chain and throughout the different life stages of the nanomaterial containing products is still needed (Koehler and Som 2008).

### 6.1 Probabilistic material flow analysis – an adequate, however also limited tool for exposure modeling

The developed probabilistic material flow analysis applies established approaches such as material flow analysis, sensitivity and uncertainty analysis, Monte Carlo simulation, Bayesian and Markov Chain modeling to calculate PECs for contaminants characterized by a distinct lack of model input data. From a methodological perspective, the use of each single technique is not new. However, the developed probabilistic material flow analysis (PMFA) includes probabilistic/stochastic computational routines that allow one to combine these different approaches into a single model framework covering the whole life cycle of potential contaminants

in complex systems of the biosphere as well as in technical compartments. Hence, the PMFA presented here includes all main natural media and main technical compartments (pollutant production; manufacturing of pollutant containing products; use, recycling and disposal of such products and pollutants' fate in waste incineration and sewage treatment plants) in addition to extending standard MFA by means of stochastic algorithms compared to generic chemical fate models.

Nevertheless, even sophisticated mathematical techniques do not create empirical model input data. Hence, a minimal input data basis is needed even in stochastic calculations to generate quantitative model input parameters. Thus, it is not surprising that the thin data base represents the key weakness in our ENM-flow modeling. For all ENM such data is very scarce and thus, the use e.g. of uniform distributions for some input parameters unavoidable. In cases where no data were available, the borders of the distributions had to be determined by experts, a fact which in turn may lead to even higher uncertainties in the input parameters. However, the case studies and first validations of the simulation results pointed out that the probabilistic material flow analysis is an adequate tool to predict ENM concentrations in the environment when little data are available. It allows using any kind of probability distribution functions for the input parameters. Such an analysis allows incorporating a large number of processes and flows in order to compute compound flows into and deposition rates in environmental and technical compartments. Another advantage of this modeling is that an improvement of prior input data by incorporating e.g. MCMC algorithms and by starting from new available e.g. simulation or measured data is possible at any time and for any part of the model.

Furthermore, the model allows one to show how relative changes of input parameters produce variations in the simulation output by means of a sensitivity analysis. This is a valuable approach to find out the most influential model input parameters. Indeed, it does not provide new empirical model output knowledge to the material flow itself. However, by incorporating in this sensitivity analysis also the uncertainty of the parameter estimation the confidence in the simulation results is evaluated by comparing the parameter sensitivity with the robustness of the parameter estimation. As a consequence, the goal of each modeling should be to avoid that the most influential parameters are based on the most uncertain data, otherwise the confidence in the simulation output would be small.

Although comparisons of the model outputs to previous studies (Blaser et al. 2008; Mueller and Nowack 2008) and first measurements (Kiser et al. 2009) had been done successfully, the discussion of the limitations of such a probabilistic/stochastic approach is essential to guarantee good scientific and practical use of the simulation outputs and to discuss the requirements for reducing the uncertainties in future simulations. There are two main limitations within the presented approach. On the one side, for several model input distributions large value ranges had to be used due to a general lack of empirical data. On the other side, all the calculations were restricted to steady state calculations for only one time period (2008). First, the data found in the literature for the key parameter, the annual production volumes of ENM, vary up to a factor of 100. Thus, large ranges of input distribution had to be modeled. Inventories listing all products containing ENMs and the used ENM masses are almost completely missing. However, an initial step was done by Schmid & Riediker (2008), who provided a first quantitative overview containing product categories allocated to incorporated ENM volumes. The second critical point is that the steady state modeling neglects storage of ENMs and ENM-containing products e.g. within the

ENM consumption processes. Data concerning such storage are missing entirely. Nevertheless, modeling time dependent ENM production quantities and storage processes would be one of the most important steps for improving the simulations.

In addition, also very little quantitative information on ENM emissions during the manufacturing of ENM-containing products and during the production of ENMs are available yet and makes the modeling difficult. Experimental data are restricted almost exclusively to ENM release from textiles (Benn and Westerhoff 2008; Geranio et al. 2009) or paints (Kaegi et al. 2008). The same absence of data is observed for the ENM release during the production of ENM and the manufacturing of ENM containing products although first measurements at companies producing ENM showed that worker exposure to these materials occurs (e.g. Yeganeh et al. 2008). The assignment of the average mass of ENMs in products lacks also on empirical information and had thus to be carried out modeling relative large distributions for the average weight of a prototypical product of each category and for the average proportion of ENM in these products.

Additional key limitations are represented by the simplification of the modeling of the ENMs' fate in nature. Fate and behavior modeling was reduced to the consideration of transfer coefficients between the single compartments. The exchange between water and sediment through resuspension and burial processes could for instance not be considered due to a lack of data. The same applied to streambed roughness and depth, flow velocity and ENM exposure to plankton and adsorbed microorganisms that undoubtedly influence e.g. ENM transport distances and accumulation in sediments as well. Especially getting results from studying aggregation behavior of ENMs under environmentally realistic conditions is needed to improve this part of the modeling. Experimental results derived under realistic conditions are needed also to biotransformation and -accumulation, or dissolution of ENMs. Lastly also the modeling of aerodynamics should not remain restricted to rough calculations of atmospheric deposition based only on data for ultrafine particles.

## 6.2 Main insights from the simulation outputs

Of all the materials considered, nano-TiO<sub>2</sub> generally showed the highest emission volumes and environmental concentrations, followed by nano-ZnO, nano-Ag, CNT and fullerenes. This reflects the chronology of the values of the most crucial input parameters, the ENM production volumes. However, similar environmental concentrations e.g. of nano-TiO<sub>2</sub> and nano-ZnO also reflect a comparable mass distribution to product categories (cosmetics and coatings and cleaning agents) that led to significant emissions into water. Consequently, water concentrations of CNTs or fullerenes might increase as well in the future if those materials were applied in product categories with significant ENM release to water. The modeled flows of nano-TiO<sub>2</sub> and nano-Ag show that for these materials the most dominant ENM transfers are from PMC to STP and WIP, STP to WIP and from there to landfills. In the case of CNTs and fullerenes, the majority of the material ended up in the WIP.

A comparison of the modeled regions illustrates that ENM concentrations for most environmental compartments are in a similar range for all regions. This may be explained with the fact that ENM production volumes were scaled according to the inhabitants of each region. Hence, regional distinctions concerning ENM applications were neglected, although they would allow one to model regional or local specific ENM flows into natural and technical environments. In order to do

this, it would be necessary to create regional databases on products containing ENM. Apart from modeling region specific ENM emissions, it would also be important to monitor continuously the development of new products containing engineered nanomaterial. Products with novel emission properties which are not on the market now could lead to significantly higher ENM release in the future. The key variations among regions are also visible in the different approaches of handling sewage sludge. Countries that dispose of waste in landfill have to deal with significant concentrations of ENMs in sludge-treated soil, while countries with complete incineration of sludge are obviously not faced with this problem.

From the sensitivity analysis, we may conclude in summary that for the metallic materials a closer look is needed at the parameters that cover the release of ENMs from the products to the STP, the STP removal efficiency and overflow and the sludge from this compartment ending up in the WIP, where it is incinerated, exported or deposited in landfills. The reason for the dominance of these parameters is that the major application volumes are in product categories such as cosmetics and coatings, paints and textiles and that releases from such applications mostly result in emissions into STP inflow. Even though CNTs and fullerenes end up in very small amounts in the STP inflow, the parameters STP overflow and STP removal efficiency influence most of all the CNT and fullerenes concentrations in water. The interpretation of these results is however complicated by the fact that very small amounts of ENMs actually reach this compartment. However, the sensitivity analysis shows that to improve the prediction of where ENMs end up, the most critical information is not related to fate and behavior in natural systems but to fate and behavior in the technosphere, all above in the application of ENMs in products and their release during the use consumption phase.

PEC calculations at high spatial resolution were carried out (ENM in Swiss rivers) in addition to regional PEC studies. Those results showed that ENM concentrations in river waters are influenced by two main parameters, the amount discharged and the water volume the compound is diluted in. Thus, calculations of PNECs for rivers at regional or national resolution provide a first rough estimation of possible concentrations. Different water flow conditions (15% and 85% quantiles of the water level distributions) may influence the concentrations up to a factor of 5. The comparison of concentrations based on different ENM loads (15% and 85% quantiles of ENM emission distribution) showed a difference of up to a factor 5, for some river sections up to 10. This makes answering the question whether the uncertainty in the input of ENM into rivers influences more or less the concentrations than the time dependent variability of the water level difficult. However, for all ENMs, scenarios and water level conditions, the calculated concentrations are in a plausible range compared to all precedent studies, and the highest concentrations were found in the midland or near urban centers or large tourist destinations in the Alps. The concentrations modeled in rural areas were negligible small even at low water levels. However, we also observed that the geographical location between a river head and an estuary in the river sequence has a significant impact on the concentrations. Locations near the river head have a small catchment area and do consequently not suffer from too high ENM input into river water, showing thus in general only marginal concentrations.

Additionally, the calculated modal risk quotients for organisms in surface water at regional resolution (nano-Ag (1.03), nano-ZnO (0.32), and nano-TiO<sub>2</sub> (0.02)) were confirmed by the last mentioned simulations at high spatial resolution. The latter results reflect the same order of PNEC exceedances for these three substances. The PNEC (base flow conditions) for nano-Ag

was exceeded in more than 90% of the time in 72% of the river sections, for nano-ZnO in 39% of the river sections and for nano-TiO<sub>2</sub> in 24% of the sections. However, the results at high spatial resolution provide also better indications than simple regional calculations to the question in which river stretches currently high concentrations and frequent PNEC exceedances of ENM can be expected and thus where effects on aquatic and benthic communities might be expected first. Such results give ecologists better information where to look for possible effects of ENM. However, they will also support analytical chemists to develop trace methods for ENM analysis in waters showing which concentration level is needed and where the highest concentrations can be found.

Concluding, one can say that the risk assessment showed that risk cannot be excluded for organisms exposed to nano-TiO<sub>2</sub> and nano-Ag in STP effluent and STP sludge and nano-Ag in water. For all other ENMs and compartments the currently (2008) calculated concentrations pose no risks to organisms. Hence above all, further investigations are needed to evaluate ENM exposure to aquatic organisms from these metallic materials. In particular, a need for further studies concerning silver concentrations in water is evidenced by the fact that silver ion release and emissions of micro-sized silver were not covered by our simulations.

We conclude that:

- data on ENM production, use and release to the environment is still very sparse;
- extending MFA to stochastic/probabilistic MFA provides a model framework to calculate PECs of contaminants although only few data is available;
- PEC simulations for different ENMs (TiO<sub>2</sub>, Ag, ZnO, fullerenes, carbon nanotubes) and different regions (Switzerland, Europe, USA) show that relevant exposure to these materials occurs for the metallic ENMs in aquatic environments;
- the uncertainty of the parameter estimation may be incorporated in the sensitivity analysis and that this is essential to study the parameter sensitivity by considering also the robustness of stochastic simulation outputs;
- the most influential model parameters cover the release of ENM to the STP, the STP removal efficiency and overflow and the sludge from this compartment reaching the WIP, where it is incinerated, exported or deposited in landfills;
- the key limitations of the approach are represented by calculations that consider partially distributions with large value ranges and parameter dynamics for only one time period, and by the simplification of the modeling of the ENMs' fate in nature by using simple mass transfer coefficients to model material exchange between the single natural compartments.

### 6.3 Further research

As seen in Helland (2007) and mentioned above, the environmental health and safety of nanomaterials will also depend to a significant extent on the voluntary initiatives by industry. However, in industry there are probably no structured methods available on how to assess the risks caused by engineered nanomaterials. Therefore, a refinement of the probabilistic/stochastic assessment framework provided here, e.g. into a user-optimized tool for private and industrial applications, could have some priority in further research. However, this cannot disguise the fact

that, in particular, improvements in the exposure modeling itself are needed. Although it is accepted (and partially already considered in toxicity studies) that ENM size may be crucial with respect to toxicity, size effects on the behavior and reactivity of ENM could, due to parametric insufficiencies caused by the distinct scarcity of empirical input data, not really be incorporated in the environmental fate modeling. Getting this type of empirical information is difficult since nanoproducts do not contain a homogeneous group of ENMs. ENMs incorporated may differ in size, shape, impurity and other physicochemical properties (Som et al. 2010). Consequently, an improved ENM emission and environmental fate modeling should also cover the different forms ENM may be released from nanomaterial containing products (single and free particles, aggregated/agglomerated material, or emissions of ENM as part of emitted nano- or micro-sized matrix particles). In addition, for future fate and behavior modeling we should consider that the used ENMs may be functionalized, e.g. to avoid aggregation and agglomeration or to stabilize the material in the product matrix, and that this could significantly affect ENM behavior in natural and technical environments (Nowack and Bucheli 2007; Som et al. 2010). However, also functionalization by environmental factors or the coating of the surface by natural compounds is neglected until now in the modeling and should therefore be integrated in future studies.

Finally, the risk assessment based on a PEC/PNEC comparison suffers from high uncertainties in the PNEC estimation. The derivation of PNECs is difficult because of the limited number of studies and the focus of such studies only on acute toxicity and only on a few numbers of test species and toxicity endpoints. ENM toxicity is mostly studied on model organisms (bacteria and algae, daphnids etc.) and by means of ENM concentrations several orders of magnitude higher than available PECs. Hence, future work should include long-term exposure to derive chronic endpoints if at all possible. This should be carried out for the largest possible range of model organisms and under environmental ENM concentrations.

One of the most important points for future research is the epistemological question as to what extent it is appropriate to model input (and structural) imprecision/uncertainty exclusively by means of precise probability distributions. Is the imprecision in the probabilities of input parameters expressed in a way sufficient to reflect an appropriate level of confidence in the modeling? Standard frameworks of decision theory do not provide any clear approach to deal with partial or fuzzy knowledge (Lossin 2005). The two fundamental ways of representing possibilities of coping with imprecision in the models are fuzzy probabilities, as initially presented by Dubois & Prade (1978), or the modeling of imprecise probabilities based more or less on upper and lower previsions, as initially proposed by Walley (1991). Both of them are similar regarding the mathematics they require, but different concerning the knowledge a decision maker needs to have about the probabilities (Lossin 2005). In this thesis we have combined data from empirical studies with expert knowledge and our own estimations of the model input to create probability distributions. In the case of nanotechnology the sample data is sparse due to the lack of experimental/empirical trials. Monte Carlo and Bayesian techniques could be used since some expert knowledge and a few empirical data were available. Such Monte Carlo Bayesian procedures have been used successfully also in other cases e.g. for modeling concentrations of DDT in the environment (Schenker et al. 2009) where calculations were carried out by means of the well established global multimedia model CliMoChem (Scheringer et al. 2000; Wegmann et al. 2004).

However, Bayesian thinking assumes that probabilities are precise. Unfortunately, in practice, the use of “precise” probabilities for the states of nature suffers from uncertainty due to the imprecision persisting in experts’ estimations or the data themselves. Hence, subsequent studies should also evaluate ways to extend such a Monte Carlo Bayesian model by integrating also imprecise uncertainties. Tu et al. (2008) present such an extension based on a decision support model that uses interval-valued probabilities to represent experts’ uncertain beliefs in Bayesian approaches. Scholz (2010) discusses Walley’s concept of imprecise probability (Walley 1991). This approach considers that exact subjective probability is unknown but that the range in which it is located may be estimated taking the lower probability to be the maximum rate at which an expert would bet on an event, and the upper probability to be the minimum rate at which it would bet against the event. However, the critical question of stochastic modeling what type of probability distribution to assume is not directly touched by such an approach. However, Fox & Rottenstreich (2003) illustrated that likelihood judgments may be biased toward an ignorance-prior probability that allocates equal credence to mutually exclusive events considered by the expert judgment. The value of the prior ignorance depends strongly on how the set of model input parameter spaces is partitioned by the judge. Thus, lower-upper probability estimations by naïve judgments may show partition dependence, despite the potential that imprecise probabilities promise avoiding it.

Another way to derive imprecise probabilities is the incorporation of logical techniques. Cozman et al. (2008) propose e.g. graph-theoretic representations for probabilistic logic providing complexity results and algorithms for their formalism. The authors examine a probabilistic logic generalizing relational Bayesian networks. Others (de Saint-Cyr and Prade 2008) propose formalisms in which uncertain default rules based on possibility theory can be expressed under incomplete information.

Finally, climate change modeling techniques may eventually help to cope with imprecise probabilities in ENM exposure assessment as well. Several facets of climate uncertainty, e.g. uncertainties in emission scenarios, may not be reflected only by means of a quantification through simple probability distributions (e.g. Grubler and Nakicenovic 2001). Hall et al. (2007) modeled e.g. socio-economic scenarios as fuzzy linguistic constructs. The emissions trajectories required for climate modeling are characterized as a degree of membership in such a fuzzy scenario. Scenario uncertainties and imprecise probabilities of model uncertainties are combined using random set theory to generate lower and upper cumulative probability distributions e.g. for the Global Mean Temperature anomaly.

In conclusion, we cannot provide here an authoritative discussion on how to deal with data and knowledge that are both uncertain and imprecise; nor can we discuss conclusively the necessity or potential that our model framework might integrate such techniques. However, it will be the task for further research to focus e.g. also on potentials of such stochastic computational routines for transformations from “precise” probabilities into other formalisms such as imprecise probabilities (lower and upper estimations, possibilities, belief functions, fuzzy sets etc.).

However, structural imprecision should not fall totally into oblivion along with parametric uncertainties. The question of to what extent more empirical data would allow one to integrate e.g. biota (bioaccumulation) also in the model framework to expand and improve the simulations has e.g. to be answered. The same applies to the question of to what extent the use of transfer coefficients is adequate to model ENM fate and behavior in natural and technical compartments.

More experimental information e.g. to material (nanomaterial containing products) degradation would help restructure, for instance, the ENM fate and behavior modeling in environmental and technical compartments. Finally, our simulations assumed, besides constant production levels for all time periods, a total use of the ENM produced and a total transfer of this material to products, technical or environmental compartments during the considered time period. Thus, temporal aspects such as e.g. storage of ENM before used in products, storage of ENM in ENM containing products before been consumed and released and ENM production volumes that vary over time should be considered as well in future studies.

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## 7. Appendix: Modeled environmental concentrations of engineered nanomaterials (TiO<sub>2</sub>, ZnO, Ag, CNT, fullerenes) for different regions

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### A. Description of the system compartments

For calculating the concentrations of ENM in water bodies the dilution factor was calculated by multiplying the relevant water mixing depth of 3 m (1) by the water surface area of the corresponding region. It was assumed that all water body reaching ENM will either infiltrate the groundwater, settle to the sediment or are exported with the system leaving water flow. According to the technical guidance document (1) a residence time of 40 days was applied.

The considered annual dry sewage treatment sludge productions for the studied regions were: 203,000 t (2) for Switzerland, 7,500,000 t (3) for the USA and 9,000,000 t (4) for the EU.

For airborne nanoparticles a residence time in the atmosphere of 10 days was assumed corresponding to ultrafine particles (5). The relevant air volume was calculated by multiplying the area of the particular region by the recommended value for atmospheric mixing height of 1 km (1). Deposition from air to soil and water occurred proportional to the land area covered by water and soil. Following water to soil proportions were used: Switzerland: 4.2% to 96.8% (6), EU: 3% to 97% (1) and USA: 6.8% to 93.2% (7).

ENM reaching the soil were assumed to accumulate within this compartment. The soil volume was calculated by multiplying the soil depth depending on the mixing depth of different soil types (natural and urban soil: 0.05 m, agricultural soil: 0.2 m (1)) by the corresponding area of the particular region. This results in relevant soil volumes of 4.1667 km<sup>3</sup> for Switzerland, 34.6602 km<sup>3</sup> for Europe and 339.358 km<sup>3</sup> for USA. The density of dry soil was calculated by subtracting the water content from the standardized value of 1,700 kg m<sup>-3</sup> recommended by the European Commission (1) resulting in 1,500 kg m<sup>-3</sup>.

ENM reaching the sediment were assumed to accumulate in this compartment. The relevant volume of the sediment was approximated by multiplying the water surface area by the depth of the sediment of 0.03 m (1). The density of dry sediment was calculated by subtracting the water content from the standardized value of 1300 kg m<sup>-3</sup> recommended by the European Commission (1) resulting in 260 kg m<sup>-3</sup>.

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Landfills were assumed to be sealed off at the bottom, and therefore almost no leachate reaches the soil or surrounding water bodies in this model.

Although recycling was implemented in the model, it was impossible to quantify the amount of ENM leaving a certain recycling process. Therefore, it was reasonably assumed that during the recycling process of ENM containing products all particles were either incinerated or aggregated to larger particles. Hence, all particles entering the recycling compartment were eliminated in this model.

## **B. ENM production volumes and allocation of these volumes to product categories**

Table 16 shows the worldwide production volumes in t per year for the studied ENM obtained from various sources. The ENM production volumes were allocated to commercially available ENM containing products. The ENM containing products themselves were grouped into product categories with similar ENM emission properties and fractions of ENMs (8). The allocation (see Table 17) of the ENM masses to the product categories was then modeled by means of probability distributions which were derived from two factors, the “number of products containing ENM” in each product category and the “average mass of ENMs” in each product (8, 9). To count the commercially available ENM containing products and allocate them to the product categories, a web search was carried out. Within the first 500 results of two common Internet search engines (10, 11) the ENM containing products were counted. Only commercially available products on manufacturer websites were considered. Furthermore, all products on a Global Marketplace Platform (12) were counted except master batches and powders. Finally, the inventory of nanotechnology-based consumer products from the Woodrow Wilson Institute (13) was considered as a representative database for the current market situation of commercially available consumer products containing ENM. Therefore, all products in this database were taken into account. Additionally, the survey of Schmid et al. (14) was used for classifying nano-ZnO, nano-TiO<sub>2</sub>, and nano-Ag and the information sheet from NICNAS (15) for nano-ZnO and nano-TiO<sub>2</sub>. For CNT the classification was also based on expert information.

The CNT results indicate that at least 90% of the ENMs are allocated to the categories composites and consumer electronics. In the case of nano-ZnO, about 65% (mean value) of the nanomaterial is applied in cosmetics. Cosmetics, coatings and cleaning agents, plastics and filter aggregates cover more than 90% of the fraction of the total ENM application for nano-TiO<sub>2</sub>. In the case of nanosized silver, the results are inconclusive. The fraction applied in textiles, paints and coatings and cleaning agents are weakly dominant and cover together about two-thirds of the mass distribution. In the case of fullerenes, the results show approximately a one-sided triangular distribution from 0.5 to 1 with a mode of 1 for the R&D sector. The remaining part was distributed uniformly to composites and cosmetics.

Table 16. Worldwide production volumes of ENM in t per year obtained from different sources.

<b>nano-TiO<sub>2</sub></b>	<b>nano-ZnO</b>	<b>nano-Ag</b>	<b>CNT</b>	<b>Fullerenes</b>					
<b>t a<sup>-1</sup></b>	<b>Reference, t a<sup>-1</sup></b>	<b>Reference, t a<sup>-1</sup></b>	<b>Reference, t a<sup>-1</sup></b>	<b>Reference, t a<sup>-1</sup></b>					
	<b>year</b>	<b>year</b>	<b>year</b>	<b>year</b>					
679	(15), 2007	18	(16), 2008	4	(17), 2005	140	(14), 2008	0.15	(18), 2002
3000	(19), 2008	20	(20), 2007	5	(21), 2008	278	(22), 2007	5	(23), 2008
5000	(20), 2007	528	(15), 2007	434	(14), 2008	295	(24), 2008	10	(25), 2005
60926	(14), 2008	1800	(19), 2008	563	(26), 2008	426	(27), 2008		
		9845	(14), 2008			473	(28), 2004		
						500	(29), 2006		

Table 17. Product categories for each ENM with the modeled input distribution. The values refer to the computed input parameters distributions extracted from the MC simulations ( $n = 100,000$ ).

Product Category	Lower Boundary	Upper Boundary	Mean
<b>nano-TiO<sub>2</sub></b>			
Cosmetics	0.0036	0.8190	0.4218
Filter Aggregates	0.0359	0.7221	0.2724
Coatings & Cleaning Agent	0.0006	0.4421	0.1051
Plastics	0.0004	0.5231	0.1258
Consumer Electronics	0.0002	0.2397	0.0397
Paint	0.0000	0.1648	0.0198
Glass & Ceramics	0.0000	0.0647	0.0099
Light Bulbs	0.0000	0.0153	0.0020
Metals	0.0000	0.0077	0.0010
Batteries & Capacitors	0.0000	0.0074	0.0010
Textiles	0.0000	0.0062	0.0008
Ink	0.0000	0.0045	0.0007
Dietary Supplement	0.0000	0.0000	0.0000
<b>nano-ZnO</b>			
Plastics	0.0000	0.0131	0.0016
Cosmetics	0.1671	0.9780	0.6489
Coatings & Cleaning Agent	0.0006	0.8108	0.3492
Textiles	0.0000	0.0021	0.0002
Dietary Supplement	0.0000	0.0004	0.0000
<b>nano-Ag</b>			
Cosmetics	0.0037	0.0191	0.0085
Filter Aggregates	0.0118	0.1059	0.0482
Coatings & Cleaning Agent	0.0808	0.5900	0.2905
Plastics	0.0086	0.0618	0.0280
Consumer Electronics	0.0209	0.1179	0.0554
Paint	0.0003	0.5277	0.2007
Glass & Ceramics	0.0000	0.0333	0.0075
Metals	0.0000	0.0042	0.0016
Textiles	0.1190	0.4900	0.2536
Dietary Supplement	0.0340	0.2825	0.1059
<b>CNT</b>			
Composites	0.0000	0.9758	0.4862
Consumer Electronics	0.0000	0.9785	0.4517
R&D	0.0000	0.8932	0.0621
<b>Fullerenes</b>			
Composites	0.0000	0.4558	0.1556
Cosmetics	0.0000	0.0335	0.0114
R&D	0.4907	0.9800	0.8330

## C. Release of ENM

Table 18. Release of engineered nanomaterials (ENM) from products, manufacturing of ENM containing products and ENM production. The values refer to the fraction of the total amount of ENM released, transferred or dissolved from a particular source.

Product Category	STP			WIP			Atmosphere			Landfill			Soil			Water			REC			Dissolution			Export					
	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH	EU	USA	CH
<b>nano-TiO<sub>2</sub></b>																														
Plastics				0.32	0.19	1.00				0.68	0.81																			
Cosmetics	0.90	0.90	0.90	0.02	0.01	0.05				0.03	0.04					0.05	0.05	0.05												
Coatings & Cleaning Agent	0.90	0.90	0.90	0.02	0.01	0.05	0.05	0.05	0.05	0.03	0.04																			
Batteries & Capacitors				0.04	0.15	0.28				0.09	0.63								0.33	0.09								0.54	0.13	0.73
Metals	0.05	0.05	0.05	0.02	0.01	0.05				0.03	0.04								0.90	0.90										0.90
Paint	0.20	0.20	0.20							0.50	0.50	0.50	0.25	0.25	0.25	0.05	0.05	0.05												
Light Bulbs				0.32	0.19	0.10				0.68	0.81																			0.91
Glass & Ceramics				0.32	0.19	1.00				0.68	0.81																			
Filter Aggregates				0.04	0.15	0.28				0.09	0.63								0.33	0.09								0.54	0.13	0.73
Consumer Electronics				0.04	0.15	0.28				0.09	0.63								0.33	0.09								0.54	0.13	0.73
Textiles	0.50	0.50	0.50	0.14	0.08	0.25				0.31	0.35								0.02	0.02								0.04	0.05	0.25
Dietary Supplement	0.90	0.90	0.90	0.03	0.02	0.10				0.07	0.08																			
Ink	0.06	0.06	0.08	0.12	0.08	0.92				0.25	0.36								0.57	0.32										0.18
Manufacturing	0.33	0.33	0.33	0.11	0.06	0.33	0.33	0.33	0.33	0.23	0.27																			
Production	0.75	0.75	0.75				0.25	0.25	0.25																					
<b>nano-ZnO</b>																														
Plastics				0.32	0.19	1.00				0.68	0.81																			
Cosmetics	0.90	0.90	0.90	0.02	0.01	0.05				0.03	0.04					0.05	0.05	0.05												
Coatings & Cleaning Agent	0.90	0.90	0.90	0.02	0.01	0.05	0.05	0.05	0.05	0.03	0.04																			
Textiles	0.16	0.16	0.32	0.05	0.03	0.16	0.02	0.02	0.03	0.10	0.11								0.01	0.01		0.65	0.66	0.33	0.01	0.01	0.16			
Dietary Supplement																						1.00	1.00	1.00						
Manufacturing	0.33	0.33	0.33	0.11	0.06	0.33	0.33	0.33	0.33	0.23	0.27																			
Production	0.75	0.75	0.75				0.25	0.25	0.25																					
<b>nano-Ag</b>																														
Plastics				0.31	0.18	0.95				0.65	0.77														0.05	0.05	0.05			
Metals	0.05	0.05	0.05	0.02	0.01	0.05				0.03	0.04								0.86	0.86		0.05	0.05	0.05						0.86
Cosmetics	0.73	0.73	0.73	0.01	0.01	0.04				0.03	0.03					0.04	0.04	0.04				0.19	0.19	0.19						
Coatings & Cleaning Agent	0.73	0.73	0.73	0.01	0.01	0.04	0.04	0.04	0.04	0.03	0.03											0.19	0.19	0.19						
Textiles	0.13	0.13	0.20	0.05	0.03	0.14	0.02	0.02	0.05	0.11	0.13								0.01	0.01		0.67	0.66	0.48	0.01	0.02	0.13			
Paint	0.16	0.16	0.16							0.41	0.41	0.41	0.20	0.20	0.20	0.04	0.04	0.04				0.18	0.18	0.18						
Filter Aggregates				0.03	0.12	0.22				0.07	0.51								0.27	0.07		0.19	0.19	0.19	0.44	0.11	0.59			
Glass & Ceramics				0.26	0.15	0.81				0.55	0.66											0.19	0.19	0.19						
Consumer Electronics				0.04	0.14	0.26				0.08	0.60								0.31	0.08		0.05	0.05	0.05	0.52	0.13	0.69			
Dietary Supplements	0.90	0.90	0.90	0.03	0.02	0.10				0.07	0.08																			
Manufacturing	0.33	0.33	0.33	0.11	0.06	0.33	0.33	0.33	0.33	0.23	0.27																			
Production	0.75	0.75	0.75				0.25	0.25	0.25																					
<b>CNT</b>																														
Composites				0.32	0.19	1.00				0.68	0.81																			
Consumer Electronics				0.04	0.15	0.28				0.09	0.63								0.33	0.09	0.73							0.54	0.13	
R&D	0.05	0.05	0.01	0.30	0.18	0.98	0.01	0.01	0.01	0.64	0.76																			
Manufacturing	0.33	0.33	0.33	0.11	0.06	0.33	0.33	0.33	0.33	0.23	0.27																			
Production	0.75	0.75	0.75				0.25	0.25	0.25																					
<b>Fullerenes</b>																														
Composites				0.32	0.19	1.00				0.68	0.81																			
Cosmetics	0.90	0.90	0.90	0.02	0.01	0.05				0.03	0.04					0.05	0.05	0.05												
R&D	0.50	0.50	0.50	0.16	0.10	0.50				0.34	0.41																			
Manufacturing	0.33	0.33	0.33	0.11	0.06	0.33	0.33	0.33	0.33	0.23	0.27																			
Production	0.75	0.75	0.75				0.25	0.25	0.25																					

<sup>a</sup>Averages enlarged and reduced by 50% (EU, USA) and 20% Switzerland (CH) to build uniform model input distributions.

## D. Considered toxicity studies

Table 19. Derived PNEC from standardized toxicity studies with an applied assessment factor of 1000 (1).

Particle	Compartment	Test Species	Toxic Endpoint	Concentration	PNEC	Ref.
nano-Ag	Water	<i>C. dubia</i>	LC50	0.696 $\mu\text{g L}^{-1}$	0.696 $\text{ng L}^{-1}$	(30)
	Air	Specific pathogen-free Sprague-Dawley rats (Slc:SD)	NOEC	100 $\mu\text{g m}^{-3}$	0.1 $\mu\text{g m}^{-3}$	(31)
CNT	Sediment	<i>Leptocheirus plumulosus</i>	LC50	68 $\text{g kg}^{-1}$	68 $\text{mg kg}^{-1}$	(32)
	Water	<i>Danio rerio</i>	NOEC	40 $\mu\text{g mL}^{-1}$	40 $\mu\text{g L}^{-1}$	(33)
	Air	Suggested Permissible exposure limit			0.1 $\text{mg m}^{-3}$	(34)
	Soil	<i>Eisenia Veneta</i>	EC50	176 $\text{mg kg}^{-1}$	176 $\mu\text{g kg}^{-1}$	(35)
Fullerenes	Water	<i>Daphnia Magna</i>	NOEC	0.2 $\text{mg L}^{-1}$	200 $\text{ng L}^{-1}$	(36)
	Soil	Microbial community, effects on basal and glucose-induced soil respiration			1 $\mu\text{g g}^{-1}$	(37)
nano-TiO <sub>2</sub>	Water	<i>Daphnia magna</i> , <i>Pseudokirchneriella subcapitata</i>	NOEC	1 $\text{mg L}^{-1}$	1 $\mu\text{g L}^{-1}$	(38, 39)
	Air	Different studies	LOEC	10 $\text{mg m}^{-3}$	10 $\mu\text{g m}^{-3}$	(40)
	Soil	Terrestrial isopods <i>P. scaber</i> Latreille, 1804			1000 $\mu\text{g kg}^{-1}$	(41)
nano-ZnO	Water	<i>Pseudokirchneriella subcapitata</i>	EC50	40 $\mu\text{g L}^{-1}$	40 $\text{ng L}^{-1}$	(39)



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## List of Publications

**Gottschalk, F.**, Ort, Ch., Scholz, R.W., Nowack, B (2010). Engineered nanomaterials in rivers – an exposure assessment for Switzerland at high spatial resolution for nano-TiO<sub>2</sub>, nano-ZnO and nano-Ag. *Environmental Science & Technology*, submitted.

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### Conference proceedings

Mueller, E., Schluep, M., Widmer, R., **Gottschalk, F.**, Böni, H. (2009). Assessment of e-waste flows: a probabilistic approach to quantify e-waste based on world ICT and development indicators. R'09 World Congress, September 14, 2009. Davos, Switzerland.

Hansen, S. F., Baun, A., Tiede, K, **Gottschalk, F.**, van der Meent, D., Peijnenburg, W., Fernandes, T., Riediker, M. (2009). Environmental fate and behaviour of nanoparticles – beyond listing of limitations. Report of The European Network on the Health and Environmental Impact of Nanomaterials, Bilthoven.

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### Oral presentations

\* Empa PhD Student's Symposium, Dübendorf, November 19, 2009: Probabilistic/Stochastic Modeling of Environmental Exposure to Engineered Nanomaterials.

\* SETAC Europe 19th Annual Meeting Göteborg, Sweden, May 31, 2009: Modeling the environmental concentrations of Engineered Nanomaterials based on a Probabilistic Material Flow Analysis.

\* 4th International Conference on the Environmental Effects of Nanoparticles and Nanomaterials, University of Vienna, September 6–9, 2009: Modeled environmental concentrations of engineered nanomaterials (TiO<sub>2</sub>, ZnO, Ag, CNT, fullerenes) for different regions.

\* The European Network on the Health and Environmental Impact of Nanomaterials, October 5–7, 2009, Bilthoven, The Netherlands: Probabilistic material flow modelling for assessing the environmental exposure to nanomaterials (TiO<sub>2</sub>, ZnO, Ag, CNT and fullerenes).

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### **Poster presentations**

\* Monte Verità Conference nanoECO “Nanoparticles in the Environment: Implications and Applications”, Centro Stefano Franscini, Ascona, Switzerland, March 2–7, 2008: F. Gottschalk, R. Scholz, B. Nowack, Modeling exposure to nanoparticles (nTiO<sub>2</sub>) in aerial, aquatic and terrestrial environments incorporating and quantifying uncertainty.

\* 3rd International Conference on the Environmental Effects of Nanoparticles and Nanomaterials, University of Birmingham, UK, September 15–16, 2008: F. Gottschalk, R. Scholz, B. Nowack, Development of a material flow modeling framework with probabilistic techniques for assessing the environmental exposure of pollutants: the case of nanoparticles.