

Draft guidelines regarding the quantification of lifecycle environmental and human health risk indicators

DELIVERABLE 3.2

Due date of Deliverable: 30.09.2020
Actual Submission Date: 05.12.2020
Responsible partner: NILU, Norway
Report Author(s): Elorri Igos, LIST, Evert Bouman, NILU, Elena Semenzin, UNIVE
Nature: R (Document, report)
Dissemination Level: PU = Public

Call: H2020-NMBP-13-2018
Topic: Risk Governance of nanotechnology
Project Type: Research & Innovation Action (RIA)
Name of Lead Beneficiary: NILU, Norway
Project Start Date: 1 January 2019
Project Duration: 50-Months



Document History

<i>Version</i>	<i>Date</i>	<i>Authors/ who took action</i>	<i>Comment</i>	<i>Modifications made by</i>
<i>0.1</i>	30-04-2020	Elorri Igos (LIST)		EI (LIST), EB (NILU), ES (UNIVE)
<i>0.2</i>	22-05-2020	Elena Semenzin (UNIVE)		ES (UNIVE)
<i>0.3</i>	06-07-2020	Elorri Igos (LIST)		EI (LIST), EB (NILU)
<i>0.4</i>	16-10-2020	Elorri Igos (LIST)		EI (LIST)
<i>0.5</i>	19-11-2020	Evert Bouman (NILU)	Draft guidelines completed for review	EB (NILU)
<i>1.0</i>	03-12-2020	Evert Bouman (NILU)	Final revision following feedback	EI (LIST), ES (UNIVE), EB, Maria Dusinska (NILU)



Abstract

This report contains draft guidelines regarding the quantification of lifecycle and human health risk indicators for engineered nanomaterials (ENMs) as may be calculated through a Life Cycle Assessment (LCA) approach. It is based on an extensive review of LCA and impact assessment literature describing the state-of-the-art approaches in the field of LCA for ENMs as well as the CEN technical specification 17276:2018 – Application of EN ISO 14044:2006 to Manufactured Nanomaterials. Written in the context of risk governance of nanomaterials, this document intends to guide the process of establishing impact assessment indicators for various levels of detail.



TABLE OF CONTENTS

Abstract	3
1 Introduction	5
1.1 Life cycle assessment methodology.....	5
1.2 Aim and scope.....	6
1.3 Challenges in relation to nanomaterials	6
1.4 Structure of this guidance	7
2 Phases in a Life Cycle Assessment of ENMs.....	8
2.1 Goal and scope definition	8
2.2 Life cycle inventory modelling	9
2.2.1 Production phase of ENMs	10
2.2.2 Manufacturing phase of ENPs	10
2.2.3 Use phase.....	11
2.2.4 End of Life	11
2.2.5 Transport of ENMs and ENPs	11
2.3 Life cycle impact assessment modelling	13
2.3.1 Introduction to USEtox modelling	15
2.3.2 Environmental fate modelling of ENPs.....	17
2.3.3 Exposure modelling of ENPs	18
2.3.4 Effect modelling of ENPs	19
2.3.5 Recommended LCIA factors for ENPs	20
2.4 Result interpretation	22
3 Guidance on practical implementation of study.....	26
3.1 Qualitative screening analysis.....	27
3.2 Screening LCA.....	27
3.3 Comparative LCA	28
4 Conclusion	29
5 References.....	30



1 Introduction

1.1 Life cycle assessment methodology

Life cycle assessment (LCA) is a standardized methodology (ISO 2006a, 2006b) which aims at evaluating the environmental impacts of products, processes or services along their lifecycle. This comprehensive approach can thus identify potential trade-offs between different life stages or environmental indicators. LCA can be applied for several purposes such as eco-design support, products benchmarking, environmental labelling, policy support, etc.

The methodology is divided into four main steps:

Goal and scope definition: This first step is essential to clearly states the objectives of the LCA study as well as its scope. It includes the definition of the studied scenarios, the system boundaries, the functional unit (quantified function to normalize results), the selected environmental indicators and other modelling

(LCI) modelling: For each process included in the defined boundaries, the inputs (e.g. consumption of electricity) and outputs (e.g. generation of waste) need to be collected. These so-called foreground data, which are specific to the studied system, are linked to background data reflecting the upstream and downstream processes (e.g. generation of electricity up to raw materials extraction). The latter are mostly generic data coming from LCI database or literature. The LCI results represent all the environmental flows (e.g. carbon dioxide emission, extraction of raw material, release of pollutants into water, etc.) normalized to the functional unit (e.g. the transport of passenger over 1 km).

Life cycle impact assessment (LCIA) modelling: In order to translate LCI results (which can be thousands of flows) into environmental impacts, LCIA methods are used. Environmental flows are classified and characterized depending on their effects. The impact due to a specific flow is obtained from the multiplication of the LCI amount (e.g. 10 kg of methane along the lifecycle) and the associated characterization factor (CF, e.g. 30.5 kg CO₂-eq./kg methane). LCIA results for an impact category is the sum of the impacts obtained for all flows contributing to this indicator.

Results interpretation: This final step intends to support the study goals based on LCIA results. The defined scenarios are compared and analyzed according to the contribution of single process or flows, in order to identify the “hotspots”. Modelling choices or uncertain parameters can be tested via sensitivity and uncertainty analyses to understand their effects on results. The related outputs can be used to review the scope choices, LCI or LCIA data in an iterative manner.

1.2 Aim and scope

This document provides guidance for application of Life Cycle Assessment relevant to both engineered nanomaterials (ENMs) as well as nano-enabled products (NEPs), i.e. products containing ENMs, for all phases along the life cycle. It aims to provide both an overview of the state-of-the-art with respect to life cycle (impact) assessment modeling of ENMs as well as pragmatic approach to conducting an LCA study for particular ENMs or NEPs. As such, the guidance provided here is in part more directive than CEN and considered complimentary to CEN technical specification on LCA of ENMs: “CEN TS 17276:2018 – Application of EN ISO 14044:2006 to Manufactured Nanomaterials.” The guidelines are primarily intended for LCA practitioners constructing LCA from either ENM production or NEP production and manufacturing perspective.

1.3 Challenges in relation to nanomaterials

The standardized LCA methodology can be applied to engineered nano-materials (ENMs) to support their eco-design (e.g. comparing different synthesis routes) or understand their environmental costs-benefits compared to conventional products they intend to substitute. In literature, LCA was applied to several types of ENMs, such as nano-TiO₂, nano-ZnO, nano-SiO₂, nano-Ag, carbon nanotubes (CNT), nano-cellulose or graphene, to analyze their impacts as ENM or used for a specific sector (Figure 1).

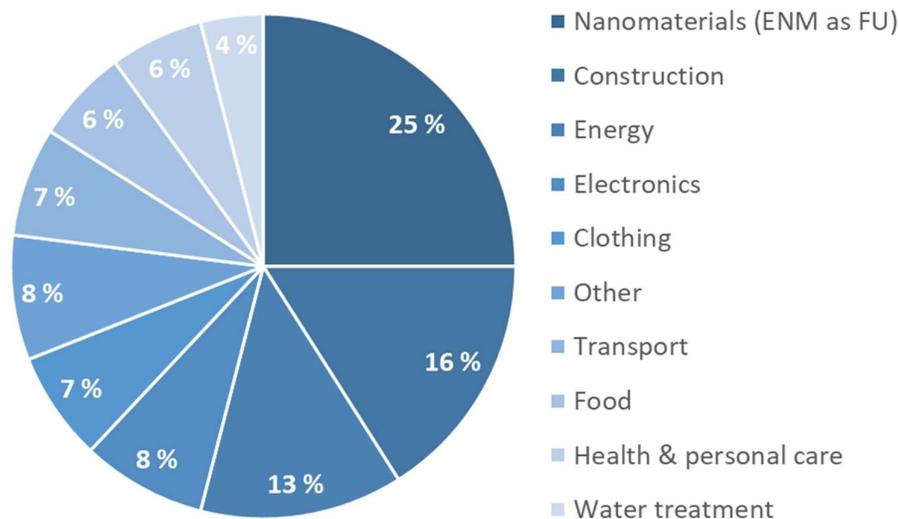


Figure 1: Classification of studies by industry of application (adapted from Cucurachi and Blanco Rocha 2019).

The LCA framework is flexible enough to be applicable to any type of product, process or service. There are however some key challenges that are specific to the evaluation of ENMs (Cucurachi and Blanco Rocha 2019; Salieri et al. 2018).

The first one is related to the system boundaries definition. Compared to conventional products, ENMs can add properties to a material. The comparison per mass of product might not be representative. The expansion of system boundaries can be applied to tackle this multifunctionality issue (e.g. add cleaning process for conventional windows to compare with self-cleaning windows enhanced with ENMs).

The second challenge is related to the availability and representativeness of LCI data. The production processes of ENMs are emerging technologies. Some production data can be available but not representative of a full-scale production (e.g. based on laboratory measurements), or they are too sensitive from a commercial point of view to be published transparently. There is also a clear lack of data regarding the emissions of nano-particles along the lifecycle of nano-enabled products. These potential releases are thus often excluded from LCA studies.

Finally, the characterization of the impacts of nano-particle emissions remains challenging. Indeed, there is no CF yet in existing LCIA methods although several authors published developed such factors. The latter still suffer from uncertainties and their quality will be improved together with the developments made in risk assessment (RA) field.

1.4 Structure of this guidance

This guidance is structured as follows. Chapter 2 details the four phases of a typical LCA study as laid out in ISO 14040, with background on goal and scope definition, life cycle inventory modelling, the choice of impact categories and application of nano-specific characterization factors, as well as results interpretation. Chapter 3 continues with guidance on practical implementation in the context of nano-risk governance. Finally, this guidance is concluded in Chapter 4.

2 Phases in a Life Cycle Assessment of ENMs

2.1 Goal and scope definition

The definition of system boundaries is a key aspect of a LCA study. Ideally, all the processes of the lifecycle of the product should be considered. In practice, it is necessary to make simplifications due to the enormous amount of data and the complexity of our globalized system of exchanges. In literature, the majority of LCA studies regarding ENMs are focused on the production steps. These so-called cradle-to-gate analyses can be useful to compare synthesis methods, as soon as the obtained product shows the same performances. The publication of LCI and LCIA data per kg of ENM produced can also be useful for other LCA practitioners who want to model the lifecycle of a nano-enabled product. To understand the environmental cost-benefits of a nano-enabled product, it is however necessary to include also the use and end-of-life stages (cradle-to-grave analysis). Indeed, ENMs can affect the function of a product and therefore the service provided during the use phase. In addition, compared to the comparative conventional products, engineered nanoparticles (ENP) could be released during the various phases of the lifecycle. If a study does not intend to analyze a specific application but the overall impacts of the ENM deployment on the market, the targeted segments should be identified (as done by Pourzahedi, Vance, and Eckelman 2017 for nano-silver enabled products). The comparison can be made per application type with conventional processes. Results could also be integrated in prospective scenarios reflecting the expected market trends.

Comparative studies rely on a common functional unit (FU) for the compared scenarios. For cradle-to-gate studies, the FU is often the production of a normalized mass of ENM (e.g. 1 kg). Some authors include the material properties in the FU to be more specific and avoid potential bias (e.g. Bafana et al. 2018 set the FU as “1 kg of 3.0 ± 1.2 nm diameter AgNPs, equivalent to an Ag surface area of 1.9×10^5 m²”). Similarly, Roes et al. 2010 proposed to apply the Ashby’s material index, considering the material properties of nanocomposites, to normalize their impacts and facilitate their comparison. For cradle-to-grave analyses, the functions provided by the nano-enabled products should be identified. The corresponding FUs can be defined as the generation of 1 kWh of electricity for nano-enable photovoltaic cells (such as in Greijer et al. 2001), the driving of 1 km with an electric vehicle powdered with nano-enabled battery (Deng et al. 2019), the protection of 1 m² of wall during 80 years (Hischier, Salieri, and Pini 2017) or the use of a food container over four washing cycles (Bi et al. 2018). The definition of such FU can be quite uncertain due to the low maturity of the studied product and variability of consumers’ behavior and can greatly influence the LCA results (Hischier et al. 2017). Such issue should be tackled by sensitivity analysis by testing the range of possible FUs (see section 2.4 for further details). When

the nano-enabled product induces a new functionality compared to the compared conventional product, the changes that will generate this co-function should be identified (e.g. less frequent washing for a nano-enabled T-shirt, longer lifetime of façade thanks to nano-enabled coating) and included in the comparison. The definition of the time period in the FU represents a key parameter for such systems.

As for the consideration of life cycle steps, it is also important to include as many environmental indicators as possible in the scope of the study to increase the coverage of environmental issues and identify potential trade-offs. This can be done by applying multi-criteria LCIA methods, such as the Environmental Footprint method from the European Commission, ReCiPe or ImpactWorld+. Previous studies on ENMs used these comprehensive methods but some also focused on indicators judged particularly relevant, such as the cumulative energy demand (CED), the global warming potential (GWP) or the (eco)toxicity related impacts.

2.2 Life cycle inventory modelling

The life cycle inventory (LCI) model in a life cycle assessment of engineered nanomaterial or nano-enabled product does not differ conceptually from an LCI of a 'traditional' product or system. LCI models are based on a vast amount of 'unit processes' that identify both environmental and economic interventions (e.g. emissions to air or water and material and energy use) which collectively form a product system with linked value chains. Traditionally, LCI modellers rely heavily on established LCI databases such as ecoinvent which provide data for key reference processes. However, data on the production and manufacturing of ENMs, their subsequent use in a NEP, disposal and waste, as well as the release of nanomaterials to the environment are at present not included in these databases, thus requiring the LCA practitioner to develop an LCI model themselves, or to rely on inventory data published elsewhere in literature. There are a number of studies published where LCI data is available as either primary data or through a synthesis of literature, and many with available data on nanomaterial emissions to environment (see e.g. Hirschier et al. 2015; Li et al. 2014; Walser et al. 2011). Finally, in the case of missing data, LCA practitioners may use scenario analysis (where e.g. a worst-case scenario with high nanomaterial emission is compared against a benchmark case based on expert opinion) to assess the severity of missing data in the LCI model. As with 'classical' LCA studies, the effect of (un)certainty and (low) data quality should be considered and addressed through thorough sensitivity and uncertainty analysis (see section 2.4).

One key departure point for an LCI of an ENM or NEP is a correct substance identification. In other words, the nanomaterial should be correctly specified beyond its chemical constitution (e.g. TiO_2). As ENMs may exhibit vastly different properties dependent for example on size and shape, this should be

documented together with the inventory. CEN TS 17272:2018 specifies as relevant properties size and shape, dissolution and dispersion properties, and surface properties and information on coating (if applied). Further, information on the potential for agglomeration and aggregation is useful for environmental fate and exposure assessment and may therefore provide useful inputs required for the development of characterization factors in Life Cycle Impact Assessment Methods.

Once the nanomaterial can be properly identified, the LCI may consider the phases in the life cycle presented in the following subsections.

2.2.1 Production phase of ENMs

Modelling of a unit process (or collection of unit processes) of an engineered nanomaterial follows in large part the same structure as the modelling the production and manufacturing. The unit process will have to define from which material resources the ENM is produced, the energy used in the production process, as well as an estimate on the infrastructure (buildings and machines) required. Here, standard processes from an LCI database may be used. However, the LCA practitioner should take care to distinguish in the LCI model the emissions of the specific ENM to the environmental compartments in addition of standard emission such as combustion products. Furthermore, the content of ENM in liquid or solid waste should be clearly documented. In the context of risk management, emissions to indoor air (leading to possible exposure of workers) may be considered in detail and added as an environmental intervention.

As for LCI models of bulk products, LCI data may be collected from a variety of sources; measured data, modelled data, or data found elsewhere in the literature and adapted to the case at hand. Uncertainty for each of these data points varies and this should be taken into account when interpreting results.

2.2.2 Manufacturing phase of NEPs

Modeling of a unit process (or collection of unit processes) for the production and manufacturing of a nano-enabled product follows the same rationale as described in the section above. Here, it is of importance to include a properly characterized and identified ENM as an input to the unit process. Special attention should be paid to the identification of (potential) pathways for ENM and NEP release to the environment in the NEP production and manufacturing process. Specific emissions of ENM and NEP to the environment, as well as output of ENM and NEP in waste flows, should be documented unless compelling reasons exist that there will not be such releases. It is recommended to include this in the unit process documentation.

2.2.3 Use phase

Modeling the unit process describing the use phase of ENMs or NEPs requires a more extensive consideration unit processes of traditional bulk products. As with ENM production and NEP manufacturing, special attention should be paid to releases of ENM or NEP to the environment during the use phase, for example as a result of product wear and tear. Note that many products may have an extensive lifetime and product properties may change over time as a result of degradation or exposure to the elements. As a result, release of degradation products of ENMs in NEPs over time could be considered and ENMs may be released during the use phase that are substantially different from the ‘virgin’ ENM used in the NEP.

Finally, for products that are used directly by humans, dermal, oral, and respiratory exposure to ENMs may be considered as a special type of ‘environmental intervention’ and documented in the unit process. It should be noted that these exposures, for example exposure to fine particulate matter, or the leaching of potentially dangerous chemicals (such as phthalates or PFAS from (micro)plastics) is at present not well included in ‘traditional’ LCAs of bulk products.

2.2.4 End of Life

Modelling the unit process for the End-of-Life (EOL) of ENMs and NEPs, as well as waste treatment processes of both industrial and consumer wastes containing these materials, should include special attention to releases of ENMs to the environment as well potential exposure routes to humans. In LCA, modelling unit processes for waste treatment is often complex and resource demanding. Waste processes are often not specific to a certain material but deal with a large variety of incoming waste streams. The complex interactions between treatment process, composition of the waste stream and ultimate disposal process are hard to capture despite extensive measurements and are often site-specific. Thus, the extraction of a generic unit process for EOL and waste treatment comes with large uncertainty. In addition, this guidance is primarily targeted at those conducting LCA studies from a production and manufacturing perspective, with little access to information on waste processing. In order to include EOL in the LCI, one pragmatic way is adapting a standard hazardous material waste process from an LCI database and include release of the ENMs to the environment as extra environmental intervention.

2.2.5 Transport of ENMs and NEPs

Transport of products between production site and manufacturing site, to retail and consumers, is often an important part in LCAs as transport may be an energy intensive contributor of emissions to the environment. This particularly holds for products transported over long distances by plane, as well as

transport by car by final consumers where the transport energy efficiency (i.e. energy used per tkm) is low. In the case of transporting ENMs or NEPs the risk of release of ENM or NEP to the environment during transport should be considered. This may happen when ENMs are loaded and offloaded prior to transport, as well as dependent on the mode of transport. This is of special relevance when the ENM or NEP has proven, or is suspected of, human and ecotoxic properties, similar to the case of all dangerous goods transport. When (unintentional) release is not envisioned (e.g. due to specific containment and mitigation measures) it is recommended to document this in the LCI process description.



2.3 Life cycle impact assessment modelling

After quantifying all the environmental exchanges (emissions into the environment and use of natural resources) along the life cycle of a product or process, the step of life cycle impact assessment (LCIA) aims at translating these flows into environmental impacts. To do so, the environmental flows are categorized (e.g. all greenhouse gas – GHG – emissions classified into climate change category) and characterized depending on their effects in function of the unit of reference for the impact category. The conversion between the physical amount and the environmental effect is done by characterization factors (CFs). For example, the CF of methane for climate change impact is equal to 30.5 kg CO₂ eq/kg, meaning that its integrated radiative forcing over 100 years is 30.5 times higher than the one of carbon dioxide. Since the consensual unit for climate change is kg CO₂-eq (IPCC 2013), the CF is expressed in kg CO₂ eq./kg to convert the mass of emitted GHGs along the life cycle into the impact unit. The European Commission developed recommendations to apply default LCIA methods for several environmental indicators. The latest version of these LCIA guidelines is called the Environmental Footprint version 3.0 (EF 3.0) with recommended CFs provided in Fazio, S. et al. 2018 (Table 1).

Table 1: Recommended LCIA methods in EF 3.0 (Fazio et al., 2018)

Impact category	Indicator	Unit	Recommended default LCIA
Climate change	Radiative forcing as Global Warming Potential (GWP100)	kg CO ₂ eq	Baseline model of 100 years of the IPCC (based on (IPCC 2013))
Ozone depletion	Ozone Depletion Potential (ODP)	kg CFC-11 eq	Steady-state ODP as in (WMO et al. 1999)
Human toxicity, cancer effects	Comparative Toxic Unit for humans (CTU _h)	CTU _h	USEtox 2.1. model (Rosenbaum et al. 2008)
Human toxicity, non-cancer effects	Comparative Toxic Unit for humans (CTU _h)	CTU _h	USEtox 2.1. model (Rosenbaum et al. 2008)
Particulate matter/Respiratory inorganics	Human health effects with exposure to PM2.5	Disease incidences	PM method recommended by UNEP (UNEP 2016)
Ionising radiation, human health	Human exposure efficiency relative to U ²³⁵	kBq U ²³⁵	Human health effect model as developed by Dreicer et al., 1995 (Frischknecht et al. 2000)
Photochemical ozone formation	Tropospheric ozone concentration increase	kg NMVOC eq	LOTOS-EUROS (van Zelm et al. 2008) as applied in ReCiPe 2008
Acidification	Accumulated Exceedance (AE)	mol H+ eq	Accumulated Exceedance (Posch et al. 2008; Seppälä et al. 2006)
Eutrophication, terrestrial	Accumulated Exceedance (AE)	mol N eq	Accumulated Exceedance (Posch et al. 2008; Seppälä et al. 2006)
Eutrophication, aquatic freshwater	Fraction of nutrients reaching freshwater end compartment (P)	kg P eq	EUTREND model model (Struijs et al., 2009) as implemented in ReCiPe (Goedkoop et al. 2009)

Eutrophication, aquatic marine	Fraction of nutrients reaching marine end compartment (N)	kg N eq	EUTREND model (Struijs et al., 2009) as implemented in ReCiPe (Goedkoop et al. 2009)
Ecotoxicity, freshwater	Comparative Toxic Unit for ecosystems (CTU _e)	CTU _e	USEtox 2.1 (Rosenbaum et al., 2008)
Land use	Soil quality index (Biotic production, Erosion resistance, Mechanical filtration and Groundwater replenishment)	Dimensionless, aggregated index of kg biotic production/(m ² *a) kg soil/(m ² *a) m ³ water /(m ² *a) m ³ g. water/(m ² *a)	Soil quality index based on LANCA (Beck et al., 2010;Bos et al. 2016)
Water use	User deprivation potential (deprivation-weighted water consumption)	kg world eq. deprived	Available Water Remaining (AWARE) in (UNEP 2016)
Resource use, minerals and metals	Abiotic resource depletion (ADP ultimate reserves)	kg Sb eq	CML (Guinee 2002) and (Van Oers et al. 2002)
Resource use, energy carriers	Abiotic resource depletion – fossil fuels (ADP-fossil)	MJ	CML (Guinee 2002) and (Van Oers et al. 2002)

In literature, only a few authors applied EF 3.0 recommended methods to assess the environmental impacts of nanomaterials (Cossutta, McKechnie, and Pickering 2017; Marimón-Bolívar and González 2018; Serrano-Luján et al. 2019), while most of the case studies used other methods such as ReCiPe, CML or TRACI. In priority the EF 3.0 method should be applied since it is based on the qualitative analysis of all available methods. However, the use of other methods can be useful, in particular to understand the sensitivity of the results to the LCIA modelling assumptions. Some studies focused only on a few indicators such as GWP or cumulative energy demand (CED). To identify potential burden shift, a comprehensive panel of indicators should be considered.

The ecotoxicity and human toxicity categories are particularly relevant for the LCA of nanomaterials due to the potential risks associated to ENPs release. As observed in Table 1, the recommended EF method is called USEtox, which comes from a scientific consensus from the UNEP-SETAC Life Cycle Initiative (Rosenbaum et al. 2008). The latter characterizes freshwater ecotoxicity, carcinogenic and non-carcinogenic human toxicity impacts, following the cause-effect chain of substances, including fate, exposure and effect modelling. The CFs for freshwater ecotoxicity express the potentially affected fraction (PAF) of species integrated over time and volume per kg of emitted substance (PAF.m³.day/kg), also referred as comparative toxic units for ecosystems (CTU_e/kg). For human toxicity (carcinogenic or not), the CF reflects the increase of (disease) cases per kg emitted (also referred as CTU for humans – CTU_h/kg), which can be further translated into disability-adjusted life years (DALYs) depending on the effect severity. The current version of USEtox does not include CFs for the emission of nanoparticles.

Several authors nevertheless tackled this issue by developing CF for ENPs based on available data and partly adapting USEtox method. In literature, twelve studies with this objective were found, sometimes only focusing on part of the cause-effect chain (e.g. fate modelling). Thanks to this effort, about 20 other studies could include the characterization of ENP emissions within the LCA application cases. Despite the fact that Cucurachi and Blanco Rocha 2019 compiled into one table all available CFs for ENPs in literature, it is important to understand the strengths and limitations of these results, facilitate the choice of CFs when several values exist and also compile partial data (e.g. fate, exposure or effect factors) that can further be combined to obtain a new CF. Such data transparency was implemented in the EF3.0 Ecotox Explorer developed by the European Commission to support a better understanding of the CFs and related data and assumptions. A similar approach could be followed in RiskGONE for the assessment of ENPs.

In the next sections, the best available practices and factors to characterize ENPs are detailed, while recommendations to further improve (eco)toxicity modelling in LCIA models are developed in the discussion section (which can further be fed by outcomes from Task 3.1 of RiskGONE).

2.3.1 Introduction to USEtox modelling

In this report, an introduction to USEtox model is made to understand how it was applied and adapted to ENPs. However, the reader should refer to the USEtox user manual for a complete guidance.

USEtox CF is based on the multiplication of the fate (FF), exposure (XF) and effect factors (EF):

$$CF=FF \times XF \times EF$$

First, fate modelling, used to predict the behavior of a substance in the environment, relies on a steady-state multimedia model (adapted from SimpleBox). Fate factors (FFs) implemented in a matrix give the increase of mass of a given substance (in kg) in a receiving environmental compartment (columns) due to its emission (in kg/day) in a source environmental compartment (rows). In case the emission and receiving compartments are the same, FF can be interpreted as the total residence time in that compartment (in days). USEtox represents environmental compartments as well-mixed boxes, described by their total mass, total volume, solid-phase mass, liquid-phase mass, and gas-phase mass. Fate modelling considers a series of transport and transformation processes (first-order losses equations), which depend on the physicochemical characteristics of the substance and the characteristics of the compartments.

For freshwater ecotoxicity, the exposure factor (XF) describes the fraction of the chemical in freshwater that is bioavailable for uptake by freshwater ecosystem species (expressed in $\text{kg}_{\text{bioavailable}}/\text{kg}_{\text{freshwater}}$). The dissolved fraction was used to be in accordance with ecotoxicity test results. The exposure model for humans transfers the amount found in a given environmental compartment to a chemical intake by humans, distinguishing direct intake (e.g. air breathing) and indirect intake through bioconcentration processes in animal tissues (e.g. meat, milk). The intake by dermal contact is not yet implemented in USEtox. The human exposure factors are represented in a matrix with rows representing the seven exposure pathways (inhalation, drinking water, above ground produce, below ground produce, meat, dairy products and fish) and columns representing the receiving compartment. The human intake fractions (iFs in $\text{kg}_{\text{intake}}/\text{kg}_{\text{emitted}}$) is obtained from the multiplication of fate and exposure matrices (i.e. a matrix with exposure pathways as rows and source compartment as columns).

The ecotoxicological effect factor (EF) represents the chronic toxicity of the substance to a freshwater ecosystem. The chronic toxicity is chosen to be consistent with the objective of LCA to integrate long-term impacts. Ecotoxicity test results are preferably taken from chronic or sub-chronic tests at the EC50-level (statistical robustness fitting the comparative purpose of LCA) for at least three trophic levels (typically algae, crustacean and fish). The ecotoxicological EF (expressed in $\text{PAF}\cdot\text{m}^3/\text{kg}$) is calculated as $0.5/\text{HC50}$, where HC50 (calculated as geometric mean of selected EC50 values), representing the hazardous concentration at which 50% of the species are exposed above their EC50 value. The human toxicity EF (in $\text{cases}/\text{kg}_{\text{intake}}$) is calculated similarly, relying on ED50 value, i.e. the estimated lifetime dose for humans related to inhalation or oral exposure that causes an increase in disease probability of 50%. For carcinogenic effects, ED50 is usually derived from animal cancer tests based on the tumorigenic dose rate for 50% over background in a standard lifetime (TD50) or from low-dose slope factor. For non-carcinogenic effects, ED50 values are rarely available and NOEL or LOEL values are applied using conversion factors to ED50.

USEtox mostly characterizes organic substances (3077 chemicals included in the latest version 2.12) while only metals are characterized within inorganic substances (27 metal ions in v2.12). Some adaptations were required for the modelling of the latter. The fate model is primarily designed for organic substances that can be degraded in the environment. For metals, the Henry coefficient or degradation rates are thus set at $1.10^{-20} \text{ Pa}\cdot\text{m}^3/\text{mol}$ or $1.10^{-20} \text{ s}^{-1}$ to reflect the negligible transfer via volatilization or the lack of degradation in the environment. Additional partitioning coefficients need to be provided to model the fate of metals (between suspended solids and water, sediment particles and water and soil particles and water). For ecological exposure factor, the truly dissolved mass of metal in freshwater is

considered, based on the geochemical model WHAM 7.0 run for freshwater archetypes, describing water chemistry parameters (e.g. pH, presence of anions and cations) influencing the metal species fractions. The ecotoxicological effect factor is also derived from the truly dissolved metal species due to the very limited bioavailability of other species (geochemical speciation model applied to calculate EC50 for truly dissolved metal compared to total EC50 reported in literature).

The evaluation of impacts in LCA is by default linear. For example, the emissions of a pollutant X in air are quantified along the life cycle of a product and normalized to the evaluated function (e.g. the transport of one car over 1 km). Within this lifecycle, the pollutant X can be released during the production of a component of the car, its assembly, use or disposal. The quantities emitted in each step are normalized to the evaluated function, e.g. if the mileage of a car is 200 000 km, the emissions due to the production of one car are divided by 200 000. This unitary normalization, done in all LCA database tools to be able to calculate lifecycle impacts for products and processes, prevents the LCA practitioner to model the real absolute values of emissions. The same CF is thus applied to all emissions of pollutant X along the life cycle, without considering if these emissions represent a risk or not. The LCA methodology aims first at comparing impacts between products or systems. If the lifecycle of product A generates 10% less emissions of pollutant X than product B, the related impacts are also 10% lower. Recently, regionalization of LCIA methods is being developed to account for local effects (e.g. the stress induced by water consumption in Finland is lower than the one in Greece). In USEtox, specific data (e.g. wind speed, human population) for 24 regions (e.g. Europe) are provided in order to regionalize fate and exposure modelling. It means that all the emissions of pollutant X within the same region are summed along the life cycle and are converted into impacts via a CF, which is different from the emission of pollutant X in another region. The temporalization of USEtox to obtain dynamic results has been investigated in literature but is not yet implemented in the default use of the method.

2.3.2 Environmental fate modelling of ENPs

Meesters et al. 2014, 2016 developed SimpleBox4Nano (SB4N), which adapts the steady-state model SimpleBox (used by USEtox for fate modelling) to nanomaterials. The multimedia fate model aims at calculating predicted environmental concentrations (PECs) of ENPs species (free, aggregated, and attached) in five different environmental media (air, rain, freshwater, sediment and soil). SB4N is based on pseudo first-order rate constants to represent transformation processes (hetero-aggregation and attachment of free ENP) and transport processes between compartments (dry/wet deposition, soil run-off, sedimentation, resuspension, soil leaching and sediment burial). A few authors used SB4N to adapt the fate modelling in USEtox for ENP release (Deng et al. 2017; Ettrup et al. 2017; Pini et al. 2016; Pu et al. 2016; Salieri et al. 2019; Salieri, Pasteris, et al. 2015).

The fate model proposed by Salieri et al. 2019 is the most recent and integrated approach developed. The authors took particular care to harmonize the definition of the environmental compartments and to evaluate the fate of total species, considering fixed ratios between free, attached and aggregated species, to be consistent with USEtox framework. The developed model is based on four compartments (air, soil, freshwater and sediment), where the rain and air compartments of SB4N were merged. Further disaggregation of compartments as done in USEtox (rural and urban air, natural and agricultural soil, seawater) should be investigated in the future. The authors applied the new fate model to nano-TiO₂ and found a good fit with the original SB4N matrix results. The comparison with dynamic modelling showed that soil behaves as a storage compartment. To improve the model representativeness, further efforts on spatialization should be done, which would also allow to validate results with measured data. The availability of data regarding the aggregation and attachment parameters (rate constant, efficiencies...) of ENPs also represents a challenge for future research.

2.3.3 Exposure modelling of ENPs

By simplification and in a conservative approach, the exposure factor for aquatic ecosystems is often set to 1 in literature (Ettrup et al. 2017; Miseljic and Olsen 2014; Pu et al. 2016; Salieri, Pasteris, et al. 2015), i.e. the concentration of ENP in freshwater (calculated from fate modelling) is fully available for aquatic species. However, the bioavailability of ENPs can be hampered by the attachment to organic matter or to the concentration in biota. Salieri et al. 2019 proposed to distinguish between soluble and insoluble ENPs. In the first case, the dissolved fraction should be considered since dissolution is the main transformation process. For insoluble ENPs, the bioavailable fraction can be derived from the species smaller than 0.45 µm (as for metals and following REACH definition, (ECHA 2008)). For nano-TiO₂, Salieri et al. (2019) considered that this bioavailable fraction was the sum of free and aggregated ENP species (the attached fraction is excluded). A different approach was taken by Deng et al. 2017 who considered only the free fraction of graphene oxide, i.e. excluding the fraction absorbed on humic substance (calculated from Langmuir adsorption equation) or accumulated in biota (based on bioconcentration factors found in literature). In general, there is a need to further investigate the bioavailability of ENPs in freshwater and its calculation.

For human exposure, Pini et al. 2016 focused on inhalation and derived XF with USEtox equations to convert the ENP concentration in air (considering the sum of free, aggregated and attached ENP species) into an uptake by humans (depending on compartment characteristics). The uptake factor is then adapted to consider the lung retention factor defined by Walser et al. 2015. Indeed, these authors recommended to adapt the exposure factor to lung physiology, because of the specific behavior of small

particles in lungs. The uptake via air inhalation is thus determined by the effective ENP dose in the target organ for local effects or in the entire human body for systemic effects, based on the total lung retention fraction and on the mass of the target organ in which toxic effects are observed. A similar approach was followed by Tsang et al. 2017 by applying physiologically-based pharmacokinetic (PBPK) model to determine the deposition and retention of nano-TiO₂ in lung over time. The authors derived retained-intake fraction, which is the ratio of the average internal wet lung mass dose of TiO₂ per average lifetime emitted mass of TiO₂, for working exposure scenarios. Regarding other exposure routes than inhalation, Ettrup et al. 2017 applied USEtox equations for direct (air inhalation and water drinking) and indirect exposure pathways (excluding exposure via meat and milk due to lack of data). The bioaccumulation factors for fish, above-ground produce and below-ground produce were derived from literature (the two latter factors assumed equal due to a lack of data for the BAF_{above-ground}).

2.3.4 Effect modelling of ENPs

The selection of tests and endpoint values is crucial for the quality of the developed CF. This was highlighted by Salieri, Righi, et al. 2015 who pointed the influence of the type of ENP (crystalline structure, nominal size, impurities content), the test procedure (suspension preparation method) and the mode of exposure (time, UV) to the ecotoxicity results. The authors therefore applied criteria to select nano-TiO₂ endpoints: tests on anatase form (more toxic than rutile form), exclusion of tests with different treatments (chemical solvents, filtration, UV radiation) and preference of primary producer tests with fluorimetric method (due to algae-particle interactions). Ecotoxicity values are reported, together with information about the tests (primary size, method, type and endpoints) and the applied inclusion/exclusion criteria by the authors. Ettrup et al. 2017 also followed a qualitative selection of aquatic ecotoxicity data, shortlisting studies presenting EC50 data, following standardized test methods (ISO, OECD, ATSM, etc.), while tests with severe alterations were excluded. Information about the testing conditions are transparently reported (particle type, specie, exposure time, size, test method, specific surface area, zeta potential). The authors calculated the EF based on different subsets of data for sensitivity analysis: USEtox-compliant, “adequate quality” from (Lützhøft, et al. 2015) “adequate quality” studies from Lützhøft et al. (2015) without Protozoa, and all rutile nano-TiO₂. The third subset (i.e. following guidelines from Lützhøft et al., 2015, that could be used for regulatory purpose but excluding protozoa that are highly sensitive) is used as baseline.

It is interesting to note that the criteria proposed by (Salieri, Pasteris, et al. 2015) and (Ettrup et al. 2017) are quite different. The procedure of (Ettrup et al. 2017) seems nevertheless more robust since it relies on existing guidelines. In the studies of (Miseljic and Olsen 2014) and (Pu et al. 2016) no qualitative

approach was detailed to select tests. However, they both provide the list of EC50 data with tests information (size, type and endpoint).

For human health effect factor, previous studies proposed approaches to select and use toxicity data. In particular, for inhalation effects, (Buist et al. 2017) developed a stepwise approach described in a decision tree, including the establishment of the hazard profile, the selection of relevant studies, the choice of relevant dose metric, derivation of point of departure (based on USE EPA Benchmark Dose Software – BMDS), extrapolation to human ED50 and conversion to mass intake. Compared to the default USEtox method, the authors applied dose deposited or retained in the lungs instead of the mass intake because it is often more relevant for nanoparticles. To facilitate the use of such metric and conversion (based on particle size distribution), they suggest to couple USEtox model with multiple-Path Particle Dosimetry (MPPD) model. The limitation of using mass intake was also highlighted by (Pini et al. 2016), (Tsang et al. 2017) and (Walser et al. 2015), who applied benchmark dose (BMD) for surface area based dose metric. The other adaptation from USEtox is to use lower effect doses (e.g. ED10 or ED4) when relevant (such as in (Buist et al. 2017; Ettrup et al. 2017; Pini et al. 2016), to avoid extrapolation factors to ED50 and potential bias due to non-linear dose-response relationship. In addition, (Buist et al. 2017) took into account a severity factor to derive ED50, such weighting should be based on expert judgement following defined procedures (from the scientific community or regulatory bodies). Finally, (Walser et al. 2015) proposed a decision tree to determine the effect factor based on available data, if it is a high aspect ratio ENP or a soluble metal (oxide). The authors suggest to group nanomaterials with similar modes of toxic action and/or toxicity profiles to avoid the case by case assessment and create consistency. All the cited studies provided detailed information about the selected toxicity tests and data, which ensures the transparency and reusability of the results.

2.3.5 Recommended LCIA factors for ENPs

Based on the analysis of the modelling assumptions, the recommended CFs from availability data in literature were compiled (Table 2). For the freshwater ecotoxicity CF of nano-TiO₂, the values of (Salieri, Pasteris, et al. 2015) are not displayed since they were updated in (Salieri et al. 2019). For the human toxicity of nano-TiO₂, the CFs of (Pini et al. 2016) were preferred for the emissions to air since the authors made the distinction between indoor and outdoor emission and they included the lung retention factor for exposure (these aspects are not covered by (Ettrup et al. 2017)). The CFs for indoor exposure scenarios proposed by (Tsang et al. 2017) could also be used if information about the emission scenario(s) is available and matches the assumptions made by the authors (advanced modelling). (Eckelman et al. 2012) also proposed a CF to characterize the freshwater ecotoxicity of carbon

nanotubes. However, they did not make the distinction between SWCNT and MWCNT (as done in (Rodriguez-Garcia, Zimmermann, and Weil 2014) and followed a very conservative approach (e.g. selecting the lowest EC50 instead of applying a geometric mean as recommended in USEtox).

In Table 2, the CFs for nano-TiO₂ are the most robust, thanks to the advanced fate modelling in Salieri et al. (2019), Pini et al. (2016) and Ettrup et al. (2017), but also the careful selection of effect data. While Ettrup et al. (2017) developed human toxicity and ecotoxicity CFs for the release of nano-TiO₂ in the three compartments, Pini et al. (2016) focused on human toxicity CF for air emission (indoor or outdoor, with greater details than in Ettrup et al., 2017), and Salieri et al. (2019) focused on freshwater ecotoxicity CF (applying a more advanced fate model than in Ettrup et al., 2017). The combination between fate factors from Salieri et al. (2019) and exposure and effects factors from Pini et al. (2016) and Ettrup et al. (2017) could be envisioned to update CF values for all impact categories and emission compartments, to take advantage of the state-of-the-art in fate, exposure and effect factor modelling. For the freshwater ecotoxicity of nano-Cu and graphene oxide, the authors (Pu et al., 2016 and Deng et al., 2017, respectively) also relied on SB4N modelling (or similar colloidal model), the quality of the obtained CFs is thus quite high. Unfortunately, only the emission to freshwater is characterized. For SWCNT and MWCNT, Rodriguez-Garcia et al. (2014) applied the default USEtox model. The related CFs should be used carefully, especially due to the lack of specific nano-fate modelling. This caution applies even more for the CF of nano-Ag from Miseljic and Olsen (2014) who applied the default USEtox model with very basic assumptions (in particular the fate factor is set to 1 day assuming short residence time in freshwater). Due to modelling and qualitative differences, it might be difficult to compare the CFs between ENPs and analyse the obtained variations.

Besides these available CFs, the effects factors from Buist et al. (2017) for MWCNT inhalation could be applied with the intake fractions from Rodriguez-Garcia et al. (2014). In particular, the authors derived carcinogenic effect factors that were not included in Rodriguez-Garcia et al. (2014). Buist et al. (2017) also calculated human effect factors for carbon black and nano-Ag that could be applied if fate and human exposure factors would be available for these ENPs.

Even if we could identify several CFs for ENPs release and some of them with high quality (in particular for nano-TiO₂, as well as for nano-Cu and graphene oxide for freshwater ecotoxicity only), the development of CFs should be pursued to fill data gaps or update previous CFs calculated with basic assumptions (this is the case for nano-Ag, SWCNT and MWCNT).

Table 2: Best available CFs in literature for freshwater ecotoxicity and human toxicity (non-carcinogenic and carcinogenic effects) of ENPs, with [1](Miseljic and Olsen 2014); [2] (Pu et al. 2016); [3] Salieri et al. (2019); [4] Pini et al. (2016); [5] Ettrup et al. (2017); [6] Deng et al. (2017) and [7] Rodriguez-Garcia et al. (2014)

Impact	Freshwater ecotoxicity			Human toxicity, non-cancer			Human toxicity, cancer		
	PAF.m ³ .day/kg (or CTU _e /kg)			cases/kg (or CTU _h)			cases/kg (or CTU _h)		
Emission compartment	Air	Freshwater	Soil	Air	Fresh-water	Soil	Air	Fresh-water	Soil
nano-Ag		8.57x10 ³ [1]							
nano-Cu		5.96x10 ³ [2]							
nano-TiO ₂	3.69x10 ² [3]	3.37x10 ³ [3]	2.08x10 ³ [3]	In [4]: 1.43x10 ⁻² Out [4]: 1.34x10 ⁻⁴	1.25x10 ⁻⁶ [5]	1.42x10 ⁻⁸ [5]	In [4]: 4.19x10 ² Out [4]: 1.77x10 ²	0 [5]	0 [5]
Graphene oxide		7.78x10 ² [6]							
SWCNT	Rur [7]: 3.04x10 ⁻³ Urb [7]: 4.85x10 ⁻³	1.25x10 ¹ [7]	5.32x10 ⁻⁵ [7]	Rur [7]: 6.75x10 ⁻⁵ Urb [7]: 7.50x10 ⁻⁵	6.60x10 ⁻⁴ [7]	2.80x10 ⁻⁷ [7]			
MWCNT	Rur [7]: 1.88x10 ² Urb [7]: 1.91x10 ²	7.40x10 ² [7]	2.26x10 ² [7]	Rur [7]: 2.60x10 ⁻³ Urb [7]: 2.50x10 ⁻³	2.70x10 ⁻³ [7]	8.30x10 ⁻⁴ [7]			

2.4 Result interpretation

This phase aims at interpreting the LCIA results obtained according to the goal and scope of the study. It usually includes the following steps (ISO 2006b):

- Identification of significant issues
- Completeness, sensitivity and consistency checks
- Conclusions, limitations and recommendations

Most of LCA studies are comparative, i.e. the objective is to compare the environmental impacts of several systems providing the same function. The results interpretation therefore analyses the environmental impacts and benefits of the compared scenarios for the different environmental indicators considered, highlighting the potential trade-offs. In the case of LCA study applied to ENMs, the environmental impacts are usually compared with a conventional reference system, and a nano-enabled product can induce environmental benefits on some categories but not on others. In order to solve these conflicting results, several approaches can be applied, such as the aggregation of midpoint indicators into endpoint indicators (impact on human health, ecosystem quality and resources) which can be further normalized (e.g. per person equivalent), the monetarization of the impact scores or multi-criteria decision analysis (MCDA). For MCDA, weighting factors are applied to the various criteria considered,

based on opinion from experts or stakeholders, linear programming, willingness to pay or distance to target techniques. Regarding ENM evaluation, MCDA was applied on LCA indicators by Hicks 2017, where several weighting scenarios were tested (equal, environmental or pro nano weighting factors).

Besides these potential environmental trade-offs, LCA evaluation relies on several value-choices, uncertain assumptions and variable parameters that can affect the conclusions of the study. As stated by the ISO standard 14044 (2006), uncertainty and sensitivity analyses shall be conducted for comparative studies disclosed to the public (such analyses are also recommended in other situations). Uncertainty analysis (propagation of input uncertainty to LCA results) and sensitivity analysis (influence on input uncertainty on output uncertainty) can provide an estimation of the variability of the LCA results (as well as the difference of LCA results between two scenarios) and identify the main contributors explaining this variability, which can be used to refine model parameters and assumptions, and determine conditions for which one scenario should be preferred (e.g. calculation of break-event point).

For the LCA of nano-enabled product or technology, several sources of uncertainty could be critical (Cucurachi and Blanco Rocha 2019):

The definition of the functional unit: As seen in section 2.1, ENM-based product can provide several functional properties, which could be captured by different formulations of the functional unit. In addition, the related parameters can be variable and uncertain due to the lack of return of experience and the influence of the user behavior.

The definition of the conventional system used as reference for the comparison: As seen in section 2.1, the identification of the product that will be replaced by the ENM-based product can be difficult because of the potential multi-functionality (several references to be included) and the uncertainty related to market deployment (depending on the maturity of the product).

The determination of LCI data: As seen in section 2.2, due to the low maturity of ENM-based products, large uncertainty remains on inventory data along their lifecycle (e.g. energy and materials used for production and use, disposal routes), in particular the potential release of ENP emissions.

The environmental impacts of ENP emissions: As observed in section 2.3, there is not yet characterization factors for ENP in LCIA methods and the CFs developed in literature suffer from high uncertainties due to necessary model adaptations to reflect the cause-effect chain of ENP emissions.

Several nano-LCA studies investigated the effects of these uncertainties, mostly applying scenario analysis. Such technique was applied for example to consider future improvements when upscaling a nanotechnology (e.g. Cossutta et al. 2020; Cossutta, McKechnie, and Pickering 2017; Fransman et al.

2017) or worst-case and realistic scenarios for ENP release and impact evaluation (e.g. Garvey et al. 2019; Hischier, Salieri, and Pini 2017) extended the scenario analysis by covering a large panel of uncertainty sources, from the definition of the functional unit, to the production data, ENP release and CF for ENP. By combining all the possible alternatives, the authors could define the range of LCA results (uncertainty analysis) and identify the factors with the highest influence (sensitivity analysis). Probability distribution sampling was also applied to determine the distribution of LCA results due to inventory variability (e.g. Fransman et al. 2017; Hicks et al. 2015) of the distribution of CF due to LCIA model parameters variability (e.g. Eckelman et al. 2012; Garvey et al. 2019). Monte Carlo sampling, i.e. random sampling of inputs within their probability distribution, is usually applied since this technique is available in most of LCA software tools. The sensitivity of LCA results due to input uncertainty can be tested by varying one parameter at a time (OAT method also called perturbation analysis) on a defined variability range and analyse the parameters which induce the largest variations on LCA results (e.g. Ahmed et al. 2017; Wu et al. 2020).

In order to increase the reliability and relevance of LCA results, it is important to generalize the use of sensitivity and uncertainty analyses. Even if there is not a standard protocol to perform these analyses, some authors provided recommendations, as in Igos et al. (2019), which could be followed. Based on this paper, the first step is to list all the possible sources of uncertainty. For modelling choices (e.g. definition of system boundaries, functional unit, reference scenario, LCIA method), alternative scenarios should be defined, covering the maximum of relevant possibilities (scenarios development with relevant experts is therefore encouraged). For quantitative data (e.g. functional properties, inventory data or CFs), the minimum and maximum values should be at least defined (e.g. as used by Garvey et al. 2019 with worst-case and realistic values), and complemented with probability distributions if possible (e.g. as done by Fransman et al. 2017). It is important to carefully define these uncertainty ranges or distributions (e.g. based on experts' review or literature data review) to obtain representative results. Indeed, the use of a generic variation for all parameters (e.g. $\pm 10\%$), which has been done for example by Ahmed et al. 2017, can generate unrealistic sensitivity measures. Since the characterization of inputs uncertainty (both modelling assumptions and parameters) can be time-consuming, a prioritization can be applied, depending on the contribution of flows to baseline LCA impacts and on a qualitative assessment of input uncertainty.

The variability of LCA results, i.e. uncertainty analysis, can be obtained by calculating the impacts for all alternative scenarios defined, and by using the minimum and maximum values of input data. When input probability distributions are defined, Monte Carlo sampling can be performed, or other more advanced sampling methods depending on the level of competences (e.g. stratified sampling like Latin hypercube).

When comparing scenarios, it is important to run the uncertainty analysis on the difference between two scenarios (discernibility analysis) in order to consider the common uncertain factors. As mentioned above, the easiest way to identify the key inputs contributing to LCA uncertainty, i.e. perform sensitivity analysis, is the scenario analysis or individual parameters variation (OAT). With advanced competences and LCA tools (e.g. Brightway2), screening or global sensitivity analysis techniques, such as the method of elementary effects (MoEE) or Sobol method, can provide more relevant and reliable information (e.g. quantification of non-linear effects, interactions and significance of the obtained sensitivity measures). The obtained results from sensitivity and uncertainty analyses should be clearly communicated in the LCA study, so that the reader can understand the limitations, confidence and reliability of the presented results.

3 Guidance on practical implementation of study

This guidance document is written in mainly to benefit LCA practitioners performing an ex-ante study on the potential environmental and human health related impacts occurring over the full (anticipated) life cycle of a nanomaterial or nano-enabled product in the context of a risk governance process focusing on risks and benefits associated with ENMs and NEPs.

Recognising that resources or competences may be limited in this perspective, here three types of study are outlined with different degrees of complexity: i) a qualitative screening analysis, ii) a screening LCA study, and iii) a full comparative LCA study. A decision tree as to how to select between these studies, as well as a short summary of the guidance is included in Figure 2. Each of the study types is discussed in the following sections.

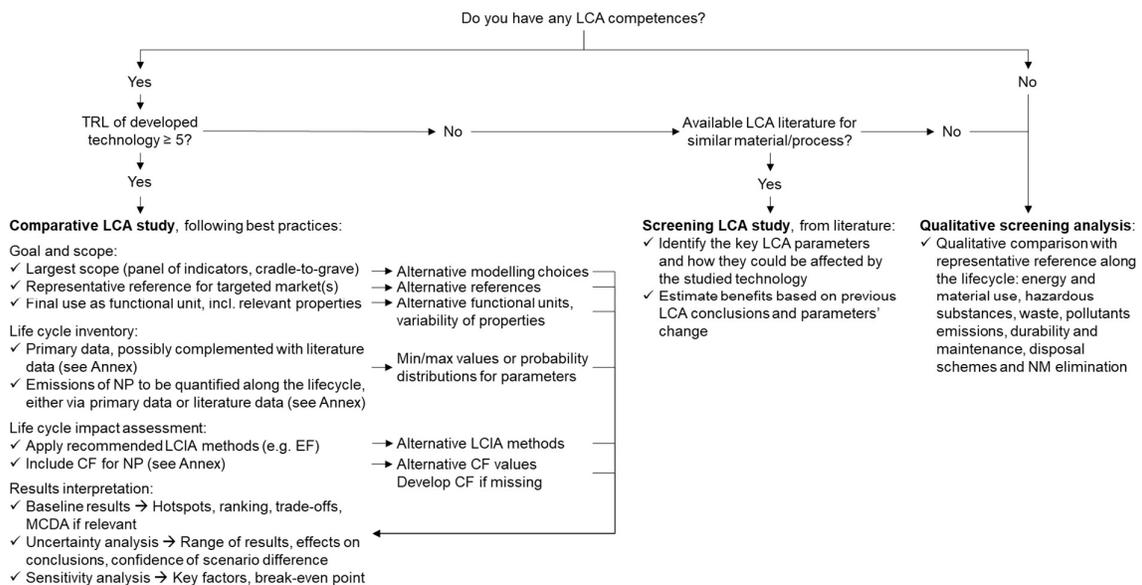


Figure 1: Overview on the type of studies that can be performed.

3.1 Qualitative screening analysis

For those projects where the ENM or NEP is in a very early stage of development or where LCA resources are not readily available a qualitative screening analysis from a life cycle perspective is recommended to provide a notion of potential risks and benefits along the life cycle associated with the envisioned product. Such a qualitative screening would have to include at least an estimate of key parameters and elements along the life cycle of an ENM or NEP. Example elements to include are: energy use, material Use, use of hazardous substances, estimation of waste generation, estimation of pollutant emissions including an estimation of the likelihood of emission of ENM or NEP, estimation of durability and maintenance of the ENM/NEP and its recycling potential, as well as any potential risks in relation to waste processing in end-of-life. Some of these estimates may have a quantitative value attached, but a qualitative scheme classifying estimates as being *high*, *medium*, or *low* would suffice at this stage. The use of the LICARA nanoSCAN tool, included in Tier 1 assessment of SUNDS decision support system, can facilitate this analysis (see: <https://sunds.gd>).

While in itself not sufficient to be a basis for decision making in Risk-Benefit analysis of ENMs and NEPs (frankly, this procedure does not qualify as an LCA) such an analysis may act as first screening and give valuable inputs and perspectives into the design process, until the stage where a more extensive analysis is required or warranted.

3.2 Screening LCA

Depending on resources a qualitative screening analysis may be passed to perform a screening LCA immediately. This is recommended for project still in the design phase (evidenced by low Technology Reference Level), but where capacity to conduct LCA is available to the organization. A screening LCA has a purpose to identify key parameters and hotspots in the value chain where data exists or may be lacking for a full comparative LCA. The screening LCA is mainly built upon data found in literature for similar processes, as well as crude quantitative estimates of process parameters. All of the phases described in the life cycle inventory modelling part of the guidance may be included, though not necessarily with a high degree of certainty associated with parameter values. This should be acknowledged in the conclusion and can to some extent be mitigated by using tools such as scenario analysis, in order to investigate how the product system responds to what-if situations (e.g. what if energy use was three times higher than initially anticipated?). The screening LCA may also act as a pre-study for a full comparative LCA in order to map knowledge gaps and steer data collection efforts for a full comparative LCA study.

3.3 Comparative LCA

An ENM or NEP that already is at a high TRL benefits best from a full comparative LCA in order to demonstrate its potential risks and benefits to environment in comparison to a traditional (bulk) product or another ENM or NEP. This guidance provides elements to include in such a study as well as an overview of potential challenges in relation to LCA.

A full comparative LCA is likely resource intensive, as many key elements will not be available from either standard LCI databases or in the literature. Thus, sufficient resources have to be allocated towards data collection through measurement or modelling. In the case of NEPs containing 'standard' ENMs this guidance provides characterization factors for both the freshwater ecotoxicity and human toxicity impact categories.

However, specification of custom impact categories and impact indicators (for example related to direct worker exposure) may fall within the scope of such a study. The added benefit of this approach is that much of the thus developed knowledge may provide input to other parts of the risk governance process such as risk management or health, safety and environmental management.



4 Conclusion

In this report, we detail various approaches to perform Life Cycle Assessment of engineered nanomaterials and nano-enabled products. The guidelines are complimentary in nature to CEN-TS-17276:2018. Many of the traditional elements in LCA procedure do not change whether LCA is conducted on an ENM, NEP, or bulk product and we refer to the existing standard and framework text provided by ISO 14040, ISO 14044 and CEN-TS-17276:2018. This guidance focuses on construction of the Life Cycle Inventory model, as well as a state-of-the-art overview and recommendations for Life Cycle Impact Assessment modelling for ENMs and NEPs, while highlighting challenges for goal and scope and interpretation phases.

Recommendations are given on how to model the life cycle inventory for production, use, and end-of-life phases of an ENM or NEP, intended for LCA practitioners working from the perspective of ENM or NEP production and manufacturing. These guidelines are meant to be used in parallel to other tools in a Risk Governance process of ENMs covering various aspects of risk management and perspectives in risk-benefit analysis. Therefore, special attention to include direct human exposure as well as release of nanomaterial or degradation products to the environment are emphasized in all unit processes of the life cycle inventory.

The overview of nano-related LCIA details state-of-the-art in fate, exposure and effect modelling for nanomaterials and contains a recommendation on specific characterization factors to be used for a limited list of specific ENMs in the midpoint impact categories freshwater ecotoxicity and human toxicity.

Lastly, recognizing that both the knowledge base and resources may be limited depending on organizational characteristics, the guidance emphasizes different ways to use life cycle considerations in the context of Risk Governance, ranging from qualitative screening analysis to a full comparative LCA study with custom application of life cycle impact indicators and development of characterization factors.

5 References

- Ahmed, Abdelsalam, Islam Hassan, Taofeeq Ibn-Mohammed, Hassan Mostafa, Ian M. Reaney, Lenny S. C. Koh, Jean Zu, and Zhong Lin Wang. 2017. "Environmental Life Cycle Assessment and Techno-Economic Analysis of Triboelectric Nanogenerators." *Energy & Environmental Science* 10(3):653–71. doi: 10.1039/C7EE00158D.
- Bafana, Adarsh, Shishir V. Kumar, Sila Temizel-Sekeryan, Si Amar Dahoumane, Liv Haselbach, and Clayton S. Jeffryes. 2018. "Evaluating Microwave-Synthesized Silver Nanoparticles from Silver Nitrate with Life Cycle Assessment Techniques." *Science of The Total Environment* 636:936–43. doi: 10.1016/j.scitotenv.2018.04.345.
- Bi, Yuqiang, Edward I. Westerband, Absar Alum, Frank C. Brown, Morteza Abbaszadegan, Kiril D. Hristovski, Andrea L. Hicks, and Paul K. Westerhoff. 2018. "Antimicrobial Efficacy and Life Cycle Impact of Silver-Containing Food Containers." *ACS Sustainable Chemistry & Engineering* 6(10):13086–95. doi: 10.1021/acssuschemeng.8b02639.
- Bos, Ulrike, Rafael Horn, Tabea Beck, Jan Paul Lindner, and Matthias Fischer. 2016. *LANCA - Characterization Factors for Life Cycle Impact Assessment: Version 2.0*. Stuttgart: Fraunhofer Verlag.
- Buist, H. E., R. Hirschier, J. Westerhout, and D. H. Brouwer. 2017. "Derivation of Health Effect Factors for Nanoparticles to Be Used in LCIA." *NanoImpact* 7:41–53. doi: 10.1016/j.impact.2017.05.002.
- Cossutta, Matteo, Jon McKechnie, and Stephen J. Pickering. 2017. "A Comparative LCA of Different Graphene Production Routes." *Green Chemistry* 19(24):5874–84. doi: 10.1039/C7GC02444D.
- Cossutta, Matteo, Viliam Vretenar, Teresa A. Centeno, Peter Kotrusz, Jon McKechnie, and Stephen J. Pickering. 2020. "A Comparative Life Cycle Assessment of Graphene and Activated Carbon in a Supercapacitor Application." *Journal of Cleaner Production* 242:118468. doi: 10.1016/j.jclepro.2019.118468.
- Cucurachi, Stefano, and Carlos Felipe Blanco Rocha. 2019. "Life-Cycle Assessment of Engineered Nanomaterials." Pp. 815–46 in *Nanotechnology in Eco-efficient Construction*. Elsevier.
- Deng, Yelin, Jianyang Li, Ming Qiu, Fan Yang, Jingyi Zhang, and Chris Yuan. 2017. "Deriving Characterization Factors on Freshwater Ecotoxicity of Graphene Oxide Nanomaterial for Life Cycle Impact Assessment." *The International Journal of Life Cycle Assessment* 22(2):222–36. doi: 10.1007/s11367-016-1151-4.
- Deng, Yelin, Lulu Ma, Tonghui Li, Jianyang Li, and Chris Yuan. 2019. "Life Cycle Assessment of Silicon-Nanotube-Based Lithium Ion Battery for Electric Vehicles." *ACS Sustainable Chemistry & Engineering* 7(1):599–610. doi: 10.1021/acssuschemeng.8b04136.
- ECHA. 2008. *Guidance on Information Requirements and Chemical Safety Assessment - Appendix R.7.13-2: Environmental Risk Assessment for Metals and Metal Compounds*.
- Eckelman, Matthew J., Meagan S. Mauter, Jacqueline A. Isaacs, and Menachem Elimelech. 2012. "New Perspectives on Nanomaterial Aquatic Ecotoxicity: Production Impacts Exceed Direct



- Exposure Impacts for Carbon Nanotubes." *Environmental Science & Technology* 46(5):2902–10. doi: 10.1021/es203409a.
- Ettrup, Kim, Anna Kounina, Steffen Foss Hansen, Johannes A. J. Meesters, Eldbjørg B. Veia, and Alexis Laurent. 2017. "Development of Comparative Toxicity Potentials of TiO₂ Nanoparticles for Use in Life Cycle Assessment." *Environmental Science & Technology* 51(7):4027–37. doi: 10.1021/acs.est.6b05049.
- Fazio, S., Castellani, V., Sala, S., Schau, E.M., Secchi, M., and Zampori, L. 2018. *Supporting Information to the Characterisation Factors of Recommended EF Life Cycle Impact Assessment Methods: New Methods and Differences with ILCD*. Ispra: European Commission. Joint Research Centre.
- Fransman, Wouter, Harrie Buist, Eelco Kuijpers, Tobias Walser, David Meyer, Esther Zondervan-van den Beuken, Joost Westerhout, Rinke H. Klein Entink, and Derk H. Brouwer. 2017. "Comparative Human Health Impact Assessment of Engineered Nanomaterials in the Framework of Life Cycle Assessment: Comparative Human Health Impact Assessment." *Risk Analysis* 37(7):1358–74. doi: 10.1111/risa.12703.
- Frischknecht, R., A. Braunschweig, P. Hofstetter, and P. Suter. 2000. "Human Health Damages Due to Ionising Radiation in Life Cycle Impact Assessment." *Environmental Impact Assessment Review* 20(2):159–89. doi: 10.1016/S0195-9255(99)00042-6.
- Garvey, Therese, Elizabeth A. Moore, Callie W. Babbitt, and Gabrielle Gaustad. 2019. "Comparing Ecotoxicity Risks for Nanomaterial Production and Release under Uncertainty." *Clean Technologies and Environmental Policy* 21(2):229–42. doi: 10.1007/s10098-018-1648-6.
- Goedkoop, M., R. Heijungs, MAJ Huijbregts, A. De Schryver, J. Struijs, and R. Van Zelm. 2009. *ReCiPe 2008: A Life Cycle Impact Assessment Method Which Comprises Harmonised Category Indicators at the Midpoint and the Endpoint Level. First Edition: Report I: Characterisation*. The Hague, The Netherlands: Dutch Ministry of the Environment.
- Greijer, Helena, Lennart Karlson, Sten-Eric Lindquist, and Anders Hagfeldt. 2001. "Environmental Aspects of Electricity Generation from a Nanocrystalline Dye Sensitized Solar Cell System." *Renewable Energy* 23(1):27–39. doi: 10.1016/S0960-1481(00)00111-7.
- Guinee, Jeroen B. 2002. *Handbook of Life Cycle Assessment: Operation Guide to ISO Standards*. Kluwer Academic Publishers.
- Hicks, Andrea L. 2017. "Using Multi Criteria Decision Analysis to Evaluate Nanotechnology: NAG Enabled Textiles as a Case Study." *Environmental Science: Nano* 4(8):1647–55. doi: 10.1039/C7EN00429J.
- Hicks, Andrea L., Leanne M. Gilbertson, Jamila S. Yamani, Thomas L. Theis, and Julie B. Zimmerman. 2015. "Life Cycle Payback Estimates of Nanosilver Enabled Textiles under Different Silver Loading, Release, And Laundering Scenarios Informed by Literature Review." *Environmental Science & Technology* 49(13):7529–42. doi: 10.1021/acs.est.5b01176.
- Hischier, Roland, Bernd Nowack, Fadri Gottschalk, Ingrid Hincapie, Michael Steinfeldt, and Claudia Som. 2015. "Life Cycle Assessment of Façade Coating Systems Containing Manufactured

- Nanomaterials." *Journal of Nanoparticle Research* 17(2):68. doi: 10.1007/s11051-015-2881-0.
- Hischier, Roland, Beatrice Salieri, and Martina Pini. 2017. "Most Important Factors of Variability and Uncertainty in an LCA Study of Nanomaterials – Findings from a Case Study with Nano Titanium Dioxide." *NanoImpact* 7:17–26. doi: 10.1016/j.impact.2017.05.001.
- IPCC. 2013. *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*. Cambridge (UK) and New York (USA): Cambridge University Press.
- ISO. 2006a. *14040:2006. Environmental Management - Life Cycle Assessment - Principles and Framework*. Geneva, Switzerland: International Organization for Standardization.
- ISO. 2006b. *ISO 14044:2006: Environmental Management - Life Cycle Assessment - Requirements and Guidelines*. Geneva, Switzerland: International Organization for Standardization.
- Li, Bingbing, Xianfeng Gao, Jianyang Li, and Chris Yuan. 2014. "Life Cycle Environmental Impact of High-Capacity Lithium Ion Battery with Silicon Nanowires Anode for Electric Vehicles." *Environmental Science & Technology* 48(5):3047–55. doi: 10.1021/es4037786.
- Lützholt, H-C.H., Hartmann, N.B., Brinch, A., Kjølholt, J., and Baun, A. 2015. *Environmental Effects of Engineered Nanomaterials: Estimations of Predicted No-Effect Concentrations (PNECs)*. Danish Environmental Protection Agency.
- Marimón-Bolívar, Wilfredo, and Edgar E. González. 2018. "Green Synthesis with Enhanced Magnetization and Life Cycle Assessment of Fe₃O₄ Nanoparticles." *Environmental Nanotechnology, Monitoring & Management* 9:58–66. doi: 10.1016/j.enmm.2017.12.003.
- Meesters, J. A. J., J. T. K. Quik, A. A. Koelmans, A. J. Hendriks, and D. van de Meent. 2016. "Multimedia Environmental Fate and Speciation of Engineered Nanoparticles: A Probabilistic Modeling Approach." *Environmental Science: Nano* 3(4):715–27. doi: 10.1039/C6EN00081A.
- Meesters, Johannes A. J., Albert A. Koelmans, Joris T. K. Quik, A. Jan Hendriks, and Dik van de Meent. 2014. "Multimedia Modeling of Engineered Nanoparticles with SimpleBox4nano: Model Definition and Evaluation." *Environmental Science & Technology* 48(10):5726–36. doi: 10.1021/es500548h.
- Miseljic, Mirko, and Stig I. Olsen. 2014. "Life-Cycle Assessment of Engineered Nanomaterials: A Literature Review of Assessment Status." *Journal of Nanoparticle Research* 16(6):2427. doi: 10.1007/s11051-014-2427-x.
- Pini, Martina, Beatrice Salieri, Anna Maria Ferrari, Bernd Nowack, and Roland Hischier. 2016. "Human Health Characterization Factors of Nano-TiO₂ for Indoor and Outdoor Environments." *The International Journal of Life Cycle Assessment* 21(10):1452–62. doi: 10.1007/s11367-016-1115-8.
- Posch, Maximilian, Jyri Seppälä, Jean-Paul Hettelingh, Matti Johansson, Manuele Margni, and Olivier Jolliet. 2008. "The Role of Atmospheric Dispersion Models and Ecosystem Sensitivity in the Determination of Characterisation Factors for Acidifying and Eutrophying Emissions in LCIA."



- The International Journal of Life Cycle Assessment* 13(6):477–86. doi: 10.1007/s11367-008-0025-9.
- Pourzahedi, Leila, Marina Vance, and Matthew J. Eckelman. 2017. “Life Cycle Assessment and Release Studies for 15 Nanosilver-Enabled Consumer Products: Investigating Hotspots and Patterns of Contribution.” *Environmental Science & Technology* 51(12):7148–58. doi: 10.1021/acs.est.6b05923.
- Pu, Yubing, Feng Tang, Pierre-Michel Adam, Bertrand Laratte, and Rodica Elena Ionescu. 2016. “Fate and Characterization Factors of Nanoparticles in Seventeen Subcontinental Freshwaters: A Case Study on Copper Nanoparticles.” *Environmental Science & Technology* 50(17):9370–79. doi: 10.1021/acs.est.5b06300.
- Rodriguez-Garcia, Gonzalo, Benedikt Zimmermann, and Marcel Weil. 2014. “Nanotoxicity and Life Cycle Assessment: First Attempt towards the Determination of Characterization Factors for Carbon Nanotubes.” *IOP Conference Series: Materials Science and Engineering* 64:012029. doi: 10.1088/1757-899X/64/1/012029.
- Roes, A. L., L. B. Tabak, L. Shen, E. Nieuwlaar, and M. K. Patel. 2010. “Influence of Using Nanoobjects as Filler on Functionality-Based Energy Use of Nanocomposites.” *Journal of Nanoparticle Research* 12(6):2011–28. doi: 10.1007/s11051-009-9819-3.
- Rosenbaum, Ralph K., Till M. Bachmann, Lois Swirsky Gold, Mark A. J. Huijbregts, Olivier Jolliet, Ronnie Juraske, Annette Koehler, Henrik F. Larsen, Matthew MacLeod, Manuele Margni, Thomas E. McKone, Jérôme Payet, Marta Schuhmacher, Dik van de Meent, and Michael Z. Hauschild. 2008. “USEtox—the UNEP-SETAC Toxicity Model: Recommended Characterisation Factors for Human Toxicity and Freshwater Ecotoxicity in Life Cycle Impact Assessment.” *The International Journal of Life Cycle Assessment* 13(7):532–46. doi: 10.1007/s11367-008-0038-4.
- Salieri, Beatrice, Roland Hischier, Joris T. K. Quik, and Olivier Jolliet. 2019. “Fate Modelling of Nanoparticle Releases in LCA: An Integrative Approach towards ‘USEtox4Nano.’” *Journal of Cleaner Production* 206:701–12. doi: 10.1016/j.jclepro.2018.09.187.
- Salieri, Beatrice, Andrea Pasteris, Jonas Baumann, Serena Righi, Jan Köser, Rosaria D’Amato, Benedetta Mazzesi, and Juliane Filser. 2015. “Does the Exposure Mode to ENPs Influence Their Toxicity to Aquatic Species? A Case Study with TiO₂ Nanoparticles and *Daphnia Magna*.” *Environmental Science and Pollution Research* 22(7):5050–58. doi: 10.1007/s11356-014-4005-2.
- Salieri, Beatrice, Serena Righi, Andrea Pasteris, and Stig Irving Olsen. 2015. “Freshwater Ecotoxicity Characterisation Factor for Metal Oxide Nanoparticles: A Case Study on Titanium Dioxide Nanoparticle.” *Science of The Total Environment* 505:494–502. doi: 10.1016/j.scitotenv.2014.09.107.
- Salieri, Beatrice, David A. Turner, Bernd Nowack, and Roland Hischier. 2018. “Life Cycle Assessment of Manufactured Nanomaterials: Where Are We?” *NanoImpact* 10:108–20. doi: 10.1016/j.impact.2017.12.003.
- Seppälä, Jyri, Maximilian Posch, Matti Johansson, and Jean-Paul Hettelingh. 2006. “Country-Dependent Characterisation Factors for Acidification and Terrestrial Eutrophication Based on



- Accumulated Exceedance as an Impact Category Indicator (14 Pp).” *The International Journal of Life Cycle Assessment* 11(6):403–16. doi: 10.1065/lca2005.06.215.
- Serrano-Luján, L., S. Víctor-Román, C. Toledo, O. Sanahuja-Parejo, A. E. Mansour, J. Abad, A. Amassian, A. M. Benito, W. K. Maser, and A. Urbina. 2019. “Environmental Impact of the Production of Graphene Oxide and Reduced Graphene Oxide.” *SN Applied Sciences* 1(2):179. doi: 10.1007/s42452-019-0193-1.
- Tsang, Michael P., Dingsheng Li, Kendra L. Garner, Arturo A. Keller, Sangwon Suh, and Guido W. Sonnemann. 2017. “Modeling Human Health Characterization Factors for Indoor Nanomaterial Emissions in Life Cycle Assessment: A Case-Study of Titanium Dioxide.” *Environmental Science: Nano* 4(8):1705–21. doi: 10.1039/C7EN00251C.
- UNEP, United Nations Environment Programme. 2016. *Global Guidance for Life Cycle Impact Assessment Indicators*, Vol. 1.
- Van Oers, L., Arjan De Koning, J. B. Guinee, and G. Huppes. 2002. *Abiotic Resource Depletion in LCA*. Road and Hydraulic Engineering Institute, Ministry of Transport and Water.
- Walser, Tobias, Evangelia Demou, Daniel J. Lang, and Stefanie Hellweg. 2011. “Prospective Environmental Life Cycle Assessment of Nanosilver T-Shirts.” *Environmental Science & Technology* 45(10):4570–78. doi: 10.1021/es2001248.
- Walser, Tobias, David Meyer, Wouter Fransman, Harrie Buist, Eelco Kuijpers, and Derk Brouwer. 2015. “Life-Cycle Assessment Framework for Indoor Emissions of Synthetic Nanoparticles.” *Journal of Nanoparticle Research* 17(6):245. doi: 10.1007/s11051-015-3053-y.
- WMO, United States, United States, United Nations Environment Programme, and European Commission, eds. 1999. *Scientific Assessment of Ozone Depletion, 1998*. Washington, DC : Nairobi, Kenya : Geneva, Switzerland : Brussels, Belgium: National Oceanic and Atmospheric Administration : National Aeronautics and Space Administration ; United Nations Environment Programme ; World Meteorological Organization ; European Commission.
- Wu, Fan, Zheng Zhou, Sila Temizel-Sekeryan, Ramin Ghamkhar, and Andrea L. Hicks. 2020. “Assessing the Environmental Impact and Payback of Carbon Nanotube Supported CO₂ Capture Technologies Using LCA Methodology.” *Journal of Cleaner Production* 270:122465. doi: 10.1016/j.jclepro.2020.122465.
- van Zelm, Rosalie, Mark A. J. Huijbregts, Henri A. den Hollander, Hans A. van Jaarsveld, Ferd J. Sauter, Jaap Struijs, Harm J. van Wijnen, and Dik van de Meent. 2008. “European Characterization Factors for Human Health Damage of PM₁₀ and Ozone in Life Cycle Impact Assessment.” *Atmospheric Environment* 42(3):441–53. doi: 10.1016/j.atmosenv.2007.09.072.



www.riskgone.eu | riskgone@nilu.no

KJELLER, 05-12-2020

The publication reflects only the author's view and the European Commission is not responsible for any use that may be made of the information it contains.



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 814425.