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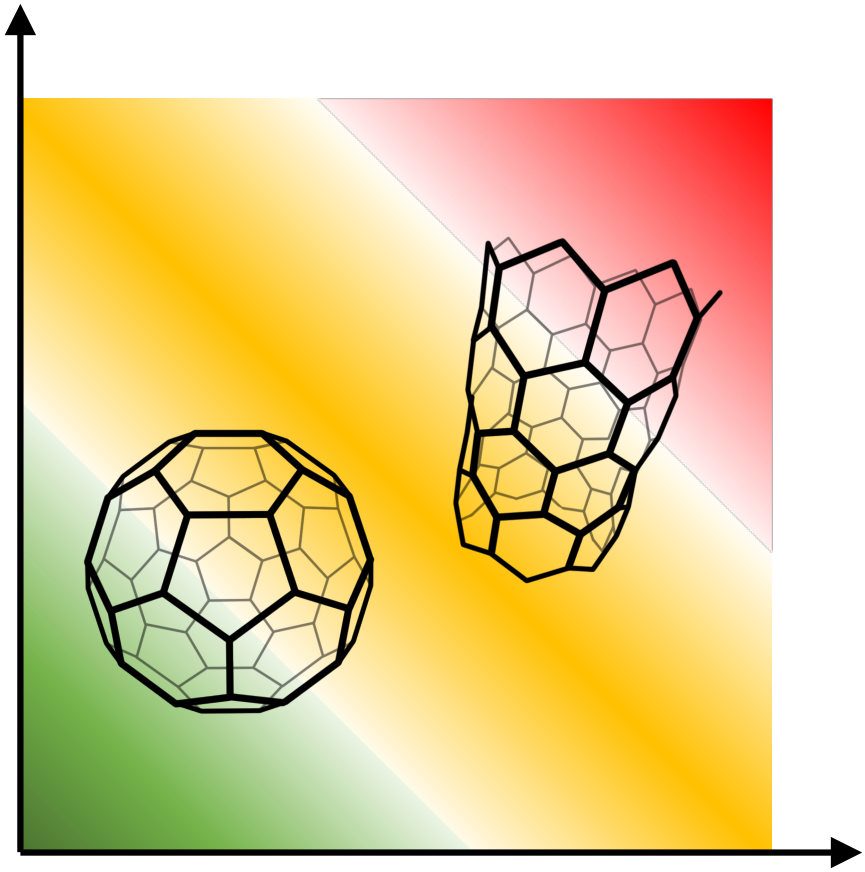

Review of Screening Risk Assessment Methods for Nanomaterials

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Cover:
Schematic illustration of a typical risk ranking matrix. The axes represent two hazard scales, and the colour indicates the scoring and ranking of the nanomaterials, going from green (low risk), via yellow (medium risk), to red (high risk). A fullerene and a carbon nanotube are shown as two examples of nanomaterials, and they were drawn by Rasmus Arvidsson.

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SUMMARY

Nanomaterials are a new and growing type of material, and concerns have been raised regarding their potential risks to human health and to the environment. These concerns have spurred the development of risk assessment methods with the purpose of assessing risks related to nanomaterials. However, such developments have proven to be challenging, both with regard to assessing toxic effects of nanomaterials and to predicting human and environmental exposure to nanomaterials. In response to these challenges, a number of screening risk assessment methods for nanomaterials have been developed. In contrast to full risk assessments, screening risk assessments typically assess risk in a qualitative manner, for example on an ordinal scale from 1 to 3. The aim of this report is to investigate existing screening risk assessment methods for nanomaterials and provide recommendations on their further development. In order to fulfil this aim, a background section about three general and often-used screening risk assessment approaches is first provided. Second, screening risk assessment methods developed specifically for nanomaterials are reviewed. Third, recommendations on potentially beneficial developments within the field are provided in a concluding discussion.

The review showed that many quite different screening risk assessment methods for nanomaterials exist. A total of 20 were identified: ANSES, CB Nanotool 2.0, early warning signs, Genaidy's method, Groso's method, Guidance, Hierarchical Rank Aggregation, LICARA nanoSCAN, Nano-Evaluris, NanoHAZ, NANoREG, NanoRiskCat, NanoSafer, Occupational Hazard Band for Nano, Precautionary Matrix, Relative Risk Analysis, Risk Trigger Scores, Stoffenmanager Nano, TEARR, and the WCD model. These methods share many features, such as the scoring and ranking of risk on ordinal scales. However, they are also different in several respects. The exact scales used in the different methods differ, and, more importantly, they vary concerning the complexity of the scoring and ranking procedure, and which hazard input parameters are used in order to conduct the scoring and ranking. Some methods are relatively simple and require few hazard input parameters, while others are more complex, and require many input parameters, some of which are difficult to determine. It was also noted that most methods focused on occupational human health risks, while fewer focused on environmental risks.

Based on the review, we propose three main recommendations. First, the further development of screening risk assessment methods focusing on environmental risks is warranted. Second, modest complexity and input data requirements are beneficial for the applicability of the method and more in line with the spirit of screening risk assessment. Third, since ordinal scales have problems related to mathematical operations and scale compression, we recommend they be used with caution.

Keywords: Risk assessment, chemical, risk ranking, control banding, chemical scoring and ranking, nanoparticle.

Preface and acknowledgement

History suggests that new materials often bring new and sometimes unexpected environmental risks – risks that society find difficult to deal with (Harremoës et al. 2001). For example, the book *Plastic: A Toxic Love Story*, provides an overview of environmental risks related to society's ever increasing use of plastic, which is a comparatively new material in the history of humankind (Freinkel 2011).

Nanomaterials constitute another new category of materials used in society. Considerable effort is currently ongoing in order to develop relevant risk assessment methods for these materials, potentially enabling the detection and management of nanomaterial risks before they happen. One such effort is the Mistra Environmental Nanosafety programme. The vision and overall goal of the programme is to:

> "establish a strong research environment capable of substantial contributions to the development of generic and applicable environmental risk assessment methodology adapted for anthropogenic and engineered nanomaterials (NMs) to support a development of nanotechnology that considers the environmental, health, and safety (EHS) aspects."

More information about this programme can be found on its webpage (Mistra Environmental Nanosafety 2015). One specific aim of this programme is to review and develop screening risk assessment methods for nanomaterials, as a complement to full risk assessments. This report and the review it contains are a part of that aim, and were written as a deliverable to the Mistra Environmental Nanosafety programme (deliverable 4.2.1). The funding from Mistra – the Swedish Foundation for Strategic Environmental Research – is thus gratefully acknowledged.

The authors,
Gothenburg, September 2016

Contents

Abbreviations

ADI: acceptable daily intake

ANSES: *Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail* (French Agency for Food, Environmental and Occupational Health Safety)

BAF: bioaccumulation factor

BCF: bioconcentration factor

BMDL: benchmark lower confidence limit

CEDL: critical effect dose lower confidence limit

CHEMS: Chemical Hazard Evaluation for Management Strategies

CLP: Classification, Labelling and Packaging

COSHH: Control of Substances Hazardous to Health Essentials

CR: causes of risk

CRIRS: Chemical Risk Ranking and Scoring

CSI: Chemistry Scoring Index

DDT: dichlorodiphenyltrichloroethane

EURAM: European Union Risk Ranking Method

IEH: Institute of Environmental Health

NM: nanomaterial (only used in some figures)

NOEC: no observed effect concentration

NOEM: Nanomaterial Occupational Exposure Management

NP: nanoparticle (only used in some figures)

PBT: persistent, bioaccumulating, and toxic

PCB: polychlorinated biphenyls

PDI: predicted daily intake

PEC: predicted environmental concentration

PNEC: predicted no-effect concentration

PU: protected units

RCR: risk characterisation ratio

SCRAM: Scoring and Ranking Assessment Method

TEARR: Tool for Engineered Nanomaterial Application Pair Risk Ranking

WCD: Worst Case Definition

1 Introduction

1.1 Chemicals and risk assessment

Human-made chemical substances – although useful in many ways – are also one of the main risks to society (Rockström et al. 2009). This fact has spurred the development of methods to assess risks of chemicals, thereby enabling society to manage these risks in advance. These efforts have resulted in the *risk assessment of chemicals* method, also referred to as *chemical risk assessment* (van Leeuwen and Vermeire 2007; European Chemicals Agency 2011; European Chemicals Bureau 2003). The procedure of this environmental assessment method is shown in Figure 1. The core idea of the method is that risks related to chemicals can be modelled, calculated, and assessed using cause-effect chains as bases. These cause-effect chains link the chemical substances to target organisms in terms of quantitative relationships. Exposure to chemicals is modelled for some organisms of choice, and then quantified in terms of a predicted environmental concentration (PEC) or, for human health risk assessment, a predicted daily intake (PDI). In parallel, toxic effects of the same substance to the target organisms are investigated and assessed, resulting in a predicted no-effect concentration (PNEC) or, for human health risk assessment, an acceptable daily intake (ADI). Based on these two parameters quantifying exposure and effects, a risk characterisation ratio (RCR) is calculated according to the following equations:

$$RCR_{eco} = \frac{PEC}{PNEC} \qquad \text{(Eq. 1)}$$

$$RCR_{human} = \frac{PDI}{ADI} \qquad \text{(Eq. 2)}$$

If the RCR is below one, the risk is said to be controlled, which means that no unacceptable effects are expected. If not, then the risk in not controlled, which means that unacceptable effects may happen. Similar approaches are employed in *ecological risk assessment*, which is a somewhat broader and often more location-specific assessment method for which risks related to chemicals are commonly also considered (Suter II 2007).

Despite being an established method, some have suggested that chemical risk assessment has inherent problems. The main reason for this is the high complexity of the natural environment, and the formidable challenge that this creates for assessing risks of chemical substances. In other words, the cause-effect chains linking chemical substances to target organisms are considered to be too complex to allow an adequate quantification. The work of Berg and Scheringer (1994) constitutes an example of this view. They wrote about the *overcomplexity* of the environment, by which they mean that "the reactions of environmental systems to human interventions cannot be

predicted in terms of cause-effect relationships." As an alternative approach to risk assessment, the same authors suggest persistence and ability to travel long distances as *proxy measures* for assessing risks of chemical substances (Scheringer and Berg 1994).

This dichotomy can be expressed as *hazard versus risk* (Löfstedt 2011; Swanson and Socha 1997). *Hazard* here means the inherent potential of a substance to cause adverse effects.[1] It is thus assessed based on some inherent properties of the substance, such as toxicity and persistence. Sometimes, less inherent but still basic properties of the substance are also employed in the hazard approach, such as annual production and emissions of the substance. In any case, assessing hazard does not require any detailed modelling of the complex cause-effect chains connecting the substance to organisms in the environment. *Risk*, on the other hand, is a combination of both exposure and effects, and requires a detailed cause-effect modelling of these. Stated in other terms, a risk perspective includes some assessment of how likely it is that the inherent hazard properties of the substance will actually cause adverse effects.

In addition to constituting an alternative to risk-based approaches, hazard-based approaches can also be pre-steps to risk assessments. The results from hazard-based approaches can then be used to prioritise substances to assess in subsequent risk assessments.

We here refer to hazard approaches by the term *screening risk assessments*. A general mathematical description of screening risk assessments is shown here:

$$f: \{p_1, \cdots, p_n\} \rightarrow S \qquad \text{(Eq. 3)}$$

Essentially, a screening risk assessment method is a function *f*. The input to that function is a set of basic hazard parameters p_1,…, p_n, or proxy risk measures as Berg and Scheringer (1994) would call them. The function then transforms the parameters and the chemicals to a scoring scale *S*. This is typically an ordinal scale, which means that the data is ranked, but the degree of difference between them is relative rather than absolute (Hubbard and Evans 2010; Stevens 1946). A scale from low, to medium, to high is a typical ordinal scale. The chemical substance's position on the scoring scale constitutes its ranking. The main differences between screening risk assessment methods are thus which hazard parameters are included, how the transformation to a scoring scale is conducted, and which scoring scale is used. In some cases, there are several scoring scales employed, such as an exposure scoring

[1] Note that the term *hazard* has, in fact, two slightly different meanings in the risk assessment field. One is indeed the inherent ability to cause risk, as opposed to the term *risk* itself. The other is a synonym for effects or toxicity. For example, the effect assessment part of a chemical risk assessment (Figure 1) can sometimes be referred to as *hazard assessment*. In several of the studies described in Section 4, it is this second meaning that is used. Unfortunately, both these meanings are established, and thus the reader must understand from the context, to which one is being referred.

scale and an effect scoring scale, without combining them into one final scoring scale. Risk acceptability can be determined based on such scoring scales, for example by saying that some parts of the scale *S* are acceptable, whereas others are not.

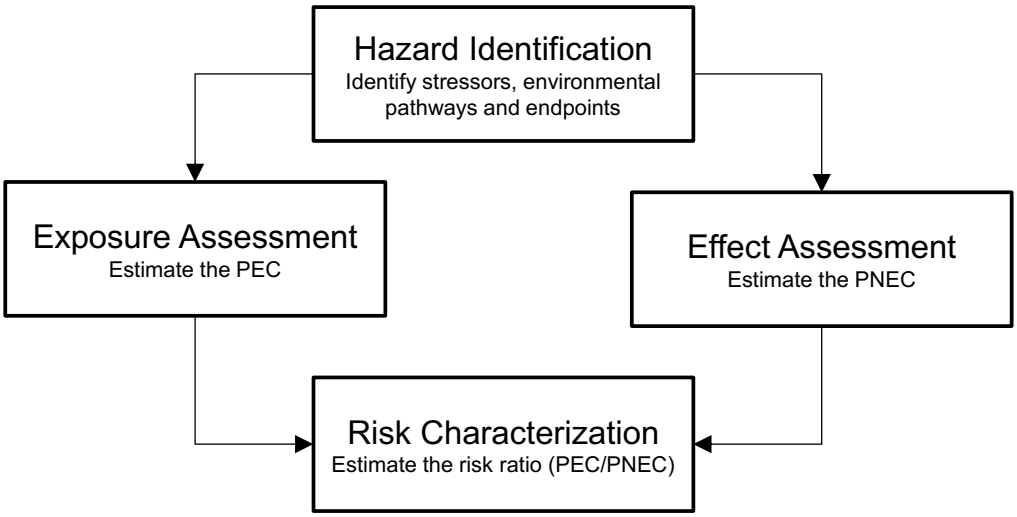

Figure 1. Graphical illustration of the risk assessment of chemicals framework. PEC stands for predicted environmental concentration, and PNEC stands for predicted no-effect concentration. Figure obtained with permission from Arvidsson (2012), and based on a similar figure by van Leeuwen and Vermeire (2007).

1.2 Nanomaterials and risk assessment

Nanomaterials can be defined as "an entity that is relevantly measured in nanometres in at least one of its dimensions or an entity that contains such entities" (Boholm and Arvidsson 2016). Sometimes, the size range is specified to be approximately within the 1-100 nm range (ISO 2008). Nanomaterials are increasingly produced and used in society (Peralta-Videa et al. 2011). According to the most comprehensive database on consumer products containing nanomaterials, there are currently more than 1600 products on the market, and the number has increased notably between 2006 and 2013 (Vance et al. 2015; Project on Emerging Nanotechnologies 2013). Examples of nanomaterials that are produced today include nanomaterials made from titanium dioxide, silver, iron and zinc oxide, as well as carbon nanotubes and graphene. Titanium dioxide nanomaterials are used in self-cleaning windows (Sanderson et al. 2003) and self-cleaning cement (Cassar et al. 2003) due to their photocatalytic properties, as well as in sunscreen to block and absorb ultraviolet light (Nohynek et al. 2007). Silver nanomaterials are primarily used for their antibacterial properties in consumer products (Luoma 2008; Wijnhoven et al. 2009). Iron nanoparticles can be used for soil remediation (Schmidt 2007). Zinc oxide nanoparticles are also used in sunscreen (González et al. 2008). Carbon nanotubes have potential uses in a number of products, including lithium ion batteries and synthetic textiles (Kohler et al. 2008). Graphene is beginning to be produced on a large scale with potential applications in composites and electronics (Segal 2009).

Most of these nanomaterials and their applications are currently in early product development, although some, such as titanium dioxide nanoparticles in sunscreen and silver nanoparticles for antibacterial purposes, have already become commercialised. Nano-sized silver in antibacterial applications has even existed commercially for more than 100 years (Nowack et al. 2011).

According to a recent review by Furberg et al. (2016), the current total global production of engineered nanomaterials is in the order of 300 thousand metric tonnes per year. The most produced of these nanomaterials are metal and metal oxide nanomaterials, including titanium dioxide, iron and iron oxide, aluminium oxide, silicon oxide and zinc oxide. In addition, about 10 million tonnes of the traditional but nano-sized material carbon black is produced each year (Furberg et al. 2016). Following the increase in production and use, the risks of nanomaterials have begun to be investigated. The dominating idea has been that nanomaterials could pose risks to humans and the environment in a similar manner as toxic chemicals (Scheringer 2008). Such risks of nanomaterials were first highlighted in scientific literature by Colvin (2003) and the Royal Society (2004), and later in a large number of studies. The high surface area of nanomaterials, which follows from their small size, and their unique surface properties, are two major hazardous properties often discussed in the literature (Christian et al. 2008; Handy et al. 2008; Nel et al. 2006; Ju-Nam and Lead 2008). Regarding exposure, studies have shown that nanomaterials can travel long distances, in a manner similar to traditional long-range pollutants (Praetorius et al. 2012).

In response to these concerns, a number of risk assessment studies of nanomaterials have been conducted, as reviewed by Arvidsson (2015), Arvidsson et al. (2013), Grieger et al. (2012a), and Gottschalk et al. (2013). After these reviews, additional risk assessment studies have been conducted and models have been developed, including the SimpleBox4nano model (Meesters et al. 2014) and the MendNano model (Liu and Cohen 2014). In general, these studies follow the principles and framework of chemical risk assessment as described in Figure 1.

Despite the number of risk assessment studies conducted, there has been considerable critique against this use of chemical risk assessment to assess nanomaterials. For example, Wiesner et al. (2009) commented on the risk assessment study by Gottschalk et al. (2009), writing that "[s]uch simple models are entirely appropriate for poorly characterized systems, but they offer limited guidance." An even more fundamental critique was formulated by Syberg and Hansen (2016), who argued that "since the quantification of risk is dominated by uncertainties, [chemical and ecological risk assessments] do not provide a transparent or an objective foundation for decision-making and they should therefore not be considered as a 'holy grail' for informing risk management [of chemicals and nanomaterials]." Along the same lines, Grieger et al. (2010) questioned the idea that chemical risk assessment can be applied for assessing risks related to nanomaterials within a foreseeable future. They write:

> "This analysis has shown that despite the recognized serious challenges that [nanomaterials] present for fulfilling traditional chemical-based risk assessment frameworks and the time this will likely take, the large majority of decision support research is directed to fit ultimately within this framework. Decision makers, therefore, may not be well equipped to make decisions concerning [nanomaterials] under conditions of extensive uncertainty in relation to environmental and human health protection in the near term. It is clear, in our view, that there is a need for a program of research and knowledge transfer specifically aimed at supporting near- and medium-term decision making, in real time and at the same pace as nano-innovation itself."

These concerns are essentially the same as those described for chemical substances in Section 1.1. Nature is regarded as overly complex, so consequently the cause-effect chains between uses of nanomaterials in society and subsequent risks to organisms are not possible to model quantitatively. Indeed, it is commonly acknowledged that both exposure assessment (Arvidsson et al. 2011; Abbott and Maynard 2010) and effect assessment (Dhawan et al. 2009; Maynard et al. 2011) of nanomaterials have proven to be challenging. These challenges mean that the development of chemical risk assessment methods adapted to nanomaterials will probably be costly and time-consuming (Grieger et al. 2012b).

As a potential alternative to applying the chemical risk assessment method in some modified form to assess risks related to nanomaterials, using some form of simplified risk assessment method has been proposed (Maynard 2007; Beaudrie and Kandlikar 2011; Grieger et al. 2012b). Considering that adequate risk assessment methods for nanomaterials – if at all possible – would take long time to develop, Grieger et al. (2010) suggested that the main benefit with such simplified risk assessment methods would be that they can be developed and applied within a relatively short time. The rapid increase in the production and consumption of nanomaterials does indeed make methods that can be applied with little time delay for assessing risks of nanomaterials highly warranted. In addition to constituting an alternative to chemical risk assessment, simplified risk assessments could also be a pre-step conducted for the prioritisation of nanomaterials to study in detailed risk assessments. Such simplified risk assessment methods go by different names (see further Section 2), but they are here referred to by the generic term *screening risk assessment methods*. It is such methods, and particularly their application to nanomaterials, that are the focus of this study.

1.3 Aim and scope of the study

The aim of this study is to investigate existing screening risk assessment methods for nanomaterials and provide recommendations on their further development. In order to fulfil this aim, a background section regarding some general and often-used screening risk assessment approaches is first provided. Second,

screening risk assessment methods developed specifically for nanomaterials are reviewed. Third, recommendations for developments of screening risk assessment methods for nanomaterials are provided in a concluding discussion. The review is intended to be inclusive, and consequently contains all identified publications where some kind of screening risk assessment method for nanomaterials is presented.

2 Background

As background, three common variants of screening risk assessment methods will be described in more detail in this section. The first is *risk ranking*, the second is *chemical ranking and scoring*, and the third is *control banding*. These approaches share many features, and all adhere to the generic Eq. 3. However, which hazard parameters are typically included, and how their scoring and ranking is conducted, differs between the three approaches. They are also typically employed in different domains. Risk ranking is the broadest of the approaches, and is not limited to assessing chemical substances (nor nanomaterials). It is a subjective approach for estimating risk, and often includes probability and consequence as the only hazard parameters. In contrast, chemical ranking and scoring methods often rely on complex systems of equations, and contain several hazard parameters related to chemical properties. Control banding can be said to be a variant of chemical ranking and scoring, but is specifically applied to manage occupational chemical risks to workers. All three approaches are general, and many specific methods exist within these broad groups. Here, we provide general descriptions of the approaches, and descriptions of some specific methods are given as examples.

2.1 Risk ranking

Risk ranking is one of the most common ways to assess risk, which is probably primarily due to its simplicity (Burgman 2005). Its uses stretch far beyond the areas of chemicals and nanomaterials, and into engineering, mining, land use, and industry. The risks assessed can be related to such varying events as nuclear power and aerospace accidents. In contrast to chemical risk assessment, risk ranking is often principally based on expert judgment (Baybutt 2015a). Estimates are often qualitative rather than quantitative.

In a proposal of a framework for risk ranking, Burgman (2005) suggested a five-step approach. In the first step, the procedure of the risk ranking is decided upon. This involves the selection of relevant experts, on whose judgement the risk ranking rests. Second, events to be assessed are identified. Third, each event is assessed. In the fourth step of the risk ranking, the now-assessed risks are compared to criteria for acceptable levels, and a prioritisation between different risks is conducted. Fifth, selected risks are managed.

Focusing on the third step of event assessment, and referring to Eq. 3, there are typically two hazard parameters that are employed in risk rankings (Baybutt 2015a). The first is *probability* or *likelihood* of an adverse event. This parameter shows the likelihood of the event occurring – for example, how likely a nuclear power plant accident is. It often follows an ordinal scale from unlikely and occasional, via likely, to frequent. It can also be assigned numerical values, for example from 1 to 5. The second parameter is *consequence*, which depicts the consequences of the event in terms of monetary value or other units. Note that sometimes roughly synonymous

terms, such as *severity*, are used instead. This parameter also often follows an ordinal scale, from negligible and marginal, over critical, to catastrophic. It too can be assigned numbers, such as 1 to 5. The risk of an event is then assessed based on both its probability and its consequences, for example by multiplying the two parameters if they have been assigned numerical values.

Important outputs from risk rankings are *risk matrices* (Burgman 2005; Baybutt 2015b, 2015a). Figure 2 provides an illustration of such a risk matrix. It is often a two-dimensional space, with probability and consequence as the two dimensions or axes. Some examples of risks are included in Figure 2 as illustrations.

An example of a risk ranking study in an environmental risk context is the study by Hammar et al. (2014) about risks to cod from off-shore wind power. Different potential causes of harm from the wind power to the cod were identified and scored. The scoring was conducted based on available data, using two main parameters. The first was likelihood of effects, which was scored from 0 to 3. The second was magnitude of effects, which was also scored from 0 to 3. A final risk score was then calculated by multiplying these two parameters, and was presented in a risk matrix. The highest score of 9 was obtained for spawning cod when exposed to extreme noise from pile driving during the construction of the wind power plants. The main recommendation from the study was therefore to avoid pile driving during the spawning period of the cod.

A problem with risk ranking is its subjectivity (Burgman 2005; Cox 2008). This includes preconceptions about the risks to be assessed, and different linguistic understandings. For example, people may have different ideas of the exact meaning of words such as ‘likely’ and ‘catastrophic.’ Unfortunately, such factors are often implicit and hidden in the risk ranking. Another problem is that it is assumed that all events are discrete (Burgman 2005). This means that they either occur, or do not occur. However, in many cases, events can be more gradual – exposure to chemical substances is an example of this. Yet another problem is range compression in cases where order-of-magnitude ranges are transformed into an ordinal scale, such as one going from 1 to 5. Levine (2012) suggested that using logarithmic scoring scales for probability and consequence would reduce this problem.

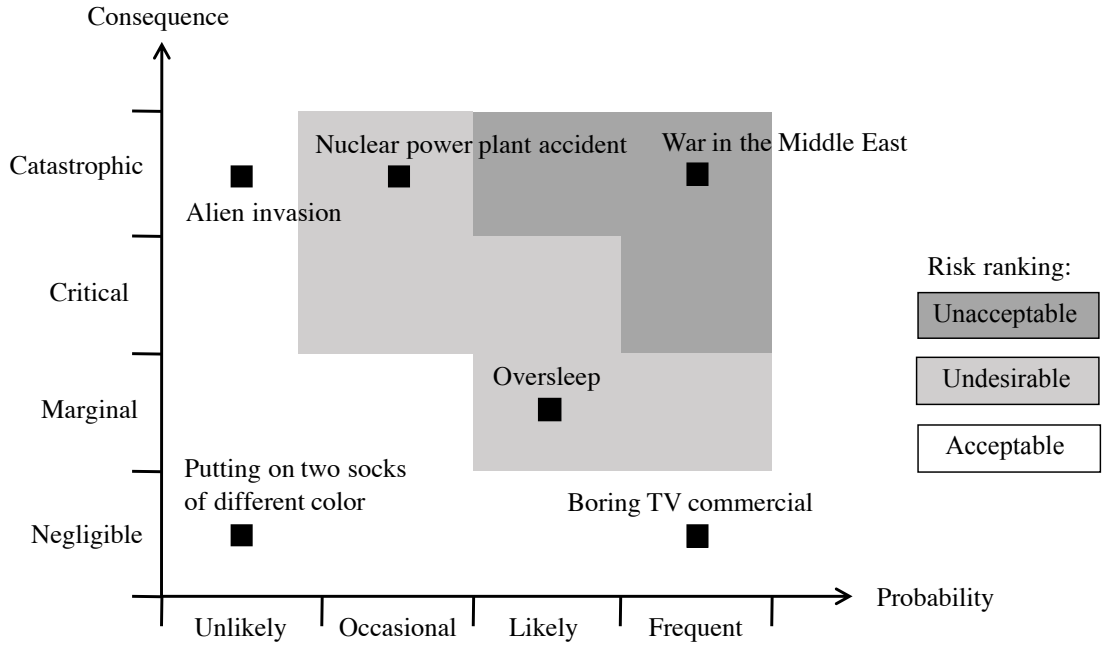

Figure 2. Illustration of a risk matrix, with probability and consequence on the axes. Some risks are added as examples, and their likelihood and consequence are estimated. Note that the estimations are meant as illustrations only, and may not reflect reality or all people's views, not even those of the authors.

2.2 Chemical ranking and scoring

Chemical ranking and scoring methods are often motivated by the need for less complex risk assessment methods for chemicals (Swanson and Socha 1997). The result of a chemical ranking and scoring is not an absolute risk in terms of, for example, the extent that organisms will become harmed by the substance. Rather, the results are a relative ranking and allow for prioritisation between substances. They can thus be utilised as pre-steps to chemical risk assessment, so that chemical risk assessments can, in turn, be focused on the substances that were highly ranked in the chemical ranking and scoring. Chemical ranking and scoring methods can be very simple categorisations based on expert judgment, in a similar manner to risk ranking (Section 2.1). They can also be conducted in a much more elaborate way, using complex algorithms that sometimes rival chemical risk assessments in terms of complexity. According to Swanson and Socha (1997), chemical ranking and scoring methods have the following features:

- They are not quantitative risk assessments, but can be part of the risk assessment paradigm (in the sense that both exposure- and effect-related properties can be included).
- There is no single chemical ranking and scoring method that is suitable for all applications.

- They are particularly useful if resources are too limited for a chemical risk assessment.

Swanson and Socha (1997) further outline a generic framework for chemical ranking and scoring, including four phases. The first phase is the *goal definition and scoping*. In this phase, the goal of the chemical ranking and scoring method is set based on which decisions the method's results will guide. The second phase is *indicator selection*, where the parameters that will be evaluated are determined (corresponding to the hazard parameters in Eq. 3). Chemical ranking and scoring methods can include numerous hazard parameters related to toxicity, persistence, production, use, and emission of chemicals (Swanson and Socha 1997; IEH 2004). This step thus also determines which data needs to be gathered. The third phase is *ranking and scoring*, during which chemicals are sorted into ordinal scales and groups based on the hazard parameters defined in the second step of the chemical ranking and scoring framework described above. Such groups could be *toxic*, *very toxic*, and *persistent, bioaccumulating, and toxic (PBT)*. The algorithms in chemical ranking and scoring can be of various types, but are often of the if-then type. For example, *if* the toxicity exceeds 1 mg/l, *then* the substance is regarded as toxic. Chemical ranking and scoring methods can also employ ordinal scoring scales with numbers, such as scales from 1 to 5. The fourth and final phase is the *output and presentation*, where results are reported in an appropriate form for the respective decision-making situation. A similar but more detailed framework was provided by the IEH (2004).

Rather than calculating a PEC as in chemical risk assessment, chemical ranking and scoring methods typically make use of different parameters as proxy measures for exposure (Swanson and Socha 1997; IEH 2004). Such parameters could be related to chemical use and emissions, for example annual production, annual use, annual disposal, and, if available, annual emissions. Different parameters that influence the fate of the chemicals in the environment can also be used as proxy measures. Examples of such parameters include molecular weight, water solubility, vapour pressure, and leaching potential. Human health effects can be ranked by toxicological parameters related to lethality, such as the dose at which half of the population would die (LD_{50}) (IEH 2004; Swanson and Socha 1997). Ecological effects are typically indicated by parameters based on ecotoxicological testing (Swanson and Socha 1997). These include the substance concentration at which half of the population would die (LC_{50}), the concentration at which half of the population would show an effect (EC_{50}), and the concentration at which no individual in the population would show an effect (no-effect concentration [NOEC]). Additional risk-related chemical properties, such as flammability and explosivity, can also be used in chemical ranking and scoring (Swanson and Socha 1997).

One example of a chemical ranking and scoring method is the European Union Risk Ranking Method (EURAM) described by Hansen et al. (1999). The method was developed to enable prioritisation between chemicals used in the European Union. The outputs of this method are an environmental score, an aquatic score, and a human

health score. All these scores range from 0 to 100 on an ordinal scale. Inputs to this model include numerous parameters linked to emissions, fate, exposure, and effects to humans and other organisms.

Although many chemical ranking and scoring systems are complex, simpler variants also exist. An example of this is a risk ranking and scoring method for pesticides from celery intake in China (Fang et al. 2015). The parameters used in the ranking included toxicity of the pesticide (denoted *A*), potency of the pesticide (*B*), proportion of celery in diet (*C*), frequency of pesticide application during planting (*D*), number of highly exposed people (*E*), and measured pesticide residue levels (*F*). The parameters were scored on an ordinal scale from 2 to 5, 0 to 3, or 1 to 4 based on both quantitative and qualitative data. A final risk score was then calculated using a relatively simple equation:

$$S = (A + B) \cdot (C + D + E) \cdot F \qquad \text{(Eq. 4)}$$

Compared to the general Eq. 3, the scoring function *f* of the celery study includes first the transformation of quantitative and qualitative data to the scores, and then the calculation of the final risk score according to Eq. 4. The considered hazard parameters are A-F.

2.3 Control banding

The history and evolution of control banding is described by Zalk and Nelson (2008) and NIOSH (2009). The aim of the approach is to control occupational exposure to hazardous chemicals. It was originally developed within the pharmaceutical industry, but has since become more widely used to control exposure in other industries as well (NIOSH 2009). Similar to risk ranking and chemical ranking and scoring, it is a qualitative method intended to be simple and understandable for users. According to Zalk and Nelson (2008), control banding has its roots in other screening risk assessment approaches, such as the risk matrices obtained from risk ranking (Figure 2). In contrast to these methods, control banding is exclusively focused on occupational health risks, and does not include environmental risks. It is particularly useful for assessments of substances for which established occupational exposure limits do not yet exist, which includes most chemical substances (NIOSH 2009).

The term *band* in control banding is to be understood as a category of relevance to risk. Based on different risk and hazard phrases, a substance can be categorised into a certain hazard-related band. In addition, based on exposure-related properties, such as volatility and dustiness, a substance can be categorised into exposure-related bands. The quantity in use can also be employed to categorise substances into exposure bands. Referring again to Eq. 3, there are typically two

ordinal scoring scales in control banding: Hazard and exposure. However, they can also be called severity and likelihood, in a way more similar to that of risk ranking.

The term *control* in control banding refers to the control of the occupational risk after categorisation into bands. Control approaches could be, for example, ventilation and good working practices. The type of control to be used is determined by the banding.

The most widely used control banding method is the Control of Substances Hazardous to Health Essentials (COSHH), developed by the United Kingdom's Health and Safety Executive (Zalk and Nelson 2008). It contains a number of hazard groups into which substances are categorised based on properties such as risk phrases, dustiness, and volatility (Brooke 1998; Garrod and Rajan-Sithamparanadarajah 2003). Comparing to Eq. 3, the risk phrases, dustiness, and volatility are thus examples of hazard parameters employed in control banding, and the hazard groups are different points on an ordinal scoring scale *S*.

3 Method

In order to identify screening risk assessment methods for nanomaterials, a number of different search terms were thus used in the scientific literature database Scopus (2016), such as ("risk ranking" AND nanomaterial*) and ("control banding" AND nanomaterial*). The reference lists of identified publications containing relevant methods were checked for additional relevant publications in a backward snowballing manner (Wohlin 2014). In addition, previous reviews were consulted (Brouwer 2012; Fleury et al. 2013; Erbis et al. In press; Grieger et al. 2012b; Hristozov et al. In press), and the relevant methods included in these reviews were also included here. Both scientific papers and reports were considered, and in one case a handbook found on a web page describing the method was also incorporated. Multi-criteria decision analysis methods for nanomaterials (Linkov et al. 2007) were not included. In total, 20 screening risk assessment methods were identified.

The review is based on a slightly modified variant of Eq. 3:

$$f_{nano}: \{p_1, \cdots, p_n\} \rightarrow S \qquad \text{(Eq. 5)}$$

In Eq. 5, f_{nano} is the function in a screening risk assessment method for nanomaterials. S is a scoring scale and p_1, …, p_n are hazard input parameters (same as in Eq. 3). In the review, the following questions, of which most are related to Eq. 5, will be answered:

- Which types of risk are assessed in the method – occupational, human health, and/or environmental risks?
- Which are the assessment objects (e.g. nanomaterials and/or nanoparticles) considered in the methods?
- Which scoring scales (i.e. S) are used to present the results of the methods?
- How is the function (i.e. f) transforming the hazard input parameters to the scoring scale formulated?
- Which hazard input parameters (i.e. p_1, …, p_n) are included in the methods?

Each method identified is described with regards to these questions in a separate section below. They are also listed in Table 1, where a summary of the results is provided. Note that the specific terminology in the reviewed methods may differ from the more general one presented here. For example, scoring scales are often referred to as bands in the reviewed control banding methods, and the hazard parameters are called criteria in one method.

4 Results

4.1 ANSES

The method described in the paper by Riediker et al. (2012) is referred to as a control banding tool for nanomaterials. Since it was developed as a commission by the French Agency for Food, Environmental and Occupational Health Safety, called ANSES (*Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*), it has been referred to by this name in previous reviews (Brouwer 2012; Fleury et al. 2013). The method was also presented in an earlier report by ANSES (2010). Focusing on occupational risks, the method is developed to assess nanomaterials in order to provide producers and users with information for risk management. The assessment object is nanomaterials.

The ordinal scoring scale used is called control bands (CB), and is based on two ordinal sub-scales. The first sub-scale is a hazard band, which contains the following categories:

- HB1: very low, no significant risk to health,
- HB2: Low, slightly toxic effects rarely requiring medical follow-up,
- HB3: moderate to significant health effects requiring specific medical follow-up,
- HB4: high, unknown health effects or serious hazard,
- HB5: very high, severe hazard requiring a full hazard assessment by an expert.

The hazard band is determined based on the procedure described in Figure 3, which also shows which hazard parameters are included. As can be seen there, most hazard parameters are based on the corresponding bulk material or some other analogous material, and not on the specific nanomaterial itself.

The second sub-scale is an emission potential band, which has the following categories: EP1, EP2, EP3, and EP4. The category is determined based on the physical properties of the nanomaterial. Solid has EP1, liquid EP2, powder EP3, and aerosol EP4. However, different specific conditions can increase the emission potential band. If a solid is friable, it gets +2 in emission potential band, meaning for example that the emission potential band could increase from EP1 to EP3. If it generates dust by external forces, it gets +3. If it melts, it gets +1. If it is dispersed in a liquid, it gets +1. If a liquid has a high volatility, it gets +1. If it generates powder by evaporation, it gets +1. If it is sprayed, it gets +2. If a powder has high or moderate dustiness, it gets +1. If it is sprayed, it gets +1. These conditions are thus also hazard parameters in this method, together with the physical form of the nanomaterial.

The hazard band and emission potential band are then combined as two axes in a risk matrix. The results of these combinations are different control bands, ranging from CB1 (lowest risk) to CB5 (highest risk). These control bands, in turn, imply different control measures, from ventilation to seeking expert advice.

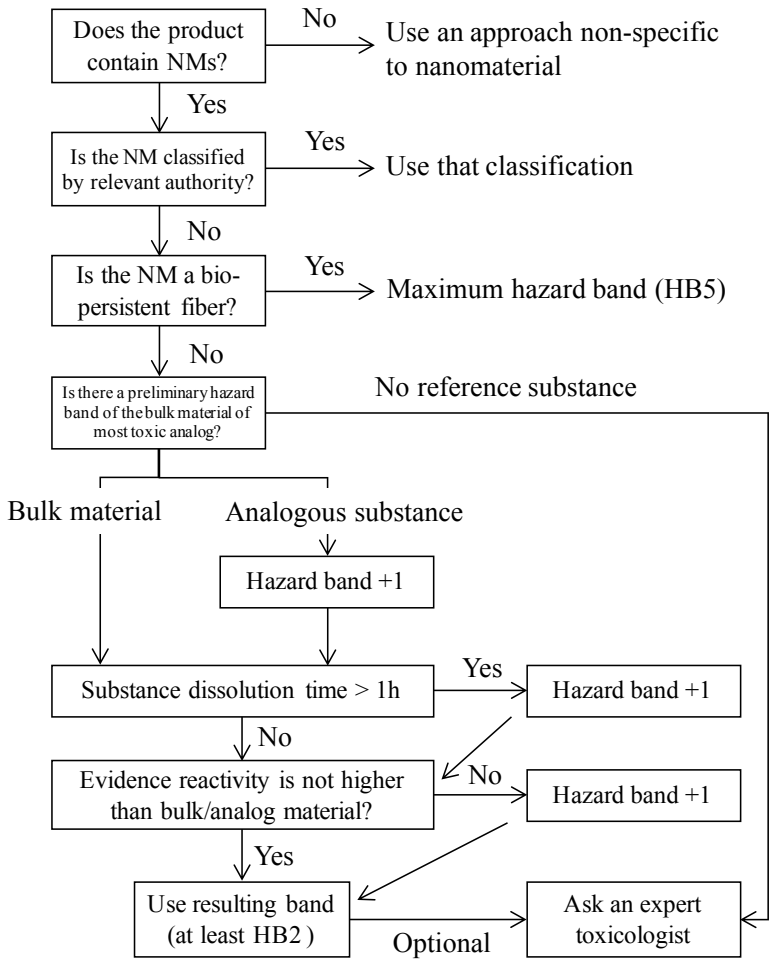

Figure 3. Procedure to derive hazard bands (HB) in the ANSES method (Riediker et al. 2012). NM stands for nanomaterial.

4.2 CB Nanotool 2.0

The CB Nanotool was first developed by Paik et al. (2008), and then a second version of the method was developed by Zalk et al. (2009). It is this second version of the method that is described here. There is also a web page dedicated to the second version of the method (CB Nanotool 2.0 2016), and the second version of the method has been further refined in order to account for uncertainties by Monte Carlo simulation (Bates et al. 2015). The CB Nanotool 2.0 method has also been used as the main part of the Nanomaterial Occupational Exposure Management (NOEM) model developed by Juric et al. (2015). As indicated by the abbreviation CB in the name, this method is a control banding-type method. It is designed to assess occupational risks related to nanoparticles, which are thus its assessment objects.

The result of the CB Nanotool 2.0 method is an ordinal scale called risk levels, which contains the categories RL1, RL2, RL3, and RL4. This scale is, in turn, a combination of two other ordinal scales: Severity score and probability score. Both these sub-scales are assessed from 0 to 100, and are divided into four equally large

categories. For severity, the categories are low (0-25), medium (26-50), high (51-75), and very high (76-100). For probability, the categories are extremely unlikely (0-15), less likely (26-50), likely (51-75), and probable (76-100). The combination of severity and probability into risk levels is conducted in a typical risk-matrix fashion. For example, the highest scores on the severity and probability scoring scales are combined into RL4.

The severity score depends on the following hazard parameters of the nanomaterials: Surface activity, particle shape, particle diameter, solubility, carcinogenicity, reproductive toxicity, mutagenicity, and dermal toxicity. In addition, the same parameters for the corresponding particulate matter of the same chemical substance (not necessarily of nano-size) are considered. Occupational exposure levels for particles of the same chemical substance as the nanomaterial are also considered. The probability score depends on the following hazard parameters: Amount of nanomaterials used in operation, number of employees experiencing exposure, and frequency of operation. Each of these hazard parameters receive different scores, adding to the final score between 0 and 100 for the severity and probability scales.

4.3 Early warning signs

In a paper by Foss Hansen et al. (2013b), they provide five criteria that should serve as early warning signs for human health and environmental risks related to nanomaterials. Although this method is not described as a risk ranking, chemical ranking and scoring, or control banding method, the authors note that the warning signs "may be used to screen nanomaterials for human health and environmental risks." It can thus be seen as a screening risk assessment method, with nanomaterials as the assessment objects. The warning signs are developed from two reports by the European Environment Agency, which show how early warnings related to environmental and human health risks have historically often been neglected (Harremoës et al. 2001; Gee et al. 2013). Examples include substances such as dichlorodiphenyltrichloroethane (DDT), asbestos, tributyl tin, and polychlorinated biphenyls (PCB).

The suggested warning signs are: Novelty, persistence, readily dispersed in the environment, bioaccumulation, and potentially irreversible action. These are thus the hazard parameters of the method. For each of the parameters, it is decided based on available scientific data whether it is *yes* or *no* for the respective nanomaterial. The scoring scale is thus a binary 0-or-1-type scale. There is no calculation of a final risk score or ranking, but it is clear that the more *yeses* a nanomaterial gets, the more severe is the warning.

The authors assess five specific nanomaterials in their study: Carbon nanotubes, titanium dioxide, nano-sized zero-valent iron, liposomes, and poly(lactic-co-glycolic acid). It is clear from the study that it is not a trivial matter to conduct the assessment in practice. In some cases, the assessment result is "yes/no", and the

authors then explain that the categorisation depends on some factors. In some other cases, the assessment result is "unknown", and the authors then explain that this is due to lack of information.

4.4 Genaidy's method

The method developed by Genaidy et al. (2009) has no particular name, and is therefore here referred to as Genaidy's method after the first author. It is developed as a low-cost tool to protect workers from occupational health hazards, specifically during the production of carbon nanofibers. Carbon nanofiber production is thus the assessment object.

In the first step of the method, the probability and severity of exposure during production are assessed. Note that it is not only exposure to the carbon nanofiber that is considered, but to also to chemicals used in the production. Probability is scored on an ordinal scale going from frequent, probable, occasional, and remote, to improbable. Severity is also scored on an ordinal scale, going from catastrophic, critical, and marginal, to negligible. In the second step, these results are then combined in a classical risk matrix, which has five coloured fields: Very high risk (red), high risk (orange), moderate risk (yellow), low risk (blue), and very low risk (green). The colours are also assigned numerical values, with red corresponding to 1, orange to 2, yellow to 3, blue to 4, and green to 5. In the third step, these five categories are transformed into three categories: Lower than 3 (red and orange), equal to 3 (yellow), and higher than 3 (blue and green). For results lower than 3, high-priority short-term improvements in the production safety are recommended. For results equal to 3, medium-priority short-term improvements are recommended. For results higher than 3, only long-term improvements are recommended.

The scoring in this method is based on observations and interviews with workers and management personnel, and was applied at a carbon nanofiber manufacturing enterprise in the United States. The scoring of the different chemicals used in that production were between 1 (for polycyclic aromatic hydrocarbons, bulk carbon nanofibers, and airborne carbon nanofibers) and 3 (for methane, ammonia, and propanol).

4.5 Groso's method

In the review by Fleury et al. (2013), the method by Groso et al. (2010) is referred to as Groso's method after the first author, and the same name is also used here. The method is presented as a user-friendly and practical procedure to be used at universities and in other laboratory environments where nanomaterials are handled. The method is presented as being similar to control banding, so the focus is on occupational human health effects. The assessment objects in Groso's method are nano laboratories.

Nano laboratories are classified into three hazard bands, called Nano 1, Nano 2, and Nano 3. Nano 1 means the lowest hazard, and Nano 3 the highest. The categorisation of laboratories into the hazard bands is conducted via a decision tree model (Figure 4). Hazard parameters required are shown in the model. As can be seen, the physical form of the nanoparticle and its medium are in focus. Based on the hazard band, suggestions are provided regarding organisational, technical, and personal safety measures.

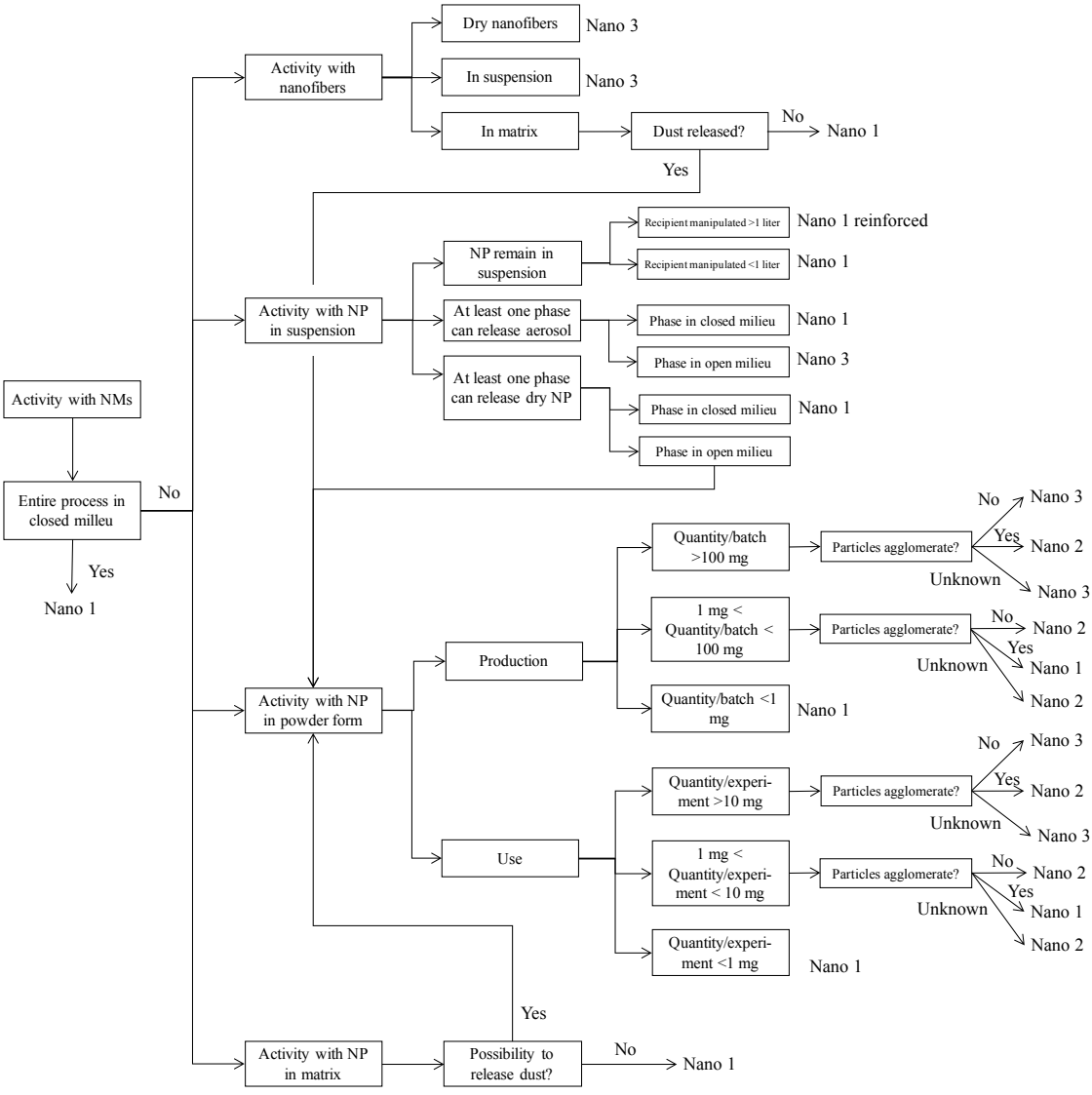

Figure 4. Procedure to derive hazard bands with Groso's method (Groso et al. 2010). NM stands for nanomaterials and NP for nanoparticles.

4.6 Guidance

The method presented in the report *Guidance Working Safely with Nanomaterials and Nanoproducts* by Cornelissen et al. (2011) was referred to as

Guidance in an earlier review (Brouwer 2012), so this name is also used here. It is intended to be a guide on how to establish a safe workplace when dealing with nanomaterials and nanoproducts, so these are thus the assessment objects of this method.

The Guidance method contains a step-wise procedure. The first step is to make an inventory of all nanomaterials and nanoproducts used by a company. In the second step, the nanomaterials and nanoproducts are classified by hazard on an ordinal scoring scale from 1 to 3, where 3 means the highest hazard. Water-soluble nanoparticles are assigned hazard class 1 (e.g. lipids), synthetic and persistent nanomaterials are assigned hazard class 2 (e.g. silver nanoparticles), and fibrous non-soluble nanomaterials are assigned hazard class 3 (e.g. carbon nanotubes). The chemical and physical composition of the nanomaterial and nanoproduct are thus required as hazard input parameters in this method. The third step contains the listing of all activities involving nanomaterials and nanoproducts in the company, along with used and emitted amounts, and the number of workers exposed. In step four, the exposure is classified on an ordinal scoring scale from 1 to 3. If there are no emissions of free particles, the exposure category is 1. If there are possible emissions of nanoparticles embedded in solid matrices, the exposure class is 2. If there are possible emissions of free nanoparticles, the exposure class is 3. The hazard input parameter for the exposure class is thus the possibility of nanoparticles becoming emitted.

In the fifth step of the procedure, using a typical risk matrix, the hazard band and the exposure category are combined into an ordinal control level scoring scale. Control levels range from A to C, where C is the worst (i.e. requires more risk reduction measures). Recommended risk reduction measures are also provided in this step, and the sixth step concerns selecting and implementing these measures. Step seven involves keeping a record of all workers dealing with nanomaterials, and step eight relates to conducting preventive medical surveillances.

4.7 Hierarchical Rank Aggregation

In the study by Patel et al. (2013), a method for hierarchical rank aggregation of nanomaterials is presented. Nanomaterials are thus the assessment objects. The ranking is based on their toxicity. The toxicity data, which are the hazard parameters considered in this method, are obtained from high throughput screening studies, which means that a large number of human cell samples are exposed to nanomaterials of different doses and for different time durations. The way in which the toxicity depends on the dose and duration can then be established. Mathematical algorithms are then applied to structure the data and rank nanomaterials relative to one another. One part of the algorithm is that different weights can be given to different cytotoxicity responses. The result is expressed as an ordinal scoring scale from 1 to 8. The method was applied for the following nanomaterials in the study: Quantum dots, zinc oxide, iron oxide, silica, aluminium oxide, gold, platinum, and silver. It was

shown that the scoring and relative ranking of these nanomaterials depended on the weight given to different cytotoxicity responses. Overall, platinum, silica, and silver were often ranked highly. This ranking can be used for prioritisation of nanomaterials for further testing.

4.8 LICARA nanoSCAN

The LICARA nanoSCAN is a tool specifically developed for small and medium-sized companies to evaluate nanoproducts (van Harmelen et al. 2016). In addition to assessing risks in a screening risk assessment fashion, the method can also be used for assessing benefits related to the nanoproducts. Three types of risks are assessed: Public health and environmental risks, occupational health risks, and consumer health risks. The result is presented on a scale from 0 to 1 for each of the three risks. These assessments are aided by the application of previously developed screening risk assessment methods. The consumer health risks are assessed using the NanoRiskCat method (Foss Hansen et al. 2013a), see further Section 4.12. The occupational health risks are assessed using the Stoffenmanager Nano method (van Duuren-Stuurman et al. 2012), see further Section 4.18. The public health and environmental risks are assessed using the Precautionary Matrix (Höck et al. 2008), see further Section 4.15. These methods are modified somewhat to fit into a common method, for example adapted to the 0-1 scale used in the LICARA nanoSCAN method.

In addition to these three risks, environmental, economic, and societal benefits are also assessed. However, since the aim of this report is to review screening risk assessment methods, these parts of the LICARA nanoSCAN method are not discussed here.

4.9 Nano-Evaluris

The Nano-Evaluris method was developed by Bouillard and Vignes (2014) in order to assess risks related to the use of nanopowders. Nanpowders are thus the assessment objects of this method. The focus is on human health in an occupational safety setting. The method is thus close to contemporary control banding methods, although the authors use the term risk ranking to describe their method. Two types of risk are considered: Inhalation and explosion.

The inhalation severity index (I_s) is calculated based on the concentration of nanoparticles in the air (OHB), emissions of nanoparticles from processes (I_{proe}), and the collective (I_{protc}) and personal (I_{proti}) protection:

$$I_s = OHB + I_{proe} - I_{protc} - I_{proti} \qquad \text{(Eq. 6)}$$

The severity is considered acceptable if the severity index is zero or negative. The *OHB* is an ordinal scale from 0 to 7, where the scoring depends on the particle concentration in air measured as μg/m^3. The I_{proe} depends on the process equipment, quantity of powder used, and the percentage of nanoparticles present in the powder that can be released to air. The I_{proti} is calculated based on percent particle penetration for the protection gear. For 10-20% penetration, the index is <1. For 1-10%, it is <2. For 0.01-0.1% penetration, it is 3. The I_{protc} is calculated similarly by considering the percent reduction in particle concentration due to collective protection.

In addition, the frequency of inhalation is considered in terms of a frequency index I_f. The value of the frequency index depends on the duration of exposure. If it is less than 5 minutes, the frequency index is -2. If the duration is 5-45 minutes, the frequency index is -1. If the duration is 45 minutes to 8 hours, the frequency index is 0. The severity and frequency indices are combined into a risk index I_r:

$$I_r = I_s + I_f \qquad \text{(Eq. 7)}$$

The risk of inhalation is acceptable if the risk index is zero or negative.

The assessment of explosion is not described in the same detail, but it is clarified that it is based on four factors: (1) Severity, (2) probability, (3) vulnerability, and (4) risk reduction barriers. Severity is assessed as the product of the quantity of the nanopowder and the explosion violence index. Quantity is assessed based on mass of the nanopowder used, which is transformed into an ordinal scale from 1 to 5. The explosion violence index is also measured on an ordinal scale, but this scale goes from 0 to 7, or sometimes higher. The hazard input parameter used to determine explosion violence index is the explosion violence parameter, measured in bar·m/s. Probability is assessed as the product of the occurrence of the formation of an explosive atmosphere (ordinal scale from 0 to 3) and the frequency of the presence of an ignition source (ordinal scale from 0 to 5). Vulnerability is modelled simply as a yes/no parameter. *Yes* means that workers are present, and *no* means that workers are not present. This is transformed to an ordinal scale, with yes corresponding to 1 and no corresponding to 0. Risk reduction barriers are assessed on an ordinal scale from 1 to 4, where 1 means inefficient reduction barriers, and 4 means a high level of efficiency.

4.10NanoHAZ

The NanoHAZ method is developed by O'Brien and Cummins (2010) for ranking nanomaterials with respect to their human and environmental risks. Nanomaterials are thus the assessment objects. The method is clearly inspired by chemical risk assessment (Eq. 1 and 2), and considers both toxicity and exposure in terms of a ratio. Four different types of risk are assessed: Environmental risk,

regulatory risk, ecotoxicological risk, and human health (i.e. toxicological) risk. The calculation of the final risk score is conducted by the following equation for all four types:

$$R = F \cdot \frac{\log_{10} C}{\log_{10} S} \qquad \text{(Eq. 8)}$$

In Eq. 8, *R* is the final risk score for each of the four considered risks. *C* is a term that describes exposure. This can be environmental concentration, human ingestion, or human inhalation, depending on which risk is considered. *S* is a term that describes toxicity. It can be an environmental limit, a provisional regulatory limit, an ecotoxicological limit, or a toxicological limit, depending on which risk is considered. *F* is a scaling factor, which is set to 5. Since the ratio of the logarithms in Eq. 8 will be 1 if the logarithms in the nominator and denominator are equal, the scaling factor makes 5 the benchmark value that tells whether there is risk or not. Since 5 is the benchmark, values between 0 and 4 mean low risk (i.e. exposure is below the limit), whereas values higher than 5 mean high risk (i.e. exposure is above the limit).

Hazard input data to exposure (i.e. *C* in Eq. 8) is obtained from numerous estimations of environmental concentrations and human intake of nanomaterials, including those by the same authors (O'Brien and Cummins 2011). Hazard input data for limits (i.e. *S* in Eq. 8) are obtained by consulting regulatory guidelines and the scientific literature on toxicity and ecotoxicity of nanomaterials. Three nanomaterials for which this data is available were assessed by the authors: Titanium dioxide, silver, and cerium dioxide. The assessment was conducted based on different environmental concentration data, and for different organisms (fish, invertebrates, and bacteria), showing different results for these different scenarios.

4.11NANoREG

In the NANoREG project funded by the European Commission, an approach for risk assessment of nanomaterials was developed (Dekkers et al. 2016). This approach is extensive, and includes three main phases: Phase I, phase II and phase III. These phases represent different levels of detail in the assessment. Phase I involves a screening and prioritisation, and thus qualifies as a screening risk assessment. Phase II and III aim to identify the most important information needed for further assessments and to allow grouping based on physiochemical properties. The assessment objects are nanomaterials, and the focus is on occupational and other human health risks.

In phase I, nanomaterials are assigned either a red, orange or green flag, with red being the most hazardous and green the least. The orange flag is then further divided into high, medium or low potential to cause harmful effects. This subdivision of the orange hazard flag level is because the authors of the approach expect this level

to contain the most nanomaterials. The orange flag signals that the nanomaterial needs further investigations. Only the orange-flagged nanomaterial will enter phase II and III of the NANoREG approach.

The general procedure of phase I is shown in Figure 5. Input data needed for this step are size, surface area, aspect ratio, rigidity, biopersistance, dissolution rate, reactivity, whether the nanomaterial is free or fixed in a matrix, production volumes, possible applications, and exposure scenarios across the applications' life cycles. First of all, the approach starts with identifying whether or not the material is in fact a nanomaterial. The determination of high, medium or low level for the orange flag is done in a classic risk ranking fashion. First, occupational exposure is ranked from high, over medium, to low, based on process and operational conditions and on production volumes. Second, consumer exposure is ranked from high, through medium, to low, based on production volumes and whether the nanomaterial is free or fixed in a matrix. Third, the hazard is ranked from high, through medium, to low, based on the reactivity and hazard classification of the non-nanomaterial or similar nanomaterials. Hazard and exposure is than combined for occupational and consumer risks separately, forming two nine-field matrices ranging from high, through medium, to low.

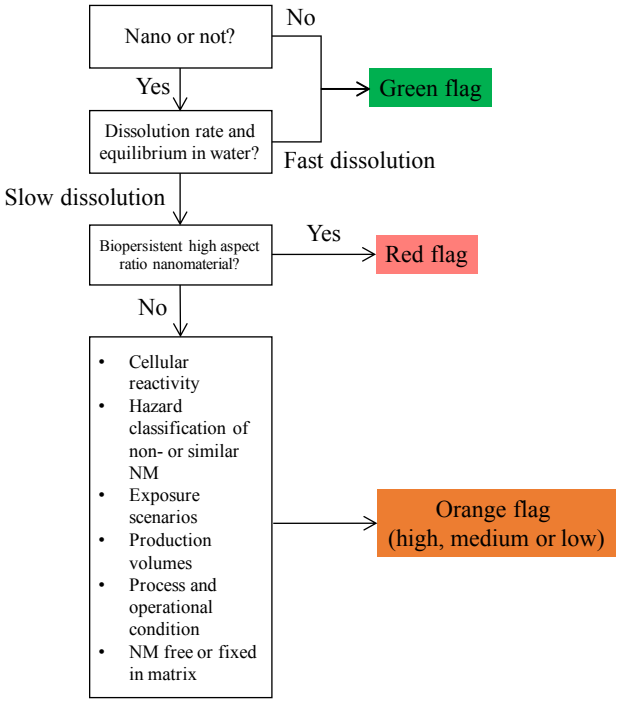

Figure 5. Phase I of the NANoREG approach (Dekkers et al. 2016). NM stands for nanomaterial.

4.12 NanoRiskCat

The NanoRiskCat method was developed by Foss Hansen et al. (2013a) as a first-tier assessment tool for assessing consumer products containing nanomaterials to be used by companies and regulators. The assessment objects are thus specific products containing nanomaterials, rather than the nanomaterial itself.

The output of the method is five coloured dots representing: (1) Exposure to professional users, (2) exposure to consumers, (3) exposure to the environment, (4) hazard potential for humans, and (5) hazard potential for the environment. Thus, the first three dots regard exposure, and the last two regard effects or hazard. The colour of the dots can be red (high risk), yellow (medium risk), green (low risk), or grey (unknown risk). No aggregation of the five dots into a final risk score is conducted.

The colour of the exposure dots is determined based on whether the nanomaterial is part of a solid material, constitutes a surface, is suspended in a liquid, or is airborne. In addition, information about the product use description is employed. Nanomaterials that are airborne or suspended in liquids are considered red. Nanomaterials bound to surfaces are considered as medium risk, unless the product use description includes sanding, in which case it is also red due to the higher probability of nanomaterial release. Nanomaterials in solids are categorised as green dots. No information about the form of the nanomaterials results in a grey-colour dot.

The assessment of human health hazard potential is based on a decision tree model. Through this model, a nanomaterial-containing product is attributed to a colour (Figure 5). For environmental hazard categorisation, a similar decision tree is used (Figure 6). A similarity to the early warning signs proposed by Foss Hansen et al. (2013b) and the hazard input parameters in Figure 6 can be noticed. Toxicity is evaluated in terms of LC_{50} values, persistence in terms of half-lives, and bioaccumulation in terms of bioconcentration and biomagnification factors.

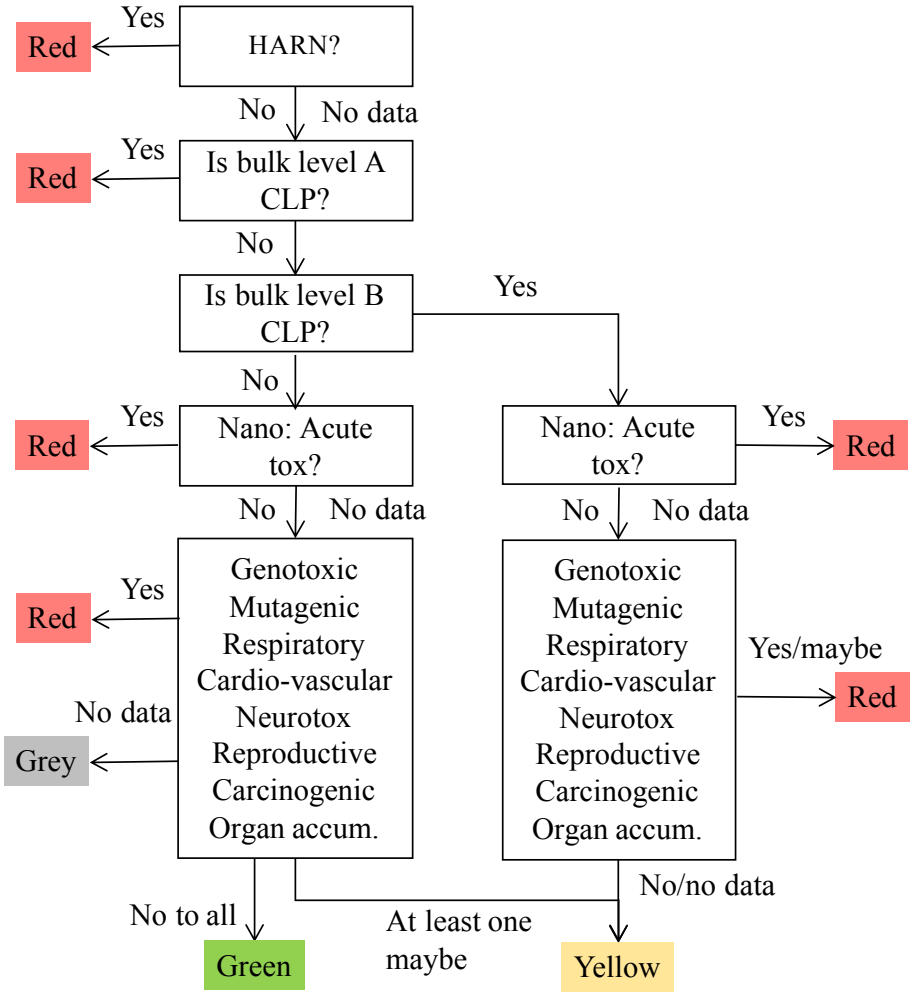

Figure 5. Procedure to derive human hazard potential with NanoRiskCat (Foss Hansen et al. 2013a). HARN stands for High Aspect Ratio Nanomaterial (meaning high surface area and high length-to-diameter aspect ratio), and CLP stands for Classification, Labelling and Packaging, and is a regulation within the European Union.

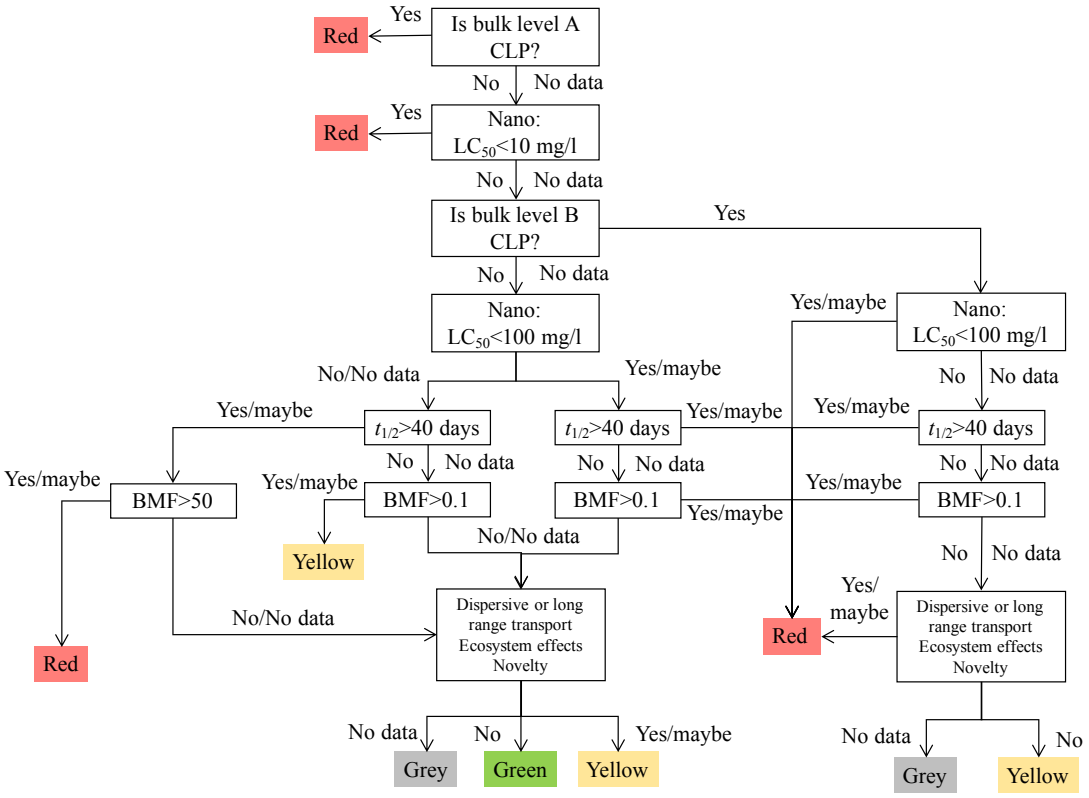

Figure 6. Procedure to derive environmental hazard potential with NanoRiskCat (Foss Hansen et al. 2013a). CLP stands for Classification, Labelling and Packaging, and is a regulation within the European Union. BMF stands for biomagnification factor.

4.13 NanoSafer

NanoSafer is a method developed in Denmark. According to its web page, it is currently available in version 1, but both a version 1.1 and a version 2.0 are being prepared (NanoSafer 2016). There seems to be no paper or report describing this method yet available, so information about it has been obtained from the web page. A digital handbook is available there, although only in Danish. NanoSafer is a control-banding tool developed for assessing risks related to nanomaterials in work environments. In addition, it is a risk management tool since it suggests control measures for reducing exposure to nanomaterials based on the previous assessment of risk. Information about the nanomaterials' size dimensions, specific surface area, density, threshold limits for the bulk material, and hazard labelling are required as input data to the model. Whether the material is in the form of a powder, and whether emissions are known, must also be provided. These are thus the hazard parameters used in the method. Based on this, NanoSafer calculates a result in terms of toxicity and exposure, and the result is presented in a risk matrix. Information about the details of this calculation is not provided on the NanoSafer webpage.

4.14 Occupational Hazard Band for Nano

A number of company representatives have proposed a development of the established control banding method called Occupational Hazard Band to also account for powders and nanomaterials (Gridelet et al. 2015). The method is suggested to apply to particle-shaped airborne materials regardless of size, thus extending somewhat beyond nanomaterials as assessment objects. The hazard band itself is not modified from the original method. It consists of a scale from 1 to 5, where materials are categorised based on available toxicological data. The hazard parameters are mutagenicity, carcinogenicity, reproductive toxicity, sensitising power, irritating power, dermal toxicity, inhalation toxicity, oral toxicity, dustiness, safety limits for the material's vapours, and hazard classification.

The exposure band considers seven hazard parameters related to the characteristics of the particulate material and its use: Hermeneticity (air tightness, *H*), characteristics of the solid material (*S*), emission potential (*E*), air containment (*C*), quantity of materials used (*Q*), frequency of operation (*F*), and duration of operation (*D*). These are also scored on an ordinal scale from 1 to 5, and an exposure index (*IE*) is calculated as:

$$IE = H \cdot S \cdot E \cdot C \cdot Q \cdot (F + D) \qquad \text{(Eq. 9)}$$

The exposure score ranges from 0 (no exposure) to >1800 (high exposure). Based on the hazard and exposure categorisation, the materials are placed in a risk matrix. This matrix has four ranking fields of different colours. The blue field is when the exposure score is zero and the risk thus is none. The green field is for low risk, the yellow is for moderate risk, and the red is for high risk. In line with the control banding philosophy, different control measures are then suggested based on the ranking.

4.15 Precautionary Matrix

The Precautionary Matrix is described in the report by Höck et al. (2008). The aim of the method is to increase the extent to which industry takes responsibility in the area of synthetic nanomaterials. The Precautionary Matrix should help such industry actors to identify sources of risk in the production, use and disposal phases of nanomaterial life cycles. Only nanoparticles and nanorods (fibres) are considered.

Risk is assessed on an ordinal scale with two classes. The first is called Class A, and means that nano-specific risks are expected to be low. The second is Class B, which means that nano-specific risks cannot be excluded. In the latter case, further investigations are needed, and risk reduction measures should be taken "with a precautionary approach in mind." Risks related to workers, consumers, and to the

environment are considered. The following equation is employed for scoring of risk (R):

$$R = (W \cdot E + S2) \cdot S1 \qquad \text{(Eq. 10)}$$

The first parameter in Eq. 10 is the potential effect (W). Its calculation requires information about the following hazard parameters: Redox activity, catalytic activity, and stability in terms of half-life under physiological and environmental conductions. The second parameter is the potential exposure to humans or the environment (E). It requires knowledge of the following hazard parameters: Potential release related to exposure of humans and to the environment, possible amount of nanoparticles handled by employees per day, possible amount of nanoparticles employees come in contact with, frequency with which employees handle the nanoparticles, amount of nanoparticles that consumers handle daily, frequency with which consumers handle the nanoparticle-containing product, amount of nanoparticles disposed of as waste without being subject to specific waste disposal, and the annual amount of nanoparticles in the product. The third parameter is information about the nanomaterial product life cycle ($S2$). Its calculation requires knowledge about the following hazard parameters: Whether the origin of the materials is known, whether there is a precautionary matrix evaluated for the starting material, whether the future product life cycle of the synthetic nanomaterial is known, and how accurately the material system and disturbing factors such as impurities can be estimated. The fourth parameter is the nano-relevance ($S1$). Its calculation requires knowledge of the following hazard parameters: Size order of primary particles, under which physiological conditions deagglomeration of formed agglomerates occurs, and under which environmental conditions deagglomeration of formed agglomerates occurs.

Risk potentials are calculated for normal use and for a worst-case scenario. The input parameters W, E, $S1$, and $S2$ are scored from 1 to 9, with 1 corresponding to low risk, 5 to medium risk, and 9 to high risk. If information is lacking, the highest risk is chosen. A value between 0 and 20 for R results in Class A, and a value higher than 20 results in Class B.

4.16 Relative Risk Analysis

Robichaud et al. (2005) describes a relative risk analysis method. The assessment objects are nanomaterial production processes. The method is explicitly developed to inform the insurance industry, and considers occupational as well as human health and environmental risks. The calculation procedure follows that of the XL Insurance database.

Three types of risk are assessed: Incident risk, normal operations risk, and latent contamination risk. These are scored on separate ordinal scales from 0 to 100. A

number of substance-related hazard parameters are considered. Note that it is not the parameters of the nanomaterials that are assessed, but those of input materials to the production process. A flammability risk class (*F*) is scored on an ordinal scale from 1 to 4 based on the flammability of the substance. LC_{50}, LD_{50}, and carcinogenicity are used to derive a toxicity risk class (*Tox*) on an ordinal scale from 1 to 4. Photolysis and biodegradation rates are used to derive a persistence risk class (*Per*) on an ordinal scale from 1 to 4. Molecular weight, solubility, and other such parameters are used to derive a mobility risk class (*Mob*), also on an ordinal scale from 1 to 4. A substance hazard risk class (*Sub*) can then be calculated as:

$$Sub = Tox \cdot x \cdot Per \cdot y \cdot Mob \qquad \text{(Eq. 11)}$$

where *x* and *y* are multipliers, which magnitude are determined by the toxicity risk class, and the persistence risk class, respectively.

Some process-related hazard parameters are also considered. The temperature is used to determine a temperature risk class (*Tem*), the pressure is used to derive a pressure risk class (*Pre*), the reaction enthalpy is used to derive an enthalpy risk class (*Ent*), and the explosion potential is used to derive a special hazard risk class (*Spe*). These four terms are all scored on an ordinal scale from 1 to 4, and based on this, a process incident probability class (*Inc*) can be calculated:

$$Inc = Tem + Pre + Ent + Spe - 3 \qquad \text{(Eq. 12)}$$

In addition to these, a material amount risk class (*Mat*) is determined based on process properties such as raw materials. An emission risk class (*Emi*) is also determined based on emissions in kg/ton product under normal operation. From this, the indecent risk score (*IRS*) and the normal operations risk score (*NRS*) are calculated:

$$IRS = (Inc + Sub + Mat - 1 - 2) \cdot \frac{99}{21} + 1 \qquad \text{(Eq. 13)}$$

$$NRS = (Emi + Sub - 2) \cdot \frac{99}{18} + 1 \qquad \text{(Eq. 14)}$$

The *IRS* and *NRS* are calculated for three different environmental compartments: Air, water and soil. Based on these, the latent risk score (*LRS*) is then calculated for each compartment. The *LRS* of soil is calculated as follows:

$$LRS_{soil} = \frac{IRS_{soil}+NRS_{soil}+0.5\cdot(IRS_{water}+NRS_{water})}{3} \quad \text{(Eq. 15)}$$

Production processes for five nanomaterials were assessed in the study: Carbon nanotubes, fullerenes, quantum dots, alumoxane nanoparticles, and nano-sized titanium dioxide. Representative production processes with potential for scale up were selected. For *IRS*, fullerenes had the highest score (around 75 of 100). For *NRS*, nano-sized titanium dioxide had the highest score (around 50 of 100). For *LRS*, fullerenes again had the highest score (around 53 of 100). The nanomaterials' production processes were also compared to those of conventional products, such as wine, petroleum, and aspirin. In general, the scores of the nanomaterials' production processes were neither higher nor lower than those of the conventional products.

4.17 Risk Trigger Scores

In order to identify risks in the early stages of product development, Wardak et al. (2008) developed a method where risk trigger scores are calculated. The assessment objects are nanoproducts, and the method is not specific for occupational, human health or environmental risks. The risk trigger scores are used to rank nanomaterial products with regard to risks. Experts were asked to estimate scores for both hazard (meaning toxicity) and exposure. The hazard parameters for this method are thus the experts' scoring of hazard and exposure. The scoring was conducted from 1 (low) to 5 (high). Results are then presented in a risk matrix, with hazard and exposure on the two axes. In order to incorporate a life cycle perspective in the assessment, different life cycle stages of nanomaterial-containing products were assessed. In addition, different exposure scenarios were considered. An example of a scenario for a specific product, life cycle stage, and exposure pathway could be: Skin absorption during the use phase of an air freshener spray.

Eight products were assessed in the study: Sunscreen containing titanium dioxide nanoparticles, toothpaste containing silver nanoparticles, air fresheners containing silver nanoparticles, lithium ion batteries, food supplement containing calcium and magnesium nanopowders, tennis racquets containing carbon nanotubes, and magnetic resonance imaging contrast agents containing metallofullerenes. The sunscreen scored most highly on hazard, whereas the magnetic resonance imaging contrast agent received the highest score on exposure.

4.18 Stoffenmanager Nano

This method, developed by van Duuren-Stuurman et al. (2012), is another control banding tool aimed at improving occupational health and safety for employees. It builds on the Stoffenmanager method, which is a web-based control-banding tool developed to assess and manage hazardous chemicals (Marquart et al.

2008). It is stated that the information needed to use the tool should be accessible and understandable for the user. The assessment object is reported to be nanoparticles between 1 and 100 nm.

Similar to many of the other methods, Stoffenmanager Nano has two main parameters: A hazard band and an exposure band. Nanomaterials are categorised into hazard bands based on whether they are soluble, whether they contain persistent fibres, and whether they are toxic, carcinogenic, mutagenic, irritant, and other such properties. There are five hazard bands, ranging from A (lowest hazard) to E (highest hazard). The exact procedure is presented in Figure 7, which shows which hazard parameters are required as input to the method.

The exposure band is based on nine main factors: Substance emission potential, handling, localised controls, segregation, dilution/dispersion, personal behaviour, separation (personal enclosure), surface contamination, and respiratory protective equipment. Based on these factors, an exposure score is calculated, which is translated to an exposure band that goes from 1 (low exposure) to 4 (high exposure). The hazard and exposure bands are then combined into priority bands in the typical risk matrix fashion.

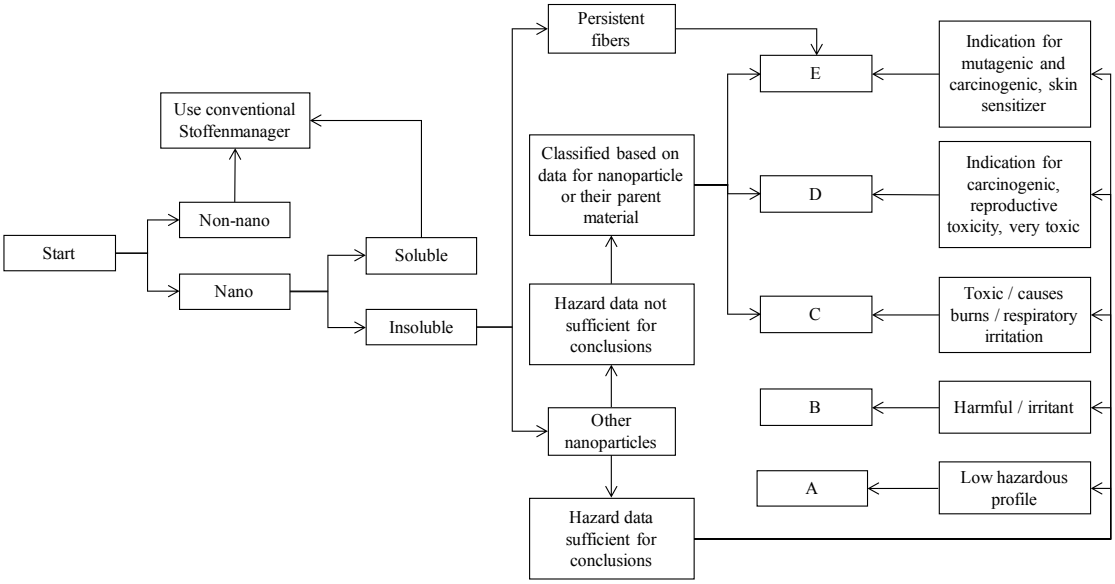

Figure 7. Procedure to derive hazard potential with Stoffenmanager Nano (van Duuren-Stuurman et al. 2012). A to E represent different hazard bands.

4.19 TEARR

The Tool for Engineered Nanomaterial Application Pair Risk Ranking (TEARR) is a risk ranking method based on both quantitative and qualitative information about potential human health risks of nanomaterials (Grieger et al. 2015). The specific focus is on the health of workers and soldiers, and on nanomaterials used in army equipment. The assessment objects are thus nanomaterial-containing army materials.

A list of 27 hazard parameters related to the nanomaterial were included in the method. These parameters include degradation potential, dispersibility, persistence, bioaccumulation, toxicity, surface charge, surface reactivity, flammability, explosivity, particle size, density, chemical composition, porosity, dustiness, solubility, aggregation, form, and shape. In addition, ten hazard parameters related to the army material were also considered, including the amount of nanomaterial in the army material, number of people exposed, and use pattern. Expert interviews and a literature review were employed to collect required information about both nanomaterial-related and army material-related hazard parameters. The values of these parameters were used to obtain ordinal scale values for release, exposure, and toxicity of the nanomaterials. Similarly, scores were assigned to the army material characteristics. Based on these numbers, a relative risk score *R* was calculated by the following equation:

$$R_{h,i,j} = \sum_1^m \left[\frac{1}{n_1}\sum_1^{n_1}\left(RS_{k_1,m} \cdot w_{k_1,m}\right)\right] \cdot \left[\frac{1}{n_2}\sum_1^{n_2} IS_{k_2}\right] \qquad \text{(Eq. 16)}$$

where *h* is either dermal exposure, ingestion, or inhalation; *i* is either civilian, worker, or soldier; *j* is either occupational or accidental; *m* is either 1, 2, or 3 and corresponds to the score for release, exposure, and toxicity potential for a specific hazard parameter k_1; n_1 is the total number of hazard parameters included; *RS* is either 1, 3, or 5 and is a score for the nanomaterial-related hazard parameters; *w* is either 0, 1, or 2 and means the ranking weight assigned by a user; n_2 is the number of army material-related hazard parameters; and *IS* is either 0, 0.5, 1, 2, 5, 10, or 100 and means the risk score for a particular army material k_2. The risk *R* is measured on an ordinal scale from 0 to 3000.

A number of different nanomaterial-containing army materials were assessed in the study. Communication devices were found to have the lowest risk, whereas smokes and obscurants were found to have the highest risk.

4.20 WCD model

The Worst Case Definition (WCD) model was first developed by Sørensen et al. (2010) and later applied by Grieger et al. (2011). The method can be used to assess nanomaterials, but also chemical substances in general. It is described as a conceptual model able to define worst-case conditions in the complex risk management of nanomaterials and chemicals. A central concept in this model is protected units (PU), which is something considered valuable by society.[2] The life of a human being could

[2] The concept seems to have a similar meaning as the concept *endpoint* in chemical and ecological risk assessment (Suter II 2007; van Leeuwen and Vermeire 2007).

be a PU in a human health risk assessment. Another central concept is causes of risk (CR). Application of a moisturizer onto human skin could be a CR. The first two steps in the model are all about identifying relevant PU and CR.

The third step of the model concerns scoring the importance of the PU, and also the importance of the relationships between PU and CR. Any combination of PU and CR could lead to risk, but not all CR are relevant for all PU. Both the PU and the relationships between PU and CR are scored on an ordinal scale from 1 to 3 and results are combined in a risk matrix. Based on this, the most important risk factors are selected for further assessment.

Table 1. Screening risk assessment methods for nanomaterials identified in the literature review.

Method	Occu-pational risk	Human health risk in general	Environ-mental risk	Assessment object	Reference
ANSES	x			Nanomaterials	Riediker et al. (2012)
CB Nanotool 2.0	x			Nanoparticles	Zalk et al. (2009)
Early warning signs		x	x	Nanomaterials	Foss Hansen et al. (2013b)
Genaidy's method	x			Carbon nanofiber production	Genaidy et al. (2009)
Groso's method	x			Nano laboratories	Groso et al. (2010)
Guidance	x			Nanomaterials and nanoproducts	Cornelissen et al. (2011)
Hierarchical Rank Aggregation		x		Nanomaterials	Patel et al. (2013)
LICARA nanoSCAN	x	x	x	Nanoproducts	van Harmelen et al. (2016)
Nano-Evaluris	x			Nanopowders	Bouillard and Vignes (2014)
NanoHAZ		x	x	Nanomaterials	O'Brien and Cummins (2010)
NANoREG	x	x		Nanomaterials	Dekkers et al. (2016)
NanoRiskCat	x	x	x	Nanoproducts	Foss Hansen et al. (2013a)
NanoSafer	x			Nanomaterials	NanoSafer (2016)
Occupational Hazard Band for Nano	x			Airborne particles	Gridelet et al. (2015)
Precautionary Matrix	x	x	x	Nanoparticles and nanorods	Höck et al. (2008)
Relative Risk Analysis	x	x	x	Nanomaterial production processes	Robichaud et al. (2005)
Risk Trigger Scores	x	x	x	Nanoproducts	Wardak et al. (2008)
Stoffenmanager Nano	x			Nanoparticles	van Duuren-Stuurman et al. (2012)
TEARR	x			Nanomaterial-containing army materials	Grieger et al. (2015)
WCD model		x	x	Nanomaterials (and chemicals)	Sørensen et al. (2010), Grieger et al. (2011)

5 Concluding discussion and recommendations

As can be seen in Section 4 and Table 1, the screening risk assessment methods for nanomaterials reviewed are different in many regards. Some are simpler, and some are more complex. Some require many hazard input parameters to be known, others only a few. Results are presented by different names, such as hazard bands, risk potentials, and risk levels. Which hazard parameters are included and the level of detail of the assessment are clearly matters of choice and ambition. These choices vary substantially between methods, to the extent that comparisons of results between methods are difficult. It seems clear that the choices in the methods much influence the outcomes. Below, we discuss the five choices that were the focus of this review (Section 3):

- Which types of risk are assessed in the method – occupational, human health, and/or environmental risks?
- Which are the assessment objects (e.g. nanomaterials and/or nanoparticles) considered in the methods?
- Which scoring scales (i.e. S) are used to present the results of the methods?
- How is the function transforming the hazard input parameters to the scoring scale formulated (i.e. f)?
- Which hazard input parameters (i.e. $p_1, \ldots, p_n$) are included in the methods?

5.1 Risks and objects assessed

Regarding which types of risk that are assessed, it can be noted from Table 1 that most of the reviewed methods focus on occupational human health, and are control-banding methods. Such risks are surely relevant, since people working with nanomaterials are likely to face higher exposure than the general population. However, this emphasis on occupational human health also shows the need for the development of methods focusing on human health in general and on the environment. Notably, less than half of the methods include the environment, and none of the methods focus exclusively on environmental risk, although the early warning signs employed by Foss Hansen et al. (2013b) may be said to primarily focus on the environment and only more indirectly on human health. This dominance of occupational risks and the lack environmental focus among screening risk assessment methods was also pointed out by Grieger et al. (2012b). Further development of screening risk assessment methods with a focus on environmental risks of nanomaterials is thus recommended.

Regarding assessment objects, it can be noted from Table 1 that most methods assess nanomaterials and nanoparticles. However, a number of methods instead assess products containing nanomaterials and nanoparticles – called nanoproducts. We see reasons for both product-specific and material-generic assessments. Most

nanomaterials will probably not be used in pure form, but rather as a constituent of a product. It is then reasonable that the product, its features, and how it is used, will influence exposure and consequently risks. A product where the nanomaterials is tightly bound in a solid matrix should be less risky than a product where the nanomaterials are used in free form, such as a spray. This is captured by, for example, Groso's method described in Figure 4 (Groso et al. 2010). For nanomaterials that can appear in many different types of products, with different likelihood of exposure, it would even be difficult to talk about a general, non-product-specific risk related solely to the nanomaterial. However, in production facilities, it is possible that nanomaterials would appear in free form. For control banding methods focusing on occupational human health risks during production, the consideration of free nanomaterials may therefore be justified.

5.2 Scoring scales

Regarding scoring scales, all the methods reviewed in Section 4 rely on some ordinal scale, for example from A to C as in the Guidance method (Cornelissen et al. 2011). One may even say that many methods rely on layers of ordinal scales, since different scoring scales are often aggregated into – or otherwise used to derive – a final scoring scale. Such final scoring scales can theoretically be as simple as a scale with only the two categories *risk* and *no risk*. The relative ranking of assessment objects (e.g. nanomaterials) that follows from their placement on the final scoring scale also, in itself, constitutes an ordinal scale (e.g. nanomaterial 5, nanomaterial 1, nanomaterial 2, and so on). Most of the ordinal scoring scales are based on natural numbers (i.e. 1, 2, 3, and so on) or the Latin alphabet (i.e. A, B, C, and so on). The scoring scales are arbitrary and defined by the method, rather than being based on some existing physical scale, such as mass or concentration. Methods employing these scales therefore benefit from simplicity and transparency provided that the number of categories on the scale remains fairly low, which is the case for most of the methods covered in this review.

Although ordinal scales are conveniently easy to grasp, they have also been criticised for a number of reasons. One reason is the implication for mathematical calculations. The sizes of the intervals between the ordinal scale categories may not be equally large (Wheeler 2011). This creates problems when attempting to use ordinal scale values in mathematical equations, since it is not certain that 1+1=2 on an ordinal scale. Interval or ration scales are strictly needed for any of the mathematical operations of addition, subtraction, multiplication, and division to be conducted (Wheeler 2011). A ratio scale is strictly also required for any type of statistical inference, including calculating average values and confidence intervals (Hubbard and Evans 2010).

Another critique of the use of ordinal scales is that of range compression (Hubbard and Evans 2010). Order-of-magnitude differences on rational scales can be transformed into much smaller differences on an ordinal scale, thereby masking the large differences. For example, instead of a difference between 1 mg/l and 1 μg/l on a ratio scale, the difference can become that between 1 and 3 on an ordinal scale.

It is seldom that the reviewed studies reflect on these problems related to ordinal scales. Although ordinal scales are common in risk ranking, chemical ranking and scoring methods, and control banding, we recommend that that these problems are kept in mind, and that ordinal scales are used with caution. In some cases, it may be possible to use logarithms instead of ordinal scales in order to transform parameter values to a scale that is easy to grasp (similar to the pH scale) (Baybutt 2015a; Levine 2012). Using such ratio scales instead would bring the benefit of enabling conventional quantitative uncertainty and sensitivity analyses, such as calculating confidence intervals. Considerations of uncertainty are otherwise unusual in risk ranking (Burgman 2005), but are important when assessing nanomaterials due to the many uncertainties associated with these new materials.

5.3 Transformation function and hazard parameters

The ideal situation for a risk assessment includes detailed knowledge of the cause-effect chains leading to risk, making quantitative estimations of emissions, exposure and effects possible by models and measurements. However, such mechanistically based risk assessments are challenging even in cases when the data and knowledge available is far more extensive than it is for nanomaterials at the moment. Screening risk assessment methods, such as the ones reviewed here, have in common that they aim for initial results that can give guidance regarding handling of risks at hand, in awaiting of further, more detailed, assessments of risk (Grieger et al. 2010). Results are therefore to be seen as preliminary and uncertain due to the present status of scientific knowledge and data availability.

Although all reviewed methods thus are simplifications in some sense, some are simpler than others, and do not include any complicated aggregation algorithms. The early warning signs proposed by Foss Hansen et al. (2013b), which are assessed on a binary yes/no scale, belong to the most simple ones. In contrast to this, some methods have a more complex algorithm. The CB Nanotool 2.0 method developed by Zalk et al. (2009) is probably among the more complex of the reviewed methods.

All screening risk assessment methods require risk-related hazard parameters at input. Such parameters can be related to the nanomaterial in itself, its interaction with various factors in the environment, or factors related to the human use of the nanomaterial. Use includes various types of formulations, where the nanomaterial occurs with other substances, and particulars of the way the nanomaterial is further transformed. In the case of titanium dioxide, it can be used in paint, where it becomes associated with polymers of the paint and no longer exists as a separate nanomaterial

(Kaegi et al. 2008). A view of the entire product life cycle, from the initial production of the nanomaterial to the waste handling of nanomaterial-containing products, can be taken in order to take such aspects into account. After use, the material may be transferred and distributed into different environmental compartments. Hazard parameters related to their further distribution, exposure and possible effects can be included in order to take this into account. Here, the reviewed methods differ in their coverage of the entire product life cycle and environmental fate after release. Some, such as the Risk Trigger Scores (Wardak et al. 2008), have a wide coverage of the nanomaterials' life cycles. Others, such as NanoHAZ (O'Brien and Cummins 2010), have a coverage of the nanomaterials' fate in the environment.

The level of knowledge about specific nanomaterials sets limits on which hazard parameters can be included in a screening risk assessment method. For some nanomaterials, many of their characteristics are well known. An example of this is titanium dioxide, which has long since had a wide application as a white pigment (Kaegi et al. 2008). Some of its known properties include the different physicochemical properties adhering to the crystal structures of the two forms of titanium dioxide employed in nanomaterials (anatase and rutile) as well as different forms of use, which may influence the release and subsequent distribution and exposure. For other, newer nanomaterials, such as graphene, less is known. Such nanomaterials may yet be produced in small amounts and with a limited number of applications, but may have a wide range of potential applications (Segal 2009). These kinds of differences in data availability will influence the possibility to both identify hazard parameters contributing to risk and data that can be used in screening risk assessments.

Sometimes, hazard parameters with a not so direct connection to risk are employed as a result of lack of knowledge of more clearly risk-related physical, chemical and biological parameters. Such hazard parameters can be seen as 'stand-ins' or proxy indicators of more risk-related parameters. On the other hand, data for such hazard parameters may be more readily available. An example is the release of dust, which is used as hazard parameter in Groso's method (Groso et al. 2010). The benefit of this kind of proxy indicator is its data availability and that it makes the method transparent in its simplicity, but the overall uncertainty must be considered to be large. In contrast, the early warning signs seem to contain a number of hazard parameters that are difficult to determine the values of for some nanomaterials (Foss Hansen et al. 2013b).

In addition to data availability for specific hazard parameters, the number of hazard parameters influences the applicability of a screening risk assessment method. The Guidance method requires comparatively few hazard parameters (Cornelissen et al. 2011). Only two pieces of information are required for this method. The first is the physiochemical form of the nanomaterials, which is often known. The second is the possibility of emissions in terms of whether the work takes place in full containment, whether emissions from a liquid or solid material are possible, and whether emissions

or primary particles are possible. Although the second parameter may be challenging to estimate, such a modest list of hazard input parameters makes a preliminary assessment more feasible. In contrast, some reviewed methods are data demanding and include numerous hazard parameters which values are not trivial to determine. The list of 27 nanomaterial-related properties and 10 army material-related properties makes the TEAR method an example of a method with many hazard parameters (Grieger et al. 2015).

Some of the methods apply expert judgement for filling data gaps. The reliability of expert judgement has been discussed by Burgman (2005). At the core of expert judgement is the expert's knowledge and experiences along with his or her ability to comprehend, integrate, and extrapolate from this knowledge and experience into the unknown. In situations with large uncertainties, the experience provided by an expert can be highly valuable. The cognitive processes involved are, however, complex and there are indications that the outcomes may show a considerable variability due to who the expert is, the way questions are formulated, and the conditions for providing the judgement (Burgman 2005).

Here, we maintain that the point of screening risk assessment methods is that they should be less complex and data demanding than is the case for chemical risk assessments. Making a screening risk assessment method too complex and data demanding – to the extent that it rivals the complexity of chemical risk assessment – thus seems to defy the very purpose of screening risk assessments. Furthermore, one important purpose of screening risk assessments is to be a pre-step prior to full risk assessments, and to provide prioritisations for such more detailed studies. Using the term suggested by Baumann and Cowell (1999), screening and full risk assessments are *consecutive* (Figure 8). We therefore recommend a modest complexity for screening risk assessment methods. Preferably, the developer of the method should provide, or at least suggest, available data sources for included hazard parameters. Examples of such sources currently available include reviews of annual production rates of nanomaterials (Furberg et al. 2016) and the recently developed NanoE-Tox database for ecotoxicological data on nanomaterials (Juganson et al. 2015).

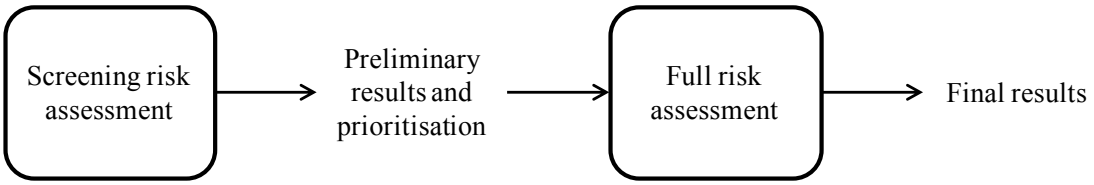

Figure 8. Illustration of the consecutive relationship between screening risk assessments and full risk assessments. Based on Baumann and Cowell (1999).

6 References

Abbott, L. C. and A. D. Maynard. 2010. Exposure Assessment Approaches for Engineered Nanomaterials. *Risk Analysis* 30(11): 1634-1644.

ANSES. 2010. *Development of a specific Control Banding Tool for Nanomaterials*. Maisons-Alfort: French Agency for Food, Environmental and Occupational Health Safety (ANSES).

Arvidsson, R. 2012. Contributions to Emission, Exposure and Risk Assessment of Nanomaterialsthesis, Environmental Systems Analysis, Chalmers University of Technology, Gothenburg.

Arvidsson, R. 2015. Life cycle assessment and risk assessment of manufactured nanomaterials. In *Nanoengineering - Global Approaches to Health and Safety Issues*, edited by P. I. Dolez. Amsterdam: Elsevier.

Arvidsson, R., S. Molander, B. A. Sandén, and M. Hassellöv. 2011. Challenges in Exposure Modeling of Nanoparticles in Aquatic Environments. *Human and Ecological Risk Assessment* 17(1): 245–262.

Arvidsson, R., J. Gallego Urrea, S. Molander, and M. Hassellöv. 2013. *Exposure assessments of nanoparticles in aquatic environments: Considerations, review and recommendations*. Sundbyberg: Swedish Chemicals Agency.

Bates, M. E., J. M. Keisler, N. P. Zussblatt, K. J. Plourde, B. A. Wender, and I. Linkov. 2015. Balancing research and funding using value of information and portfolio tools for nanomaterial risk classification. *Nature Nanotechnology* 11(198-203).

Baumann, H. and S. J. Cowell. 1999. An evaluative framework for conceptual and analytical approaches used in environmental management. *Greener Management International*(26): 109-122.

Baybutt, P. 2015a. Designing risk matrices to avoid risk ranking reversal errors. *Process Safety Progress* 35(1): 41-46.

Baybutt, P. 2015b. Calibration of risk matrices for process safety. *Journal of Loss Prevention in the Process Industries* 38: 163-168.

Beaudrie, C. and M. Kandlikar. 2011. Horses for courses: Risk information and decision making in the regulation of nanomaterials. *Journal of Nanoparticle Research* 13(4): 1477-1488.

Berg, M. and M. Scheringer. 1994. Problems in environmental risk assessment and the need for proxy measures. *Fresenius Environmental Bulletine* 3: 487-492.

Boholm, M. and R. Arvidsson. 2016. A Definition Framework for the Terms Nanomaterial and Nanoparticle. *NanoEthics* 10(1): 25-40.

Bouillard, J. and A. Vignes. 2014. Nano-Evaluris: an inhalation and explosion risk evaluation method for nanoparticle use. Part I: description of the methodology. *Journal of Nanoparticle Research* 16(2): 1-29.

Brooke, I. M. 1998. A UK Scheme to Help Small Firms Control Health Risks from Chemicals: Toxicological Considerations. *Annals of Occupational Hygiene* 42(6): 377-390.

Brouwer, D. H. 2012. Control Banding Approaches for Nanomaterials. *Annals of Occupational Hygiene* 56(5): 506-514.

Burgman, M. A. 2005. *Risks and Desicions for Conservation and Environmental Management*. Cambridge, UK: Cambidge University Press.

Cassar, L., C. Pepe, G. Tognon, G. L. Guerrini, and R. Amadelli. 2003. White Cement for Architectural Concrete, Possessing Photocatalytic Properties. In *Proceedings of the 11th International Congress on the Chemistry of Cement*. Skokie.

CB Nanotool 2.0. 2016. http://controlbanding.net/Home.html. Accessed 11th of Februay 2016.

Christian, P., F. Von der Kammer, M. Baalousha, and T. Hofmann. 2008. Nanoparticles: structure, properties, preparation and behaviour in environmental media. *Ecotoxicology* 17(5): 326-343.

Colvin, V. L. 2003. The potential environmental impact of engineered nanomaterials. *Nature Biotechnology* 21(10): 1166-1170.

Cornelissen, R., F. Jongeneelen, P. van Broekhuizen, and F. van Broekhuizen. 2011. *Guidance Working Safely with Nanomaterials and nanoproducts - the Guide for Employers and Employees. Version 1.0*. Amsterdam, the Netherlands: IVAM.

Cox, L. A. T. 2008. What's Wrong with Risk Matrices? *Risk Analysis* 2: 497-512.

Dekkers, S., A. G. Oomen, E. A. J. Bleeker, R. J. Vandebriel, C. Micheletti, J. Cabellos, G. Janer, N. Fuentes, S. Vázquez-Campos, T. Borges, M. J. Silva, A. Prina-Mello, D. Movia, F. Nesslany, A. R. Ribeiro, P. E. Leite, M. Groenewold, F. R. Cassee, A. J. A. M. Sips, A. Dijkzeul, T. van Teunenbroek, and S. W. P. Wijnhoven. 2016. Towards a nanospecific approach for risk assessment. *Regulatory Toxicology and Pharmacology* 80: 46-59.

Dhawan, A., V. Sharma, and D. Parmar. 2009. Nanomaterials: A challenge for toxicologists. *Nanotoxicology* 3(1): 1-9.

Erbis, S., Z. Ok, J. A. Isaacs, J. C. Benneyan, and S. Kamarthi. In press. Review of Research Trends and Methods in Nano Environmental, Health, and Safety Risk Analysis. *Risk Analysis*.

European Chemicals Agency. 2011. *Guidance on information requirements and chemical safety assessment. Part A: Introduction to the Guidance document*. Helsinki.

European Chemicals Bureau. 2003. *Technical Guidance Document on Risk Assessment*. Ispra.

Fang, L., S. Zhang, Z. Chen, H. Du, Q. Zhu, Z. Dong, and H. Li. 2015. Risk assessment of pesticide residues in dietary intake of celery in China. *Regulatory Toxicology and Pharmacology* 73(2): 578-586.

Fleury, D., G. Fayet, A. Vignes, F. Henry, and E. Frejafon. 2013. Nanomaterials Risk Assessment in the Process Industries: Evaluation and Application of Current Control Banding Methods. *Chemical Engineering Transactions* 31: 949-954.

Foss Hansen, S., K. Jensen Alstrup, and A. Baun. 2013a. NanoRiskCat: a conceptual tool for categorization and communication of exposure potentials and hazards

of nanomaterials in consumer products. *Journal of Nanoparticle Research* 16(1): 1-25.

Foss Hansen, S., K. N. Nielsen, N. Knudsen, K. D. Grieger, and A. Baun. 2013b. Operationalization and application of "early warning signs" to screen nanomaterials for harmful properties. *Environmental Science: Processes & Impacts* 15(1): 190-203.

Freinkel, S. 2011. *Plastic: A Toxic Love Story*. New York: Houghton Mifflin Harcourt.

Furberg, A., R. Arvidsson, and S. Molander. 2016. Very small flows? Review of the societal metabolism of nanomaterials. In *Advances in Nanotechnology Volume 15*. Hauppauge: Nova Science Publishers.

Garrod, A. N. I. and R. Rajan-Sithamparanadarajah. 2003. Developing COSHH Essentials: Dermal Exposure, Personal Protective Equipment and First Aid. *Annals of Occupational Hygiene* 47(7): 577-588.

Gee, D., P. Grandjean, S. Foss Hansen, S. van den Hove, M. MacGarvin, J. Martin, G. Nielsen, D. Quist, and D. Stanners. 2013. *Late lessons from early warnings: science, precaution, innovation*. Copenhagen: European Environment Agency.

Genaidy, A., R. Sequeira, M. Rinder, and A. A-Rehim. 2009. Risk analysis and protection measures in a carbon nanofiber manufacturing enterprise: An exploratory investigation. *Science of The Total Environment* 407(22): 5825-5838.

González, S., M. Fernández-Lorente, and Y. Gilaberte-Calzada. 2008. The latest on skin photoprotection. *Clinics in Dermatology* 26(6): 614-626.

Gottschalk, F., T. Sun, and B. Nowack. 2013. Environmental concentrations of engineered nanomaterials: Review of modeling and analytical studies. *Environmental Pollution* 181(0): 287-300.

Gottschalk, F., T. Sonderer, R. W. Scholz, and B. Nowack. 2009. Modeled Environmental Concentrations of Engineered Nanomaterials (TiO2, ZnO, Ag, CNT, Fullerenes) for Different Regions. *Environmental Science & Technology* 43(24): 9216-9222.

Gridelet, L., P. Delbecq, L. HervÉ, P. Boissolle, D. Fleury, S. Kowal, and G. Fayet. 2015. Proposal of a new risk assessment method for the handling of powders and nanomaterials. *Industrial Health* 53(1): 56-68.

Grieger, K., A. Baun, and R. Owen. 2010. Redefining risk research priorities for nanomaterials. *Journal of Nanoparticle Research* 12(2): 383-392.

Grieger, K., A. Laurent, M. Miseljic, F. Christensen, A. Baun, and S. Olsen. 2012a. Analysis of current research addressing complementary use of life-cycle assessment and risk assessment for engineered nanomaterials: have lessons been learned from previous experience with chemicals? *Journal of Nanoparticle Research* 14(7): 1-23.

Grieger, K., J. Redmon, E. Money, M. Widder, W. van der Schalie, S. Beaulieu, and D. Womack. 2015. A relative ranking approach for nano-enabled applications to improve risk-based decision making: a case study of Army materiel. *Environment Systems and Decisions* 35(1): 42-53.

Grieger, K. D., S. F. Hansen, P. B. Sørensen, and A. Baun. 2011. Conceptual modeling for identification of worst case conditions in environmental risk assessment of nanomaterials using nZVI and C60 as case studies. *Science of The Total Environment* 409(19): 4109-4124.

Grieger, K. D., I. Linkov, S. F. Hansen, and A. Baun. 2012b. Environmental risk analysis for nanomaterials: Review and evaluation of frameworks. *Nanotoxicology* 6(2): 196-212.

Groso, A., A. Petri-Fink, A. Magrez, M. Riediker, and T. Meyer. 2010. Management of nanomaterials safety in research environment. *Particle and Fibre Toxicology* 7(40): 1-8.

Hammar, L., A. Wikström, and S. Molander. 2014. Assessing ecological risks of offshore wind power on Kattegat cod. *Renewable Energy* 66: 414-424.

Handy, R., F. von der Kammer, J. Lead, M. Hassellöv, R. Owen, and M. Crane. 2008. The ecotoxicology and chemistry of manufactured nanoparticles. *Ecotoxicology* 17(4): 287-314.

Hansen, B. G., A. G. van Haelst, K. van Leeuwen, and P. van der Zandt. 1999. Priority setting for existing chemicals: European Union risk ranking method. *Environmental Toxicology and Chemistry* 18(4): 772-779.

Harremoës, P., D. Gee, M. MacGarvin, A. Stirling, J. Keys, b. Wynne, and S. Guedes Vas. 2001. *Late lessons from early warnings: the precautionary principle 1896-2000*. Copenhagen: European Environment Agency.

Höck, J., H. Hofmann, H. Krug, C. Lorenz, L. Limbach, B. Nowack, M. Riediker, K. Schirmer, C. Som, W. Stark, C. Studer, N. von Götz, S. Wengert, and P. Wick. 2008. *Guidelines on the Precautionary Matrix for Synthetic Nanomaterials. Version 1.1*. Berne: Federal Office for Public Health and Federal Office for the Environment.

Hristozov, D., S. Gottardo, E. Semenzin, A. Oomen, P. Bos, W. Peijnenburg, M. van Tongeren, B. Nowack, N. Hunt, A. Brunelli, J. J. Scott-Fordsmand, L. Tran, and A. Marcomini. In press. Frameworks and tools for risk assessment of manufactured nanomaterials. *Environment International*.

Hubbard, D. and D. Evans. 2010. Problems with scoring methods and ordinal scales in risk assessment. *IBM Journal of Research and Development* 54(3): 1-10.

IEH. 2004. *A review of prioritisation methodologies for screening chemicals with potential human health effects as a result of low level environmental exposure*. Leicester: MRC Institute for Environment and Health.

ISO. 2008. *Nanotechnologies — Terminology and definitions for nano-objects — Nanoparticle, nanofibre and nanoplate*. ISO/TS 27687:2008(E).

Ju-Nam, Y. and J. R. Lead. 2008. Manufactured nanoparticles: An overview of their chemistry, interactions and potential environmental implications. *Science of The Total Environment* 400(1-3): 396-414.

Juganson, K., A. Ivask, I. Blinova, M. Mortimer, and A. Kahru. 2015. NanoE-Tox: New and in-depth database concerning ecotoxicity of nanomaterials. *Beilstein Journal of Nanotechnology* 6: 1788-1804.

Juric, A., R. Meldrum, and E. Liberada. 2015. Achieving Control of Occupational Exposures to Engineered Nanomaterials. *Journal of Occupational and Environmental Hygiene* 8(50): 501-508.

Kaegi, R., A. Ulrich, B. Sinnet, R. Vonbank, A. Wichser, S. Zuleeg, H. Simmler, S. Brunner, H. Vonmont, M. Burkhardt, and M. Boller. 2008. Synthetic TiO2 nanoparticle emission from exterior facades into the aquatic environment. *Environmental Pollution* 156(2): 233-239.

Kohler, A. R., C. Som, A. Helland, and F. Gottschalk. 2008. Studying the potential release of carbon nanotubes throughout the application life cycle. *Journal of Cleaner Production* 16(8-9): 927-937.

Levine, E. S. 2012. Improving risk matrices: the advantages of logarithmically scaled axes. *Journal of Risk Research* 15(2): 209-222.

Linkov, I., F. K. Satterstrom, J. Steevens, E. Ferguson, and R. C. Pleus. 2007. Multi-criteria decision analysis and environmental risk assessment for nanomaterials. *Journal of Nanoparticle Research* 9(4): 543-554.

Liu, H. H. and Y. Cohen. 2014. Multimedia Environmental Distribution of Engineered Nanomaterials. *Environmental Science & Technology* 48(6): 3281-3292.

Löfstedt, R. 2011. Risk versus Hazard - How to Regulate in the 21st Century. *European Journal of Risk Regulation* 2: 149-168.

Luoma, S. N. 2008. *Silver nanotechnologies and the environment: Old problems or new challanges?* Washington DC: Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies and The PEW Charitable Trusts.

Marquart, H., H. Heussen, M. Le Feber, D. Noy, E. Tielemans, J. Schinkel, J. West, and D. Van Der Schaaf. 2008. 'Stoffenmanager', a Web-Based Control Banding Tool Using an Exposure Process Model. *Annals of Occupational Hygiene* 52(6): 429-441.

Maynard, A. D. 2007. Nanotechnology: The Next Big Thing, or Much Ado about Nothing? *Annals of Occupational Hygiene* 51(1): 1-12.

Maynard, A. D., D. B. Warheit, and M. A. Philbert. 2011. The New Toxicology of Sophisticated Materials: Nanotoxicology and Beyond. *Toxicological Sciences* 120(suppl 1): S109-S129.

Meesters, J. A. J., A. A. Koelmans, J. T. K. Quik, A. J. Hendriks, and D. van de Meent. 2014. Multimedia Modeling of Engineered Nanoparticles with SimpleBox4nano: Model Definition and Evaluation. *Environmental Science & Technology* 48(10): 5726-5736.

Mistra Environmental Nanosafety. 2015. http://www.mistraenvironmentalnanosafety.org/en. Accessed 8th of February 2016.

NanoSafer. 2016. http://nanosafer.i-bar.dk/. Accessed 8th of February 2016.

Nel, A., T. Xia, L. Madler, and N. Li. 2006. Toxic Potential of Materials at the Nanolevel. *Science* 311(5761): 622-627.

NIOSH. 2009. *Qualitative Risk Characterization and Management of Occupational Hazards: Control Banding (CB). A Literature Review and Critical Analysis*. Washington DC: Department of Health and Human Services, Centers for Disease Control Prevention, National Institute for Occupational Safety and Health (NIOSH).

Nohynek, G. J., J. Lademann, C. Ribaud, and M. S. Roberts. 2007. Grey Goo on the Skin? Nanotechnology, Cosmetic and Sunscreen Safety. *Critical Reviews in Toxicology* 37(3): 251 - 277.

Nowack, B., H. F. Krug, and M. Height. 2011. 120 Years of Nanosilver History: Implications for Policy Makers. *Environmental Science & Technology* 45(4): 1177-1183.

O'Brien, N. J. and E. J. Cummins. 2010. Ranking initial environmental and human health risk resulting from environmentally relevant nanomaterials. *Journal of Environmental Science and Health, Part A* 45(8): 992-1007.

O'Brien, N. J. and E. J. Cummins. 2011. A Risk Assessment Framework for Assessing Metallic Nanomaterials of Environmental Concern: Aquatic Exposure and Behavior. *Risk Analysis* 31(5): 706-726.

Paik, S. Y., D. M. Zalk, and P. Swuste. 2008. Application of a Pilot Control Banding Tool for Risk Level Assessment and Control of Nanoparticle Exposures. *The Annals of Occupationsl Hygiene* 52(6): 419-428.

Patel, T., D. Telesca, R. Rallo, S. George, T. Xia, and A. Nel. 2013. Hierarchical Rank Aggregation with Applications to Nanotoxicology. *Journal of Agricultural, Biological, and Environmental Statistics* 18(2): 159-177.

Peralta-Videa, J. R., L. Zhao, M. L. Lopez-Moreno, G. de la Rosa, J. Hong, and J. L. Gardea-Torresdey. 2011. Nanomaterials and the environment: A review for the biennium 2008–2010. *Journal of Hazardous Materials* 186(1): 1-15.

Praetorius, A., M. Scheringer, and K. Hungerbühler. 2012. Development of Environmental Fate Models for Engineered Nanoparticles—A Case Study of TiO2 Nanoparticles in the Rhine River. *Environmental Science & Technology* 46(12): 6705-6713.

Project on Emerging Nanotechnologies. 2013. Consumer Products Inventory. http://www.nanotechproject.org/cpi. Accessed 26th of November 2015.

Riediker, M., C. Ostiguy, J. Triolet, P. Troisfontaine, D. Vernez, G. Bourdel, N. Thieriet, and A. Cadène. 2012. Development of a Control Banding Tool for Nanomaterials. *Journal of Nanomaterials* 2012: 1-8.

Robichaud, C. O., D. Tanzil, U. Weilenmann, and M. R. Wiesner. 2005. Relative Risk Analysis of Several Manufactured Nanomaterials: An Insurance Industry Context. *Environmental Science & Technology* 39(22): 8985-8994.

Rockström, J., W. Steffen, K. Noone, Å. Persson, F. S. Chapin, E. F. Lambin, T. M. Lenton, M. Scheffer, C. Folke, H. J. Schellnhuber, B. Nykvist, C. A. de Wit, T. Hughes, S. van der Leeuw, H. Rodhe, S. Sorlin, P. K. Snyder, R. Costanza, U. Svedin, M. Falkenmark, L. Karlberg, R. W. Corell, V. J. Fabry, J. Hansen, B. Walker, D. Liverman, K. Richardson, P. Crutzen, and J. A. Foley. 2009. A safe operating space for humanity. *Nature* 461(7263): 472-475.

Royal Society. 2004. *Nanoscience and nanotechnologies: opportunities and uncertainties*. London.

Sanderson, K. D., S. Hurst, T. McKittrick, D. Rimmer, and L. Ye. 2003. Photocatalytic Coatings for Self Cleaning Glass. In *Glass Processing Days*. Tampere.

Scheringer, M. 2008. Nanoecotoxicology: Environmental risks of nanomaterials. *Nature Nanotechnology* 3(6): 322-323.

Scheringer, M. and M. Berg. 1994. Spatial and temporal range as measures of environmental threat. *Fresenius Environmental Bulletine* 3: 493-498.

Schmidt, K. F. 2007. *Green nanotechnilogy: It's Easier Than You Think*. Washington DC: Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies and The PEW Charitable Trusts.

Scopus. 2016. http://www.scopus.com/. Accessed 8th of February 2016.

Segal, M. 2009. Selling graphene by the ton. *Nature Nanotechnology* 4(10): 612-614.

Sørensen, P. B., F. Giralt, R. Rallo, G. Espinosa, B. Münier, S. Gyldenkærne, and M. Thomsen. 2010. Conscious worst case definition for risk assessment, part II: A methodological case study for pesticide risk assessment. *Science of The Total Environment* 408(18): 3860-3870.

Stevens, S. S. 1946. On the Theory of Scales of Measurement. *Science* 103(2684): 677-680.

Suter II, G. W. 2007. *Ecological Risk Assessment*. Boca Raton: CRC Press.

Swanson, M. B. and A. C. Socha. 1997. *Chemical ranking and scoring: Guidelines for relative assessment of chemicals*. Pansacola: Society for Environmental Toxicology and Chemistry (SETAC) press.

Syberg, K. and S. F. Hansen. 2016. Environmental risk assessment of chemicals and nanomaterials — The best foundation for regulatory decision-making? *Science of The Total Environment* 541: 784-794.

van Duuren-Stuurman, B., S. R. Vink, K. J. M. Verbist, H. G. A. Heussen, D. H. Brouwer, D. E. D. Kroese, M. F. J. Van Niftrik, E. Tielemans, and W. Fransman. 2012. Stoffenmanager Nano Version 1.0: A Web-Based Tool for Risk Prioritization of Airborne Manufactured Nano Objects. *Annals of Occupational Hygiene* 56(5): 525-541.

van Harmelen, T., E. K. Zondervan-van den Beuken, D. H. Brouwer, E. Kuijpers, W. Fransman, H. B. Buist, T. N. Ligthart, I. Hincapié, R. Hischier, I. Linkov, B. Nowack, J. Studer, L. Hilty, and C. Som. 2016. LICARA nanoSCAN - A tool for the self-assessment of benefits and risks of nanoproducts. *Environment International* 91: 150-160.

van Leeuwen, C. J. and T. G. Vermeire. 2007. *Risk Assessment of Chemicals: An Introduction*. 2nd ed. Dordrecht: Springer.

Vance, M. E., T. Kuiken, E. P. Vejerano, S. P. McGinnis, M. F. Hochella, Jr., D. Rejeski, and M. S. Hull. 2015. Nanotechnology in the real world: Redeveloping the nanomaterial consumer products inventory. *Beilstein Journal of Nanotechnology* 6: 1769-1780.

Wardak, A., M. E. Gorman, N. Swami, and S. Deshpande. 2008. Identification of Risks in the Life Cycle of Nanotechnology-Based Products. *Journal of Industrial Ecology* 12(3): 435-448.

Wheeler, D. J. 2011. Problems with risk priority numbers - Avoiding more numerical jabberwocky. Quality Insider. http://www.qualitydigest.com/inside/quality-insider-column/problems-risk-priority-numbers.html. Accessed 27th of December 2015.

Wiesner, M. R., G. V. Lowry, K. L. Jones, J. M. F. Hochella, R. T. Di Giulio, E. Casman, and E. S. Bernhardt. 2009. Decreasing Uncertainties in Assessing Environmental Exposure, Risk, and Ecological Implications of Nanomaterials. *Environmental Science & Technology* 43(17): 6458-6462.

Wijnhoven, S. W. P., W. J. G. M. Peijnenburg, C. A. Herberts, W. I. Hagens, A. G. Oomen, E. H. W. Heugens, B. Roszek, J. Bisschops, I. Gosens, D. Van De Meent, S. Dekkers, W. H. De Jong, M. van Zijverden, A. J. A. M. Sips, and R. E. Geertsma. 2009. Nano-silver – a review of available data and knowledge gaps in human and environmental risk assessment. *Nanotoxicology* 3(2): 109 - 138.

Wohlin, C. 2014. Guidelines for Snowballing in Systematic Literature Studies and a Replication in Software Engineering. In *Proceedings of the 18th International Conference on Evaluation and Assessment in Software Engineering*.

Zalk, D., S. Paik, and P. Swuste. 2009. Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures. *Journal of Nanoparticle Research* 11(7): 1685-1704.

Zalk, D. M. and D. I. Nelson. 2008. History and Evolution of Control Banding: A Review. *Journal of Occupational and Environmental Hygiene* 5: 330-346.