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Commentary

Control Banding Approaches for Nanomaterials

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Control banding (CB) has been developed as a pragmatic tool to manage the risk resulting from exposure to a wide variety of potentially hazardous substances in the absence of firm toxicological and exposure information. Currently, the CB approach is applied for emerging risks such as nanoparticles, by the development of various CB-based tools. Six of these are compared. Despite their similarity, i.e. combining hazard and exposure into control or risk bands, the structure, the applicability domains, and the assignment of the hazard and exposure bands, show differences that may affect the consistency of the resulting outcome amongst the various CB tools. The value of the currently available CB tools for nanomaterials can be enhanced by transparently elucidating these differences for user consideration during the selection of a tool for a specific scenario of application.

Keywords: applicability domain; assignment; control banding; exposure; hazard; nano; risk

INTRODUCTION

Control banding (CB) was developed in the pharmaceutical industry as a pragmatic tool to manage the risk resulting from exposure to a wide variety of potentially hazardous substances in the absence of firm toxicological and exposure data (Zalk and Nelson, 2008). Basically, it is a risk-assessment approach in a context of uncertainty using the generally accepted risk paradigm, where risk is a function of severity of impact (hazard)and the anticipated probability of that impact (exposure). Both hazard and exposure are graded into two to five different levels, usually referred to as bands. The two sets of bands are combined, most often in a matrix, resulting into control or risk bands.

CB principles have been widely used for the last decades to implement a risk management strategy, e.g. Control of Substances Hazardous to Health (COSHH) in the UK, where R(isk) and S(afety) phrases are allocated to hazard bands (Brooke, 1998), and exposure bands are based on statistical analysis of exposure data. In the Netherlands, the Stoffenmanager evolved from a qualitative risk prioritization tool into a tool to quantitatively predict exposure (Marquart *et al*., 2008).

The production and the use of (manufactured) nanomaterials (MNM), however, may introduce new and for the time being unknown risks. In such a context of uncertainty, the CB approach can be very helpful in implementing a risk-management strategy according to a precautionary approach. Recently, worldwide several CB approaches for MNM-related exposure have been developed and published.

The International Organization for Standardization (ISO) Technical Committee (TC) 229 Nanotechnologies has adopted the use of the CB approach as a work item and is currently in the process of editing a technical specification on this topic. Unfortunately, the draft report cannot be cited in this commentary.

Note that the CB tools discussed were drafted before the EU Commission published its Recommendations on the definition of Nanomaterials; ‘Nanomaterial means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate and where, for 50% or more of the particles in the number definition, one or more

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external dimensions is in the size range 1 nm–100 nm”. (EC, 2011).

In this commentary, the CB approaches for nanomaterials published so far will briefly be described and similarities and differences will be discussed.

CB APPROACHES FOR NANOMATERIAL

The CB approach for occupational ‘nano’ exposure has firstly been proposed by Andrew Maynard; however, this was only on a conceptual level (Maynard, 2007). Paik *et al*. (2008) proposed a CB Nanotool for risk prioritization and management in a research work environment; later, a slightly adjusted version was published by Zalk *et al*. (2009). This CB Nanotool 2.0 has been launched by the same authors at http://www.controlbanding.net., where a spreadsheet and a field form can be downloaded and a field form. It will be referred to as **NanoTool**. In Switzerland, a Precautionary Matrix for Synthetic Nanomaterials was developed to empower industry, commerce and trade to take greater responsibility and to apply a precautionary approach in a targeted and cost-effective matter (Höck et al., 2008). This CB approach is a risk prioritization tool and consists of a spreadsheet that can be downloaded (www. nanotechnologie.admin.ch); however, a web application is also available. In contrast to the name, the Precautionary Matrix is not a matrix allocating hazard and exposure bands; however, it combines hazard and exposure potential in a single score. It will be referred to as **Precautionary Matrix**.

In France, ANSES developed a CB tool for nanomaterials in workplace settings (Ostiguy *et al*., 2010; Riediker *et al.,* 2012, in press). The report is available through the internet (www.anses.fr). It will be referred to as **ANSES**.

Recently, two web-based tools for workplace risk prioritization have been launched, i.e. the Dutch **Stoffenmanager Nano** 1.0 (van Duuren-Stuurman *et al*., 2011, 2012, in press) available at http://.nano.stoffenmanger.nl, and the Danish **NanoSafer** available at http://nanosafer.i-bar.dk. The Stoffenmanager Nano is a module of Stoffenmanager for ‘conventional‘ hazardous substances and aims to be a risk prioritization tool, and has both Dutch and English versions. NanoSafer facilitates a (semi-quantitative) risk evaluation, and has currently only a Danish version. Both on-line tools have a link to libraries of good practices or examples of (implemented) control measures.

To guide employers and employees, Dutch Social Partners, i.e. Employers (VNO-NCW) and Employees (FNV and CNV), developed a Guidance on Working Safely with Nanomaterials and Nanoproducts (version 1.0) (Cornelissen *et al*., 2011). It includes an action plan to implement safe work practices, and printed versions are available in Dutch and English (available through the websites of FNV, VNO-NCW, CNV, e.g. www.fnv.nl. It includes a decision matrix to determine the level of control and will be referred to as **Guidance.**

In this review, the various CB-related tools will be compared based on the similarities in: (1) scope and applicability domain, (2) parameters for severity/hazard banding, (3) parameters for exposure/probability/exposure banding and (4) classification in risk or control bands.

SCOPE AND APPLICABILLITY DOMAIN

The **Precautionary Matrix** aims to guide industries, more specifically small- and medium-sized enterprises (SMEs), to decide whether the production or the application of synthetic nanomaterials needs ‘nano-specific measures’. The **Precautionary Matrix** not only is limited to workplace exposure but also addresses consumer exposure and potential release to environmental compartments**. NanoTool** was developed to support first-line occupational health professionals and researchers to evaluate the potential risks related to production and down-stream use of nanomaterials in a research work environment. **ANSES** and **Stoffenmanager Nano** explicitly focus on the work environment. **ANSES** is intended to be used by persons ‘adequately qualified in chemical risk prevention’. Stoffenmanager Nano is intended to be used by non-expert SME employers and employees (e.g. Environment, Health and Safety (EHS) responsible persons). Both tools cover activities across the life cycle of nanomaterials, varying from the synthesis of MNM, its down-stream use, the application of ‘ready-to-use’ nanoproducts, e.g. sprays, coatings, machining or abrasion of nanoproducts, e.g. sanding coated surfaces, which is in line with the ‘source domains’ in the conceptual model by Schneider *et al*. (2011). However, for the evaluation of machining or abrasion activities, the users of **Stoffenmanager Nano** will be redirected to the conventional Stoffenmanager. **NanoSafer** is also focused on the work environment; however, its application is limited to down-stream use of the powder form of nanomaterials. Similar to tools previously described, **NanoSafer** is intended to be used by EHS responsible persons in SMEs; however, the tool requires more specific data and information of the MNM powder and workplace conditions than other CB nanotools.

Similar to **ANSES** and Stoffenmanager Nano, the **Guidance** covers a wide range over activities related

Table 1. Summary of the most important characteristics of the various CB tools

	Hazard banding			Exposure banding							Matrix	
	Allocation system			Source domains/type of activities*							Number of bands/ levels	
CB tool Short name	Binary	Score	*N*	Synthesis	Powder handling	Application ready-to-use products	Abrasion	Emission potential	Exposure potential	*N*	CB	RL
Precautionary Matrix	−	+	1	(+)	(+)	(+)	(+)	+	−	1	2	−
NanoTool	−	+	4	+	+	−	−	+	−	4	4	−
ANSES	+		5	(+)	+	+	+	+	−	4	5	−
Stoffenmanager Nano	+	−	5	+	+	+	(+)	−	+	4	−	3
NanoSafer	+	+	4	−	+	−	−	−	+	5		5
Guidance	+	−	3	+	+	+	+	+	−	3	3	−

*Based on Schneider *et al*. (2010).
1 Precautionary matrix does not distinguish separate hazard and exposure bands.
N Number of bands.
CB Control band.
RL Risk level.
+ Used/addressed by tool.
− Not used/addressed by tool.
(+) only implicitly addressed by tool.

to MNM and nanoproducts. It explicitly aims to provide a self-assessment for non-OHS professionals.

The most relevant characteristics of the various tools are summarized in Table 1 and will be further discussed.

Severity or hazard banding

Two different approaches to assign hazard bands can be distinguished: (1) a scoring system, where a score is assigned to a variety of (hazard) parameters and the hazard bands represent a range in scores, and (2) a binary (yes/no) decision tree approach. The **Precautionary Matrix** allocates a score to the potential effect of MNM on health (and the environment). The **NanoTool** uses the scoring system with usually points ranging from 0 to 6 or 10 for a single severity factor, whereas **ANSES** and **StoffenmanagerNano** follow the binary approach system. **NanoSafer** uses a mixture of both approaches. **ANSES**, **NanoSafer** and to a lesser extent Stoffenmanager Nano rely much on (known) hazards of parent or bulk materials. The **Guidance** directly classifies a MNM into a hazard band, based on some substance properties or identity.

The starting point for all tools is defining which materials can be identified as 'nanomaterials' to be addressed for CB or risk prioritization. The **Precautionary Matrix** starts with a section to determine the 'nano relevance' of substances, i.e. does the substance contain nano objects (particles, fibres, rods)? Primary particle size and the size of smaller agglomerates <500 nm are taken into account, and even for larger agglomerates (up to 10 μm), nano relevance is identified in case deagglomeration cannot be excluded (either in the body or in the environment). Even for stable agglomerates >500 nm, structural elements (nanoscale side branches) that have nano-specific toxicity when in contact with biological tissues should be treated as nano relevant! In addition, a score is assigned to the level of uncertainty, i.e. lack of sufficient information with respect to the life cycle of the materials.

In the **NanoTool**, 'nano relevance' is not explicitly addressed as a parameter of severity; however, implicitly, only particles <100 nm are taken into account. The level of uncertainty in the scoring system is addressed by assigning a score of 75% of the maximum score for a specific parameter in case of 'unknown' information.

ANSES uses the ISO (ISO/TS 27687; 2008) definition of nanomaterials. A substance is 'nano relevant' in case manufactured nanomaterials are present, either as 'raw' materials or incorporated in a matrix (liquid or solid).

Stoffenmanager Nano follows the same approach as **ANSES** does, i.e. ISO (ISO/TS 27687; 2008) definition and 'raw' materials or incorporated in a matrix (liquid or solid). However, an additional criterion is that the particle should be insoluble. For nanopowders, the SCENIHR definition is used, i.e. primary particle size ≤100 nm and Brünauer, Emmett, Teller

(BET) gas adsorption determined specific surface area (SSA–BET) ≥ (1/ρ) 60 m^2 g^{-1} (SCENIHR, 2010).

NanoSafer focuses on nanopowder products only and uses ≤200 nm (primary particle size) as an inclusion criterion and specific surface area (SSA–BET) ≥ (1/ρ) 30 m^2 g^{-1}.

The **Guidance** defines nanoparticles as having three dimensions in the range of 1–100 nm, and fibrous particles as having two dimensions in the nano range of 1–100 nm. It states that this information should be available either from the Material Safety Data Sheet or the Technical Data Sheet of the product.

Size and solubility are major hazard banding parameters that are addressed, either in the decision to assign a 'nano relevance' to the MNM or as an 'independent' parameter. The **Precautionary Matrix** does not address solubility as a hazard parameter as such, but it is implicitly addressed in the parameter stability (half-live) of the MNM in the body (or environment). The application of the size parameter has been discussed above; however, for non-specific nanoparticles, the size range <10 nm is considered to result in the highest reactivity.

In the **NanoTool**, solubility is a hazard parameter, where (water) insoluble/poorly soluble MNMs were assigned with the highest severity points. However, severity points are assigned to soluble MNMs as well, but to a lesser degree. In addition, size as such is considered to be a separate hazard parameter; however, the severity points for particles between 40 and 100 nm are zero.

ANSES uses solubility, more specifically dissolution time >1 h, as an increment factor, i.e. adding one hazard band. Size as such is not considered to be a separate hazard parameter.

Stoffenmanager Nano uses (water) solubility (< 0.1 g l^{-1}) as an inclusion criterion for further consideration. MNMs with known solubility >0.1 g l^{-1} will be redirected to the conventional Stoffenmanager to proceed the risk prioritization (not nano specific). In addition to the size criterion for definition of MNM, size, more specifically particle size ≤50 nm, is used to increase the hazard band.

NanoSafer only uses size (and density) to recalculate the Occupational Exposure Limit (OEL) of the bulk material to allocate hazard bands (see classification and labelling of parent/bulk material).

The **Guidance** does not use size as an additional criterion for hazard banding, apart from the definition. Water solubility (>0.1 g l^{-1}) is used as criterion to allocate the lowest hazard band.

Biopersistency and shape are addressed by all CB approaches, however, not always as distinct (hazard) parameters. The **Precautionary Matrix** does not cover biopersistent fibres (length >15 μm); however, shape is partly captured by assigning a high score of nano-specific (redox and/or catalytic) activity.

In the **NanoTool**, shape is a distinct hazard parameter, where tubular, fibrous MNMs are assigned with the highest severity points, and compact/spherical MNMs have no severity points.

ANSES refers to the definition of the WHO on biopersistency (aspect ratio) and assigns the highest hazard band to biopersistent-fibrous MNMs.

Stoffenmanager Nano follows the same approach as **ANSES** does and also uses the definition that the fibres should exceed a length of 5000 nm, with the other two dimensions <100 nm. Such fibres fall into the (two) highest hazard bands. **NanoSafer** defines (biopersistentfibres) with aspect ratio (≥1:3), diameter <3 μm, length >5 μm and classifies fibres into the highest hazard band with a relative hazard score of 1.

The **Guidance** does not explicitly refer to aspect ratio; however, it refers to potential effects by describing fibrous, non-soluble nanomaterials 'for which asbestos-like effects cannot be ruled out, e.g. single- and multi-wall carbon nanotubes'. This type of MNM is assigned to the highest hazard band.

Surface chemistry, redox potential and reactivity are other hazard parameters that are used. The **Precautionary Matrix** assigns scores to nano-specific (redox and/or catalytic) activity. Some examples of nanoparticles are given with low reactivity, e.g. TiO2, silica coated, or high reactivity, e.g. TiO2, uncoated.

In the **NanoTool**, the surface activity is addressed as an individual severity factor.

ANSES assigns a higher hazard band in case of evidence of higher reactivity of the MNM compared with the bulk material.

The **Stoffenmanager Nano**, the **Guidance** or the **NanoSafer** does not address surface chemistry/redox potential/reactivity as such; however, **Nano Safer** assigns MNMs that are functionalized with a relative hazard of 0.75, comparable with the relative hazard assigned to MNMs with an OEL of the parent material <1 mg m^{-3} (high toxicity).

Classification and labelling/toxicological profile of the parent/bulk material is an additional parameter that contributes to the hazard banding in CB approaches, except for the Precautionary Matrix. In the **NanoTool**, carcinogenicity, mutagenicity and/or reproduction toxicity (CMR), and general toxicity and dermal toxicity of parent material are used as distinct parameters with assigned severity points.

ANSES uses the classification, according COSHH-Essentials tool (Brooke, 1998), of either the bulk material or an analogous substance as the starting point for the hazard banding process if the MNM is not a biopersistent fibre. Hazard parameters such as dissolution time and reactivity may increase the hazard band.

In **Stoffenmanger Nano**, the classification of the parent material is used in case MNM-specific data are lacking (and in case the MNM is not a biopersistent fibre). In case of carcinogenicity, mutagenicity, teratogenicity (CMR) classification or sensitization, the highest hazard band (band E) is assigned, whereas in all other cases, the one but highest hazard band (D) is assigned for particles ≤50 nm and band C for MNM with particle size >50 nm. **NanoSafer** implicitly uses the toxicity profile of the bulk material because the OEL of the bulk material is used in the process of assigning a hazard band. More specifically, the OEL is used for a pre-classification, e.g. OEL < 1 mg m^{-3} = high hazard, relative score = 0.75; >1 mg m^{-3} = low hazard, relative score = 0.2.

The **Guidance** does not consider the toxicological profile of the parent/bulk material for hazard classification of the MNMs. However, in case the parent material has been classified as CMR(S) substance, the user is notified to comply with the appropriate legislation.

As shown earlier, both the **Precautionary Matrix** and the **Nano Tool** address the uncertainty either as a separate issue (**Precautionary Matrix**) or as to assign 75% of the highest severity points in case of lack of information. The other CB approaches implicitly address the uncertainty by applying a (very) conservative approach in the process of allocating hazard bands.

Assigning of hazard bands. The **Precautionary Matrix** does not allocate a hazard band as such, but rather adds the scores of the nano relevance, uncertainty and potential effects. In the CB **Nano Tool**, the severity points are added (max score = 100). Four hazard bands, equally divided over the range of severity scores, are distinguished.

ANSES uses five hazard bands; the maximum hazard band is used for biopersistent fibres; the allocation of the hazard band of other MNM is based on the classification of the bulk (or analogous) material, using the COSHH-Essentials classification scheme, and an increment based on the hazard parameters. In case of lacking specific information on the MNM, it is impossible to allocate the lowest hazard band.

Stoffenmanager Nano also uses five hazard bands; the highest is used for persistent fibres, and MNM with indications for (CMRS, or in case of lacking information a similar classification of the parent material. In case of lacking specific information on the MNM, it is impossible to allocate the two lowest hazard bands.

The allocation of hazard bands in **NanoSafer** is slightly more complex compared with the other CB approaches. Four equally divided hazard bands are distinguished, expressed as a relative hazard score ranging from 0 to 1. (Persistent) fibres are assigned with relative hazard index of 1 and fall automatically in the highest hazard band, whereas (not functionalized) MNMs with parent materials that have an OEL >1 mg m^{-3} fall into the lowest hazard band. Functionalized MNMs, and/or MNMs with parent materials that have an OEL of < 1 mg m^{-3}, are assigned with a preliminary hazard index of 0.75. However, based on the underlying R-phrases, the hazard index may decrease to 0.26.

The classification of MNM by the **Guidance** according to three hazard bands is relatively simple and depends on a few properties because (bio persistent) fibres are classified in the highest of the three hazard bands, whereas water-soluble particles are classified in the first hazard band. All other MNMs (particle size between 1 and 100 nm) are classified in the mid-band.

PROBABILITY OR EXPOSURE BANDING

In general, (inhalation) exposure can be described as the result of a series of processes that determine the transfer of an aerosol from the source, through emission, via the transmission compartment to the receptor (i.e. worker, consumer). This source-receptor approach for workplace aerosols has been described by Cherrie and Schneider (1999) and has been recently modified for nano aerosols by Schneider et al. (2011). Briefly, it is assumed that the potential for emission is determined by both the substance emission potential (e.g. dustiness or mistiness) and the level of energy related to activities, defined as the activity emission potential. The transport of the aerosols is modified by segregation of the source from the work environment, local controls (e.g. local exhaust ventilation), dispersion by general ventilation and loss by deposition resulting in surface contamination. At the receptor, the worker can be separated from the workplace air by a cabin) or by using personal protective equipment (e.g. a respirator). Both determine what part of the concentration of MNM in the workroom air will result in actual personal exposure of the receptor, i.e. worker or consumer. The conceptual model for the assessment of inhalation exposure to MNM (Schneider et al., 2011) offers also a framework to evaluate various emissions or releases by identifying four so-called source domains: (1) point source or fugitive emission during the production phase (synthesis) prior to harvesting the bulk material,

(2) handling and transfer of bulk MNM powders, (3) dispersion of either intermediates containing highly concentrated MNO (>25%) or application of (relatively low concentrated, <5%) ready-to-use products, (4) activities resulting in fracturing and abrasion of MNM-enabled end-products at work sites such as machining.

The conceptual model and its framework will be used both to indicate the domain of application of the various CB approaches with respect to exposure and to indicate what determinants (i.e. emission, transmission, immission) have been covered.

The **Precautionary Matrix** takes the so-called 'physical surroundings' (i.e. the physical state of the MNM either as 'free' aerosols or particles or as matrix-embedded particles) as a starting point to assess the potential for exposure. Predefined values are assigned to these physical surroundings to indicate the availability for exposure to humans or input into the environment. The next step is to estimate the maximum possible 'exposure' by assessing two parameters, i.e. the amount of MNM handled and the frequency. In view of a conceptual model approach, the factor 'physical surroundings' reflects the substance emission potential, whereas amount and frequency reflect the activity emission potential. With respect to the 'applicability domains', it is likely that implicitly source domains 1–4 are covered.

In the CB **NanoTool**, parameters related to emission potential are dustiness/mistiness (substance emission potential) and amount of MNM handled (activity emission potential). Operations resulting in emission classified as Extremely Unlikely are handling of matrix-embedded MNM or non-agitated liquids. It is likely to assume that Schneider *et al.* (2011) source domains 3 and 4 are not addressed by this tool. In addition, frequency and duration of operations are other parameters that affect the probability of exposure. The number of employees with similar exposure is another parameter that is addressed. This parameter is an integrated part of the probability score (max score = 100). The four probability or exposure bands are equally subdivided over the rangeof exposure scores.

ANSES covers emission potential by initial banding based on the physical state of the material, ranging from solid (exposure band 1) to aerosol (exposure band 4). Further modification of the bands (increment) is possible either due to the substance emission potential or due to the process operations (activity emission potential). **ANSES** covers the source domains 2–4; however, it is unclear whether the emission during synthesis (domain 1) may be covered as well.

Stoffenmanager Nano, similar to the Stoffenmanager for conventional substances (Marquart *et al.*, 2008), follows the source-receptor approach of the conceptual model (Schneider et al., 2011), which includes addressing factors that affect emission (potential), transmission and immission. It explicitly addresses the distinct source domains by proposing multipliers (or scores) for different types of activities within these source domains. However, for an evaluation of source domain 4, the user is redirected to the conventional Stoffenmanager. All multipliers of the modifying factors are fitted into an exposure algorithm (for both near-field and far-field sources of exposure). The resulting scores are allocated (on the logarithmic scale) to one of the four exposure bands.

NanoSafer exclusively focuses on handling of nanopowders. According to modified existing models, using the amount of powder handled, the activity level, e.g. the fall height in case of powder dropping, and the dustiness index of the powder, an emission rate is calculated. In more complex models, the emission rate is used to calculate the particle concentration in the near field and the far field by including ventilation factors. The most interesting part, since it actually links the exposure bands with the hazard bands, is that the allocation of the exposure band is based on the ratio of the OEL of the bulk material. The latter is recalculated to surface area concentration assuming all particles are 200 nm, and the particle concentration at the receptor is expressed (calculated) as a surface area concentration. The five exposure bands represent ratios between <0.1 (lowest) and >1.0 (highest).

Guidance uses three bands for possible exposure, based on the user estimates; the lowest band is allocated in case emission can be excluded due to the use of 100% closed system. The highest band is used for activities where emission of primary nanoparticles is possible, e.g. during production (source domain 1). The mid exposure band is used for exposure scenarios where emission would be possible of larger particles (100 nm–100 μm) composed of nanoparticles embedded in a solid or a liquid matrix, i.e. during weighing or adding nanomaterials (source domain 2), or spraying and sanding of nanoproducts (source domains 3 and 4, respectively). Clearly, only emission potential is considered for the allocation of the bands; however, it can be argued whether a 100% closed system is an emission potential or an implemented control measure.

In summary, the exposure bands are allocated based on the emission potential by the **Precautionary Matrix**, the CB **Nano Tool**, the **ANSES** and the **Guidance**, whereas **Stoffenmanager Nano** and

NanoSafer present (personal) exposure estimates generated by underlying source-receptor models, which include emission potential, the transmission mechanism and its modifying factors (such as ventilation, LEV, etc.). In the other tools, these factors are listed as control measures.

CONTROL OR RISK BANDING

In all CB approaches, the outcome of the hazard and the exposure banding are combined. However, in most cases, both hazard and exposure bands use independent ordinate scales that are not inter-linked. Two exceptions can be distinguished, the **Precautionary Matrix** and **NanoSafer**.

As previously indicated, the **Precautionary Matrix** does not distinguish hazard and exposure bands, but links estimates and parameters together into a score. The total score is subdivided into two categories (or bands) for further action: (1) nano-specific action low/not needed (total score ≤ 20) and (2) nano-specific action needed, i.e. review existing or evaluate new measures (total score >20).

Nanosafer distinguishes five risk levels, based on the combination of the five exposure bands and four hazard bands. The four hazard bands are related to the toxicological profile (of the bulk material) or reflect a precautionary approach. The risk levels are linked to control measures. Apparently, the exposure bands are leading for risk classification because the highest risk level is assigned for the highest exposure band, despite the level of the hazard band. However, because the exposure band is based on the ratio of the OEL and the actual exposure, it makes sense to allocate the highest risk band in case of ratios >1.

The CB **Nano Tool** links the hazard and exposure bands, which have the same ranges of scores into four risk levels, and consequently to control bands linked to the risk levels. The hazard band seems to dominate the allocation of the risk level because, e.g. the combination of the highest severity level and the lowest probability results in one but highest risk level (RL3), whereas the combination of the highest probability band with the lowest severity level results in the allocation of RL2.

In **ANSES,** the five hazard and four exposure (emission potential) bands are directly linked into five control bands. Definitely, the hazard band is dominating the allocation of the control band (or risk level) because the highest hazard band, e.g. in case of persistent fibres or lack of information, requires the highest control band independent of the exposure band.

Stoffenmanger Nano combines the five hazard bands and the four exposure bands into three risk prioritization bands. Similar to **ANSES**, the highest hazard band is associated with the highest risk priority, independent of the exposure band. Because the lowest two hazard bands can only be allocated to fully toxicologically characterized MNMs, it is likely that currently the lowest risk priority will only exist for the lowest exposure band.

The **Guidance** links the exposure and hazard categories into a decision matrix, which should be created for each different activity/MNM combination. Three levels of control are distinguished of the lowest refers to commonly used measures for control to comply with legislation. The level refers to the hierarchy of control, where all technical and organizational control measured should be evaluated on their economical feasibility. For the highest level of control, the condition of economical feasibility is not valid due to the precautionary approach. For fibres, the one but highest control level would be possible for closed systems.

CONCLUSION

The CB approaches presently discussed represent a wide panel of methods to indicate or prioritize risks related to the use of MNMs. At one side of the spectrum, the **Precautionary Matrix** guides potential producers, users, etc. to identify the precautionary need during production, use and waste disposal with respect to human and environmental exposure. On the other side, the **Nanosafer** tool focuses on specific occupational powder-handling scenarios and provides a close-to 'semi-quantitative' risk evaluation. This spectrum also indicates the range of different target groups of users and applicability domains.

The required input information for the various tools will affect the level of occupational health expertise needed to 'run' the tools. CB **NanoTool** specifically focuses a preliminary qualitative risk assessment for research activities and facilities with relative small-scale use of a wide variety of MNMs. The information that is required for the hazard banding is rather specific. The other tools, except the **Precautionary Matrix**, focus more on industrial scale use (and production) of MNM. **ANSES**, **Stoffenmanager Nano** and **Guidance** rely on the use of currently available hazard classification systems and in case of **Stoffenmanager Nano** and **Guidance** also rely on relatively easily to retrieve information provided, e.g. by Material Safety Data Sheet (MSDS) by MSDS and Product Information sheets. However, these sources of information should be used with the caveat that the information is incomplete. Recently, Lee *et al*. (2012) evaluated the quality and accuracy of 97 safety data sheets (SDSs) on nanomaterials and found that most of the SDSs did not include sufficient information on the safety of nanomaterials.

In order to get a more detailed tool output, **NanoSafer** requires much more detailed information, especially with respect to the substance and the workplace. From the perspective of level of details and applicability for a wide range of activities, **ANSES**, **Stoffenmanager Nano** and **Guidance** seem to be the most robust tools. CB **Nano Tool** and **ANSES** explicitly recommend or require involvement of experts in the evaluation of the CB process, whereas **Stoffenmanager Nano** and **Guidance** focus on the use by non-professionals. However, with respect to the unknown reliability of information, and without an established elicitation procedure to estimate the likelihood of emission in case of **Guidance**, the tools may not properly account for nano-specific factors . This underlines that the tools are first-tier assessments and further consultation of experts should be encouraged.

The methods and the appraisal of the parameters considered to allocated hazard bands differ between the CB approaches; scoring versus a decision tree (binary system), and the high concern related to fibres in **ANSES**, **Stoffenmanager** and **Nanosafer**. The decision tree affords to set upfront priorities by a high-concern substance, e.g. a fibre, or by a single hazard parameter, e.g. carcinogenicity, whereas in the more balanced scoring system, the effect of high concern might be damped because no more maximum points can be assigned to a single hazard parameter, e.g. particle shape.

The uncertainty of the toxicology and exposure of MNMs has been made operational in different ways. The **Precautionary Matrix** assigns a distinct set of parameters with respect to uncertainty (lack of information), whereas the CB **Nano Tool** assigns 75% of the maximum severity points for the specific parameter. The other CB approaches make uncertainty and precautionary approach operational by assigning high hazard bands, and consequently high risk or control bands, in case of lack of information.

Stoffenmanager Nano and **Nanosafer** enable a more detailed assessment of exposure; however, the underlying exposure models, including the assumptions for the efficacy of control measures, have not been validated so far (Schneider *et al.*, 2011). Precautionary Matrix and CB **Nano Tool** offer downloading of a spreadsheet to run the tool, whereas **Stoffenmanager Nano** and **Nanosafer**, being specifically designed web-based tools including libraries, have the advantage of the easy accessibility and guided use (although currently **NanoSafer** is only available in Danish language). The **Guidance** as such is also a simple and easy-to-use tool. The easiness of use, however, may introduce the caveat of misinterpretation of tool entries or outcomes by non-expert users.

In conclusion, it can be stated that a more thorough look at the various CB approaches yield more differences than a first-glance observation. At present, it is impossible to evaluate the performance of the approaches. Uncertainty and a precautionary approach seem to result in a rather conservative allocation of hazard bands, and consequently high levels of risk and control. Validation of the CB tools for nanomaterials has not been published so far; however, the CB **Nano Tool** outcomes have been compared with occupational hygienists' evaluations and show a good agreement (Zalk *et al*., 2009).

Overall, modifications, adjustments and validation of the various CB approaches will be expected in the next few years because new research initiatives arise, which are focused on the comparison of CB models. In addition, new information will become available, e.g. toxicological and exposure data and data on the effectiveness of control measures, or reliable models to predict hazards or exposure. Expert elicitation may be used to bridge knowledge gaps and improve the tools meanwhile. However, all CB tools explicitly state that the use of their approach should never replace a comprehensive risk assessment by experts.

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