Nanomaterials, a New Challenge in the Workplace

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Abstract

Nanomaterials are a nanotechnological product of increasing importance given the possibilities they offer to improve quality of life and support sustainable development. Safe management of nanomaterials is needed to ensure that this emerging technology has the highest levels of acceptance among different interest groups, including workers. This chapter reviews the current state that presents the different stages of risk management applied to nanomaterials, including standardisation, regulation, risk assessment and risk control. Particularly, the chapter contextualizes the development of nanotechnologies at European level and analyses the scientific evidence available on the risks derived from nanomaterials use. Furthermore, it highlights the required conditions to encourage the responsible development of nanomaterials, as well as reflects on the lack of consensus in terms of approaches and frameworks that could facilitate standardisation adoption, regulatory enforcement and industry intervention concerning nanomaterials.

Keywords

Health and safety · Nanoparticles · Risk assessment · Risk management

15.1 Introduction

Nanotechnology is presented as one of the greatest technological revolution of our time [31]. By manipulating the materials at scales from 1 to 100 nanometers, new properties are achieved which gives nanotechnology considerable potential for its development and application in various sectors of the industry, including chemistry, pharmaceuticals, cosmetics and electronics. This is a field full of opportunities that can significantly enhance human lives by providing improvements in medicine, creating new jobs, etc. Continuously new fields of application are discovered which could also lead to improvement in the environment, such as air pollution control or wastewater treatment.

The application of Nanotechnology and the usage of synthetic or artificial nanoparticles, however, can pose a risk to health, safety and to the environment, as already highlighted by several studies found in the literature review (see [13, 57, 85]), and thus requiring a close assessment and control in its management. Nanomaterials (NMs) can be design or produced in a variety of sizes and forms, as well as with a

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variety of surface modifications, or with their chemistry being changed too. Changes in these parameters may result in different nanoforms.[1] Due to differences in physicochemical parameters, nanoforms constituted by the same substance might potentially show distinct hazardous characteristics [20]. The lack of understanding regarding the mechanisms of effects of NMs makes necessary the assessment of their hazards and risks on a case by case basis [80].

Due to the numerous advantages, in the coming years, a great development of the use of nanotechnologies is expected, which will increase the number of workers exposed to nanoparticles [24]. Currently, specific regulatory occupational exposure assessments (OELs) for NMs have not been established by the EU or by any national authority and it is expected that it may take a long time before OELs have been derived for all highly diverse frequently used NMs. This is mainly due to the still existing large gaps in knowledge on particle toxicology, the high diversity of the newly developed, and used, NMs, the uncertainties about their hazardous nature and the on-going discussions on the metrics to be used for the nano-OELs e.g. mass-based or particle number based [67].

Therefore, due to the lack of uncertainties that still exist yet around of the nanomaterials, their management in the workplaces thus becomes a challenge for regulators, industry heads and occupational safety professionals. A certainty that exists is that a safe, integrated and responsible nanotechnology production and utilization strategy is necessary. In this chapter a literature review and the identification of challenges link to existing risk management framework and applications to occupational settings is performed, from both a technical and practical perspective. The aim is to understand whether the current risk management approaches are suitable for different organisations and whether it could be adapted and enhanced to make it more effective if that was necessary. This chapter summarises a set of information regarding the risk management of NMs in the workplace, namely, the current applicable legislation, the existing standards, the available risk management tools and the great challenges associated with the lack of nanomaterials data and information.

To this end, the chapter has been structured into four sections. Section 15.2 addresses the risk management standards landscape and the regulatory aspects for nanomaterials within the European Union (EU). Section 15.3 refers to the risk Assessment process and the three phases involved: hazard characterization, Exposure Assessment and Risk evaluation. Finally, Section 15.4 covers the risk treatment based on the hierarchy of controls applied to nanomaterials: elimination and substitution; engineering controls; administrative controls and personnel protective equipment.

15.2 Risk Management Frameworks: Advances in Standardisation and Regulation

Standardisation and regulation on health and safety (H&S) management for nanotechnologies is still on going. Some aspects related to the standardisation of nanotechnologies that are still under development include aspects such as: (1) clear definition of nanotechnology and requirements for users, (2) support legal issues (e.g. exposure assessment, hazard identification, labelling, Safety Data Sheets (SDS/MSDS); (3) promote H&S practices within organisations; and (4) define criteria for conformity assessment. According to the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) report [3], the relevance of standardisation and regulation can be helpful in tackling some of the following issues: (1) expand traditional standards frameworks to include nanomaterials properly; (2) reduce knowledge gaps regarding the hazardous properties of NMs, (3) adapt and recommend H&S measurement and methods applied to NMs; (4) to better assess risk control effectiveness, and (5) safeguarding robustness and consistency

[1] See the definition of nanoforms in Annex VI on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation [22].

across international standardisation bodies and users. The following subsections discuss the advancement and challenges regarding the standardisation and regulatory processes of risk management involving NMs.

15.2.1 Risk Management Standards Landscape

Technological developments, such as nanotechnologies, have to face different kind of factors and influences, internal (organizational) and external (from stakeholders), that create uncertainty about whether or not they could achieve the objectives for what they were created [50]. The effect of these risk could be managed though their identification, analysis and evaluation in order to satisfy a control criterion. To support these processes, different strategies and methodology for risk management have been presented in international standards. Particularly, the ISO 31000:2018 standard is the main reference regarding how to achieve risk management in a systematic way [47]. However, the specifics on how to respond to the uncertainties associated with nanotechnology, particularly as it is emerging technologies and which we have little information, require greater attention for its management [65].

International standards and relevant documentation, such as technical specifications, technical reports, and guidance materials, are currently being established for nanotechnologies, through the technical Committee TC-229 of the International Standards Organization (ISO), as well as the OECD's Working Party for Manufactured Nanomaterials (WPMN) [49, 77]. At the EU level, the H&S standard development is led by the European Committee for Standardization (CEN), more precisely by the technical committee (CEN/TC) 352 on nanotechnologies and supported by "CEN/TC 137 – Assessment of workplace exposure to chemical and biological agents" and "CEN/TC 195 – Air filters for general air cleaning". The role of these bodies compasses the understanding of what effects nanotechnology might have on health and the environment, including standards focused on the areas such as vocabulary, classification, nanometrology, measurement equipment, testing and characterisation, models development; and H&S guidelines [11].

Table 15.1 shows the approximate number of published standards related to:

1. Nanotechnology concepts and vocabulary (e.g. ISO/TR 11360:2010);
2. Nanomaterials characterisation, including physico-chemical characterisation (e.g. ISO/TR 10929:2012; ISO/TR 16196:2016);
3. Hazard identification, including safety and toxicity parameters (e.g. ISO/TR 13014:2012);
4. Exposure assessment (e.g. ISO/TR 18637:2016);
5. Risk management and/or assessment frameworks (e.g. ISO/TR 12885:2018); and
6. Other aspects such as waste management, product labelling and life cycle assessment (e.g. ISO/TS 13830:2013).

Table 15.1 Published standards and guidelines on nanotechnologies by international and European standardisation and policy development bodies (as for may-2020)

Standardisation body	ISO/TC 229	CEN	OECD – WPMN	Others
Standard category				
Concepts and vocabulary	21	13	–	
Nanomaterials characterisation	60	10	5	
Risk management framework	4	3	7	1 (IEC)
Hazard identification	19	3	9	
Exposure assessment	6	13	13	
Others (Product C&L / lifecycle)	2	7	–	
Total (by may/2020)	112	49	34	

The total number of ISO standards published by this committee is 112 (May 2020), of which 54% have focused on aspects of characterization of the NMs. However, many of these published standards indirectly provide valuable information for risk management. For their part, CEN and OECD have focused on developing standards that directly respond to H&S aspects, mainly exposure assessment. A detailed list of the standards included in this analysis can be consult in https://bit.ly/NMsStandards2020. Current publications by OECD WPMN programme are guidance documents rather than standards. Whilst OECD does publish standards and is pioneering in the nanotechnology field, there are no relevant published standards on H&S aspects, and it is expected the publication of future standards by OECD [44].

Based on the current landscape for H&S standards for nanotechnologies, the following key aspects can be highlighted:

- **Risk assessment for nanotechnologies:** Whilst data on hazardous properties and monitoring methods is currently under development, employers are forced by labour law to manage exposure to NMs in an effective level. Considering the lack of information regarding NMs hazardous and exposure routes, risk assessment is a practical approach to undertake (e.g. control banding evaluation is one way to undertake a risk assessment that have been standardised in ISO/TS 12901–2:2014).
- **Exposure Standards:** This type of specific standards covering NMs are still limited, however they are key in supporting regulation development. Furthermore, there is a need to create standards to assess NMs when they are embedded as part of a matrix or in a nano-based product.
- **Verifying conformity with standard practices:** In order to ensure conformity with standard practices, measurement of exposures and emissions will be required. If potential NMs exposure is identified, the continuation of exposure monitoring is recommended. Nevertheless, this type of standards are not fully developed yet, since most of the available guidelines have been generated for substances in bulk form.
- **Development of standards for nanotechnology H&S control:** Conventional H&S controls (e.g. process insulation or local air extraction) can aid in the prevention of NMs inhalation exposure; nevertheless, monitoring of NMs exposures and emissions is key in supporting H&S management.
- **Material Safety Data Sheets (MSDS) and labelling:** More progress needs to be done with regards to the standardisation to support the preparation of MSDS for NMs, namely the specific content and guidance about what should considered in the different mandatory sections of the MSDS. Labelling of NMs for their utilisation by workers is also an issue of concern. Independently of the size and form of chemical substances, current H&S labelling standards mandate those particular dangerous characteristics to be identified on the labels. As a result, any NMs, or products containing them, needs to be supplied with the corresponding safety statements, pictograms, and warnings. For this reason, hazard information availability is important, including precautionary information for NMs of uncertain hazards.
- **Hazard identification:** Still development needs to be made in provide protocol or guidelines for the determination of hazard characteristics (e.g. flammability) and the ability of the nano-based products containing nano-objects to be a hazardous source. These technical specifications should also provide guidelines on the reception, preparation, and characterization of samples for testing.

Standardisation is important in helping to protect the H&S of workers. A range of international and sectorial related documents are now being developed based on the information gained by research on H&S aspects of nanotechnologies. The focus of the standard development includes, among others, facilitate the design of regulatory framework to cover nanotechnologies appropriately, support toxicology research regarding the hazardous properties of new NMs, develop risk

assessment approaches, and provide guidance on effective workplace controls to support organisations.

15.2.2 Regulatory Aspects of Nanomaterials in the EU

In the European Union, nanomaterials are covered by the same regulatory framework that ensures the safe use of all chemicals and mixtures, more precisely by REACH and CLP regulations. This means that hazardous properties of nanoforms of substances will have to be assessed and their safe use needs to be ensured.

Particularly for NMs and to provide a common basis for regulatory purposes across all areas of European Union (EU) policy, the European Commission has developed the recommendation 2011/696/EU, for a definition of the term nanomaterial [23]. Since its publication, regulatory provisions were adopted in the EU jurisdiction which explicitly address nanomaterials and contain regulatory definitions of the term "nanomaterial". The latter were derived from the EC definition, adopting it either as a whole or in its core parts, for example in the biocidal products regulation (EU) n. 528/2010, the medical devices regulation (EU) 2017/745, the annexes of the chemicals regulation REACH (EC) n° 1907/2006 which were amended in 2018 [91].

Furthermore, in early 2019, two Science for Policy reports were published by the Joint Research Centre (JRC) [90, 91]. In one of the reports, the European Commission's science and knowledge service aims to provide clarifications of the key concepts and terms that are used in the EU NM definition, and discusses them in a regulatory context. The second report addresses the identification of nanomaterials by measurements and discusses options and points to consider when assessing whether a particulate material is a nanomaterial or not according to the definition of nanomaterials.

As was mentioned previously, the existent EU legislation and so the generic rules set in them, independent of the context (environmental, worker and consumer protection), applies in the same way to nanomaterials, as well as for other form of substance, although it does not refer explicitly to them. With regard to European worker protection legislation, the Framework Directive 89/391/EEC, the Chemical Agent Directive 98/24/EC, and the Carcinogen and Mutagen Directive 2004/37/EC [29] are of particular relevance whenever NMs are handled during work activities.

Regulatory decisions regarding chemical substances are commonly based on toxicological properties which in the case of nanomaterials, due to their new and specific properties, may be different when compared to those exhibited by the same substances in non-nano form. This leads to uncertainties about their safety and how to assess their risk properly. The regulatory testing of nanomaterials for safety relies on the use of standardised test guidelines that aim to ensure tests are done uniformly across different labs and deliver relevant and reliable data [89]. Through European initiatives, such as the NANoReg and Prosafe projects (see [38, 112]), and the work of the OECD WPMN, a number of existing Test Guidelines have been identified as requiring adaptation to be applicable to nanomaterials and also the need for new ones. From a regulatory point of view, the resolution of these issues becomes urgent. Taking the REACH regulation as an example, which requires information such as physicochemical, toxicological and ecotoxicological properties for the registration of nanomaterials, it has been observed a need for more test guidelines so companies can provide enough information to demonstrate the safe use of their NMs.

Further research with specific relevance for regulatory questions is needed, such as the enforcement of product labelling for the presence of NMs and indicative occupational exposure limit values establishment, contributing to reduce uncertainties with regards to the safety of NMs and for a greater availability of quality data for regulatory purpose. To this end, best practices, guidelines and assessment practices, and methods for the safety testing of nanomaterials are being developed, which will certainly contribute

to the better management of nanomaterials in the workplace.

15.3 Risk Assessment

Risk assessment is the overall process for the estimation of probabilities and expected consequences for identified risks [82]. It includes three main stages: hazard characterisation, exposure assessment, and risk evaluation. Given the many different nanomaterial types, the potential routes of exposure, nanomaterial characterization issues, limitations in research methodologies, such as time-course and dose-response issues, and inadequate *in vitro* methodologies for *in vivo* standardized and guideline toxicity testing, adequate risk assessments methods and tools for NMs are still under development [113]. The following subsections present the advancement and challenges for the different risk assessment stages for occupational settings.

15.3.1 Hazard Characterization

According Rasmussen et al. [88], the identification and characterization of NMs need more information on physicochemical properties and test methods, when compared with other chemicals in general. A degree of consensus within the scientific community has been reached in recent years, with regards to the structure of the considered properties for the characterization of NMs. These parameters has being classified in three groups [86]:

- Characterization: physical and chemical identification (e.g. composition, impurities, shape, size, size distribution, surface characteristics, etc).
- Fate: biological and environmental fate based on their solubility, hydrophobicity, dispersibility, dustiness, etc.
- (Re)activity: their reactivity, effects of their physical hazards, biological activity, etc.

In order to ensure a safe workplace with regard to the presence of chemical substances, information about their characteristics and hazards must be available to and understood by workers. Normally, information about the hazardous properties of chemicals agents present in the workplace can be obtained from material safety data sheets (MSDS), labels, European commission recommendations, occupational exposure limit values and other sources (peer reviewed data, scientific literature, relevant databases such as PubMed or ECHA, information generated by renowned institutions such as IARC, WHO, HSE, NIOSH, OSHA, ISO, etc.).

MSDSs are the first source of information on how to handle a particular product containing nanomaterials, but the information provided is still non-existent or very limited, specifically in terms of their specific hazards and risks, or incorrectly refers to "bulk material" properties rather than nano [18, 87, 101]. According to article 31 of the REACH regulation [27], the provision of MSDS for nanomaterials is mandatory only for those substances and mixtures that are classified under the CLP regulation [28] or meet the criteria established in Annex XIII of the REACH regulation as being classified as persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB substances). Nevertheless, it is a common practice by the chemical industry to provide a MSDS for non-classified substances/mixtures as well.

MSDS for NMs can be improved through a literature review which includes the latest information about the toxicological data, epidemiological studies, measurement techniques, occupational exposure values, engineering measures, and the most current regulatory requirements. In doing so, the MSDS could provide the best information as possible to the users allowing them to implement the necessary control measures to prevent or eliminate the exposure to NMs and, consequently, protect the health of workers [87].

The European Chemical Agency (ECHA), aiming to enhance the safe handling of chemicals

(including the nanomaterials) while promoting innovation and competitiveness in the EU chemical sector, introduced a dissemination tool "infocard" as a 'first tier' in disseminating information from ECHA's databases. Among the various functionalities of the infocard's user, the following stand out: highlights ECHA's preferred substance name and main substance identifiers in one location, quickly shows the most prominent hazardous and critical properties of a substance, easy access to legislative and safe use information associated with the substance, presents key substance information and permits tracking substances through the RSS feed. This tool can therefore be an important source of information when available hazard assessments of a given nanomaterial are almost non-existent.

According to Sajid et al. [95], there is sufficient evidence that nanoparticles induce toxicity to higher organisms including human and wildlife. Jeevanandam et al. [51] concluded that toxicity of nanomaterials may depend of factors such as dose and time effect, aggregation and concentration effect, Particle size effect, particle shape effect, surface area effect, crystal structure effect, surface functionalization, pre-exposure effect. The availability of occupational and epidemiological data for chemicals, including nanomaterials, is a key aspect of risk assessment. The amount of new chemicals produced and released on the market is about a hundred thousand per year [101]. However, only a small number of them have an established exposure limit values, as an example the publication 2018 TLV and BEIs from the American Conference of Governmental Industrial Hygienists (ACGIH) presents around 700 chemicals with TLV-STEL or TLV-TWA values (short-term exposure limit and time-weighted average, over the 8-hour working day). At the nanoworld, only 56 NMs have OELs proposed values [101]. Table 15.2 presents some of the particle control values (PCV) for some of nanomaterials. This reference values include a range of particle metrics such as mass, particle number concentration and could be national exposure standards set by regulatory authorities, recommended exposure limits, exposure limits proposed by researchers, and Local Background Particle Reference Values based upon background nanomaterial levels [79]. As it can be seen, the suggested values vary enormously, and no consensus exists between the authors.

Beyond human toxicity and eco-toxicity, NMs impose additional risks. For example, Khan [53] refer that one specific potential hazard posed by nanoparticles is their capacity to cause fire or explosion. This is because nanoparticles are almost certain to give a rise to a dust explosion hazard and that due to their large specific surface area, they may well be spontaneously flammable on exposure to air. This is particularly the case with metal nanoparticles as they oxidise easily. Additionally, Bouillard et al. [7] found that with the reduction of particle size, ignition temperature and minimum ignition energy also reduce. This indicates that a higher potential risk of inflammation and explosion is achieved when using nanopowders. In this regard, it was observed that carbon based nanopowders exhibit some propensity to explode while metallic nanopowders can be very reactive, thus delineating potential high explosion risks for facilities manufacturing such powders. However, the impacts of agglomeration on explosion severity and sensitivity for nanopowders were not fully understood through the study. This is why more research needs to be done in order to increase the understanding of NMs hazards.

Given the current limited availability of hazard data for most nanomaterials it will be challenging to establish the toxicological behaviour of specific nanomaterials with any degree of certainty. In most cases it will be necessary to refer to information that has been obtained for similar materials [41]. In this way, the use of a non-testing strategies like read-across in the hazard assessment of nanomaterials is desirable allowing, in due time and at lower costs, to perform the safety assessment of almost all nanomaterials [21]. The identification of physicochemical (PC) properties affecting the hazard potential of NMs is crucial, as it could enable to predict impacts from similar NMs and outcomes of similar assays, reducing the need for experimental (and in particular animal) testing [58, 99]. Furthermore,

Table 15.2 Particle control values of some nanomaterials

Types of nanocarbons	Proposed PCV for NMs	References
Multiwalled carbon nanotubes (MWCNT)	Occupational exposure limit (OEL) air <50 μg/m^3 for 8-hour TWA[a] during a 40-hour workweek	[84]
Carbon nanotubes (CNTs)	Proposed nanoreference values (NRV) <0.01 fibres/cm^3	[109]
Carbon nanotubes (CNTs)	Recommended exposure limit (REL) <1.0 μg/m^3 for 8-hour TWA during a 40-hour workweek	[71] [b]
Carbon nanofibers (CNFs)	Occupational exposure limit (OEL) <0.01 fibres/cm^3	[104]
Carbon nanotube group, SWCNT, DWCNT, MWCNT	Occupational exposure limit (OEL) <30 μg/m^3 for 8-hour TWA during a 40-hour workweek	[68]
TiO_2 (10–100 nm)	Recommended exposure limit (REL) <0.3 mg/m^3 for ultrafine TiO_2 as TWA[a] concentrations (> to 10 hours/day, during a 40-hours work week.)	[70]
TiO_2	Occupational exposure limit (OEL) <0.3 mg/m^3, respirable fraction.	[104]
Carbon black [CAS n. ° 1333-86-4]	ACGIH [c]: 3 mg/m^3 (TWA), for 8-hour workday and a 40-hour workweek.	[43]
Carbon black	Germany – BeKGS527: 0.2 x nano-GBP[d] density in g/cm^3, TWA [d], respirable — If no other relevant information is available	[43]
Carbon black	Germany – MAK[e]: 0.3 x GBP density in g/cm^3, TWA, respirable, 4.0, TWA, inhalable	[43]
Carbon black [CAS n. ° 1333-86-4]	OSHA[f]: Permissible exposure limits (PELS) 3 mg/m^3, 8-hour TWA	[43]
Carbon black [CAS n. ° 1333-86-4]	Recommended exposure limit (REL) 3.5 mg/m^3 (without PAHs [g]; when PAHs are present, NIOSH considers carbon black to be a potential occupational carcinogen.	[43] [74]
Carbon black, ultrafine	Occupational exposure limit (OEL) 0.12 mg/m^3	[55]
Amorphous silicon dioxide	Occupational exposure limits (OELs) 0.3 mg/m^3, respirable fraction, for 8-hour TWA.	[104]
Nanoclays	Occupational exposure limits (OELs) 0.3 mg/m^3, respirable fraction, for 8-hour TWA.	[104]
Low-toxicity dust	Occupational exposure limits (OELs) 0.3 mg/m^3, respirable fraction, 4 mg/m^3, inhalable fraction.	[104]
Granular biopersistent particles (insoluble nanomaterials)	Benchmark exposure level (BEL): 0.066 x bulk workplace exposure limit (WEL) (μg/m^3)	[9]
Non biopersistent granular nanomaterials (1-100 nm)	Nano reference value (NVR): Applicable occupational exposure limits (OEL), workplace exposure limit (WEL) (μg/m^3)	[109]
Soluble	Benchmark exposure level (BEL): 0.5 × bulk workplace exposure limit (WEL)	[9]
Zirconium compounds	Occupational exposure limits (OELs): 5 mg/m^3 (TWA); 10 mg/m^3, ST[h]	[1]

[a]*TWA* Time weighted average, 8 h unless otherwise specified
[b]*NIOSH* National Institute for Occupational Safety and Health
[c]*ACGIH* American Conference of Governmental Industrial Hygienists
[d]Dust of biopersistent nanomaterials without specific toxicological properties and without fibrous structures (carbon black is listed in BeKGS 527)
[e]*MAK* Maximum Workplace Concentration, *DFG* Deutsche Forschungsgemeinschaft
[f]Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELS)
[g]*PAH* Polycyclic aromatic hydrocarbons
[h]*ST* Short Term Exposure Limit

the scientific community needs to continue developing test methods that can characterize certain behaviours of nanomaterials to support read-across strategy.

15.3.2 Exposure Assessment

Occupational exposure can be defined by the direct contact to a potentially harmful chemical,

physical or biological agent as a result of work. Concerning NMs, the primary route of entry to the human body are inhalation, however it can also occur by skin exposure, and ingestion, where the toxicity targets are the respiratory, integumentary, and gastrointestinal systems respectively. While the skin is in generally an effective barrier, the lungs and gastrointestinal tract are more defenceless [45]. In order to find the agent emission, which is defined as the transfer process of liberated NMs to the workplace air, usually expressed as a flow (particles per unit time or area) [56], similarly to other chemical agents, the first phase of NMs exposure characterisation, consists of two steps: first, a workplace survey, to have an evaluation of the processes or operations, including the way of how the agents are handled and, second, the physical form of NMs. The second phase of this exposure characterization is the quantitative evaluation, through liberated agent monitoring. It aims of obtain insights regarding inferences concerning the quantification of the occupational exposure, with the purpose of making comparisons with OELs. For the NMs, all this process should be the same, but the lack of data on workplaces studies and OELs to NMs makes comprehensive exposure assessment difficult.

15.3.2.1 Workplaces/Processes

As referred before, the emission potential of an agent, in this case NMs, it depends (among other issues) on the type of process or handling operation and its ability to release them in the workplace. The likelihood of exposure to NMs during synthesis, production and manufacturing processes is highly dependent upon the type of process and the type of equipment involved in the process. For example, Dahm et al. [14] conducted exposure assessments at six manufacturers and users of carbon nanotubes and nanofibers. This study showed that the highest exposures occurred during dry powder handling tasks including mixing and weighing operations.

In order to ensure the appropriate characterisation of the exposure route, information for workplace and process survey should include: (1) identification of the source domain (SD) and activities related to handling nanomaterials (considering not just exposures during normal routine working but also possible accidental releases and maintenance); (2) identification of the physical form of the NMs in each stage of the work process (dry powder/suspension or liquid/embedded or bound in other materials); (3) identification of the presence of other processes in the workplace that can affect measurements or the measurement strategy employed; (4) identification of the presence or absence of ventilation, heating and air conditioning (HVAC) [25]. For the workplace exposure four SDs were identified by Schneider et al. [97] to describe the different processes: (1) During the production phase (synthesis) prior to harvesting the bulk material, point source or fugitive emission, e.g. emissions from the reactor, leaks through seals and connections, and incidental releases, can take place (SD1), in these cases, discrete nanoparticles and agglomerates will be formed; (2) During the manufacturing of products, the handling and transfer of bulk NMs powders with relatively low energy can release nanoparticles, e.g. collection, harvesting, bagging, bag dumping, bag emptying, scooping, weighing, dispersion/ compounding in composites (SD2); (3) During the application of products (sprays) or dispersion of intermediates containing nanoparticles (SD3); (4) fracturing and abrasion, or other mechanical release of NMs or materials containing NMs, of final products during further processing (SD4).

15.3.2.2 Physical Form

Exposure level to NMs will depend on their ability to be released directly from their dusty form or from the matrix where there are embedded, as well as due to their transformation and degradations characteristics. Different potential exposure scenarios will happen in function of different factors, linked to the nanoparticle reduced dimension, such as their final form in the product, dust generation (emission and dispersion) potential and solubility. The physical form to be considered is that of the material at the beginning of the process at the workstation being evaluated. Four

categories of physical forms have been identified by NRC [75] according to their increased emission potential:

1. Physically bound/ encapsulated (usually the lowest potential exposure).
2. Solid nanomaterials with nanostructures fixed to the material's surface.
3. In suspension in a liquid.
4. In the form of powder (usualy highest potential exposure).

Studies on the Potential Exposure to releases in the machining of nanocomposites revealed that some NMs were often detected (96% of the experimental studies). Base matrices were also analysed, which shown the presence of matrix nanoparticles (92%), and partially embedded nanomaterials among matrix particles were often detected (76%) [34].

15.3.2.3 Quantitative Evaluation and Measuring Devices

As referred above, there is not much information about exposure assessment to NMs, and so at this time, it is not clear which units of measurement associated with exposure to nanomaterials are more important from the perspective of occupational risk prevention. Therefore, the release of airborne NMs to the workplace environments could be measure with different metrics such as mass, number and/or surface area concentration. The understanding of the behaviour of these nanomaterials, when they escape to the workplace, is still very scarce and weak, therefore no international consensus exists regarding the most appropriate metrics that must be applied for NMs environmental monitoring [42] and it is important to be aware about the workplace activities around when measurements are taken like airflows and pressure differentials generated by heating, ventilation and air conditioning systems, by air movements generated when people walk, or by doors opening and closing [78]. After the revision of the guideline limit values existing in different countries at present, the units of measurement applied are based on the quantification of nanomaterials present in the air in the worker's breathing zone: (1) mass, expressed with $\mu g/m^3$ or mg/m^3; (2) number of nanoparticles/cm^3.

Studies refer that particle size plays an important role in determining the potential adverse effects of nanomaterials in the respiratory system: by influencing the physical, chemical, and biological nature of the material, affecting the surface-area dose of deposited particles, and enabling the deposited particles to more readily translocate to other parts of the body [69]. Nevertheless, mass concentration measurements can be a good approach when there is a correlation between the surface area of the NMs and mass concentration determined or if are available toxicity data based on mass dose for a specific NM.

Without harmonized guidance for the characterization of exposure, due to the absence of adequate instrumentation, the lack of appropriate exposure metrics and the lack of quantified exposure limits, considering that the exposure limits that exist are most often a concentration of mass, conjunction of qualitative and a quantitative assessment must be applied to establish the possible release of NMs. Due to the interest in knowing the mass concentration and number of particles and their surface area, the instrumentation used to characterize the exposure varies and is achieved through various sampling instruments designed to capture these metrics. These three metrics can be converted into each other if we are in presence of spherical particles and if the parameters related with density and size distribution are known [78]. Regarding the mentioned instruments they fall into two general categories: "direct reading" and "time-integrated". The former provides "real time" concentration values while the latter requires sampling over a period of time followed by an analysis to determine mass and/or chemical composition [10, 76]. Exposure studies involving count concentrations around the equipment/processes and for personal exposure measurements should chose the direct-reading combination handled instruments, that can afford the metrics, like particle number and size distribution (independently on the chemical

composition or morphology) based on different techniques, such as:

- Condensation Particle Counter (CPC) can measure particle number concentration but not particle size.
- Diffusion Charger (DC) measure the fraction of airborne particle surface area concentration that upon inhalation would deposit in the gas-exchange region, the number concentration, the average particle size or a combination thereof (20 nm to above 400 nm).
- Scanning Mobility Particle Sizer (SMPS) measure particles size distributions down to 10 nm and concentrations up to 1.000.000 particles/cm^3 [108].
- Optical Particle Counter (OPC) assesses real-time number concentration of particles >300 nm in diameter [66].
- Electrical low-pressure impactors (ELPI) Enables the measurement of real-time particle size distribution and concentration in the size range of 6 nm–10 μm.

In order to have the NMs identification and the elemental composition, "time integrated" methods and instruments should be used. Sampling could be undertaken via open-face sampling, filtration, electrostatic or thermal precipitator, size-selective collection by cascade impaction, elutriators, personal samplers, surface sampling and wiping. Subsequent chemical and electron microscopic (EM) analyses (SEM or TEM with Energy Dispersive X-Ray Spectroscopy – EDS) and or X-ray fluorescence/ inductively coupled plasma mass spectrometry (XRF/ICP-MS), Atomic Force Microscopy (AFM) and others used on chemical laboratories, for elemental composition and particle identification [78].

Whenever possible, the measurement strategies should include sampling and laboratory analysis and the use of direct reading instruments to cover all relevant readings (e.g. particle size distribution, particle count and particle surface areas). All of these techniques have limitations in some way the first ones like lack of information on fibres (CPC, DC), the size and weight and complexity of operation (SPMS and ELPI) and lacking real time data output (samplers and laboratory analysis) [36]. The lack of exposure-relevant documented evidence and the use of not-harmonized collected data methods and strategies are the greater disadvantage of this process.

To better understand the exposure assessment, several studies were carried out to the characterization of nanoparticle release. One key aspect of these occupational assessments is the need to distinguish the background and the specifically process NMs release. The main pathways for background characterization that are often used in exposure studies are:

(1) Far-Field (FF) approach: The background measures are taken in a place far from the workplace where NMs are produced/handled in order to be out of the process influence, but in the same facility. If there is a divergence between the background and workplace concentrations, this implies that the NMs process emissions under investigation should be further analysed. FF background measurements should be taken at the same time as workplace measurements.
(2) Near-Field (NF) approach: this is based on monitoring before the start of the task in the workplace. The NF background is also characterised as a "time series" approach, considering that the background concentration is assessed when the task is not occurring, and that any increases in concentration will be attributed to releases from the activity involving NMs [5].

More than 60 exposure characterization to NMs studies were done by "the National Institute for Occupational Safety and Health" (NIOSH). These studies gave NIOSH the needed information to improve an already existing technique, the "Nanoparticle Emission Assessment Technique" (NEAT 1.0), to develop the NEAT 2.0. The latter gives greater importance to integrated time, filter based sampling with elemental analysis and morphology, around breathing zone and area samples, rather than particles counters direct readings, in order to have a exposure job map [19]. NEAT

1.0 was very useful to identify the activities that leads to more nanomaterial emissions in laboratories or pilot plants but, the use of this technique in larger sites do not addresses the potential for transient or background emissions arising from normal plant operations.

Using NEAT 2.0 a quite complete perception on the overall picture of the worker exposure is given because it applies: (1) a collection of time-integrated PBZ (Personal Breathing Zone) air samples; (2) additional time-integrated air samples are collected in the PBZ for identifying task-specific exposure information during that specific task; (3) particle counters are used to supplement providing data information on peak emissions, plus (4) a collection of real-time integrated background data over the course of a full sampling period to detect background fluctuations.

It would be expensive and time consuming to carry out studies with individual exposure measurements for each chemical under every circumstance in view of the large variety of possible exposure scenarios and the amount of available data is still very scarce. When lacking relevant regulatory requirements for NMs and real time exposure data, more qualitative techniques can be implemented to characterize exposure potential. The control banding tools can be used to have an initial understanding to evaluate exposure to NMs in the workplace [97].

15.3.3 Risk Evaluation

As highlighted in the previous sections, the H&S effects of nanomaterials are currently quite unknown (e.g. there is no specific regulation, nor are there approved occupational exposure limits). However, as a potential risk factor at work, organisations still have the obligation to assess and manage NMs, as it is done with any other material introduced into the production process, considering a maximum technical approach. The complexity and level of detail required for the risk assessment depend on the hazardous substance in question and the activity being carried out; even for more complex situations, the help from experts it is recommended [4, 15]. Figure 15.1 shows the different level and kind of tools that support risk assessment based on the evaluation's aim, as well as the origin, reliability and quality of the information used. Exposure estimation can be carried out at different levels or *tiers*, starting with a more exploratory, and even pure qualitative, level to establish the least favourable scenario (Tier 1), and ending up with robust quantitative methods based on probabilistic exposure models or detailed site-specific measures (Tier 3) [78].

In recent years, several tools for assessing occupational risk have been developed. Among the Tier 1 evaluation models based on qualitative or semi-quantitative estimation from environmental concentrations, there are the Control Banding models (CB) [40]. Control banding or simplified tools are models where risk is assessed based on the severity determined through exposure parameters. These methods prioritize action on risk control, without investing excessive resources in evaluating risk in detail using quantitative exposure values. For their part, tier 2 and 3 models, based on quantitative evaluation, correspond to established measurement strategies and methodologies to proceed to obtain suitable values and, as far as possible, to compare them with the reference limit values [8]. Table 15.3 provides a summary of the most widely used nanospecific tools.

15.3.3.1 Control Banding Tools

Control banding (CB) tools calculates the severity of a task that involves NMs when information from several factors based on the physicochemical properties of the nanomaterial (surface chemistry, particle shape and diameter, and solubility), toxicological properties of the nanomaterial and the "bulk" material (carcinogenicity, toxicity to the reproduction, mutagenicity, dermal toxicity and ability to produce asthma) [96]. Probability levels are also calculated from factors such as estimated amount of nanomaterial during the task, dustiness or ability to form mists, number of workers with similar exposure, frequency and duration of the operation. When combining the severity and probability scores, a decision matrix is obtained that leads to a risk level value [16].

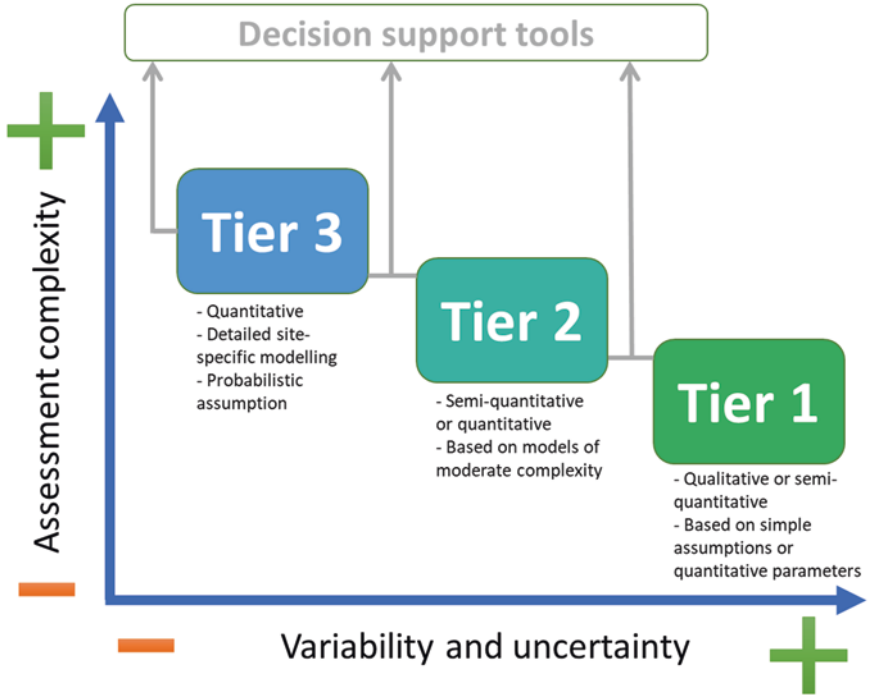

Fig. 15.1 Classification of risk evaluation tools by tiers

Table 15.3 Tiered approach tools for risk evaluation

Level	Description	Tools examples
Tier 1–2	**Control banding (CB):** (1) qualitative & semi-quantitative models. (2) based on the precautionary principle. (3) workplace safety only. *Note: There are additional CB tools that use a life-cycle approach that involve environmental and consumer aspects (also refer to as risk screening tools), however, they are out of the scope of this chapter.*	CB Nanotool [115], ANSES CB tool [81], Stoffenmanager Nano [110]
Tier 2–3	**Occupational exposure: (1)** quantitative exposure models. (2) tools based on refined information, including hazard assessment and physicochemical characterization. (3) additional tools include models to assess kinetic for human internal exposure (post-exposure risk assessment).	Nanosafer [52], ART [32], DART [37], NanoRiskCat [39], PBPK "kinetic" [105]
	RA high level models: (1) high tier quantitative models. (2) requires expertise to apply them. (3) based also in detailed information of occupational exposure, hazard assessment and physicochemical characterization.	GUIDENano [83]
	Hazard assessment: (1) determine health effects based on NMs concentrations. (2) types: In vivo (observational) and in vitro (cell) protocols. (3) in silico (computational) models. (4) it can also be applied at the kinetic level	NanoVALID – in vivo [6], EURO-NanoTox – In vitro [94], QNAR – In silico [114]
	Physicochemical characterisation: (1) protocols to characterise different physicochemical properties at each lifecycle stage	NANOREG [38]
Others	**Decision support tool:** (1) evaluation of models results in order to recommend courses of action. (2) determine and weigh benefits versus risks	LICARA [111], SUN DSS [64]

Table 15.4 CB tools specific for occupational exposure assessment

Tool	Target group	Comments	Inputs requirements	Number of bands		
				Hazard	Expos.	Risk
ANSES CB tool	All working environments	Scope considers solids, liquids, powders and aerosols. It also includes a risk control band.	Low	5	4	5
CB Nanotool 2.0	Laboratory-scale work	Risk levels include a recommended control approach.	High	4	4	4
NanoSafer	SMEs	It can be used for NMs in powder form. Assessment for NMs production, products containing them, and accidental emissions	Medium	4	5	5
Stoffenmanager Nano	All working environments	Scope considers insoluble NMs. It gives priority to the hazard assessment. It provides control measure recommendations.	High	5	4	3

Table 15.4 shows a comparison between the different CB tools available for occupational risk management:

CB method can provide an alternative risk assessment and management process, grouping workplaces with similar hazards and/or exposures into similar categories. Due to its relative simplicity and ease of application, CB can be an alternative/complementary tool to traditional occupational risk assessment, especially attractive for SMEs [63]. However, one of the biggest challenges in applying this tool to NMs lies in making decisions about assigning the hazard and exposure bands. Therefore, the successful implementation of this approach in any organisation still requires technicians with proven experience and competence in risk management and more specifically, in those issues directly related to the NMs used in industrial processes. Another issue associated to CB is the fact that it corresponds to a first screening for risks management. In the case when a high-risk band is selected, it will be required to refine the assessment with tier 2 or higher tier methods and also the best the effectiveness of the controls once implemented. Additionally, and depending on the role an organisation has in the NMs chain (development, manufacturing, use or disposal), we will need to use additional and more specific tools. For example, to fulfil REACH requirements, NMs producers will have to undertake a specific risk characterisation following the guidelines established in the ECHA R-series such as Riskofderm or Advanced REACH Tool – ART [61].

In general, the risk assessment techniques are designed to accomplish similar goals (e.g. hazard characterisation, exposure estimation, or risk valuation). Their specifications, on the other hand, differ significantly (i.e. data requirements, results, and scope of application). This makes an integration of the different tools into a unified framework difficult. Furthermore, risk assessment tools have been developed in major research projects (e.g. H2020), but most of them have not been calibrated and/or validated due to scarcity of relevant experimental data.

15.4 Risk Treatment

Due to the limited information about the health risks associated with occupational exposure to NMs, appropriate steps should be taken to minimize the risk of worker exposure through the implementation of a risk management program [69]. The application of controls aims to make sure that occupational exposure is as low as possible. This exposure should be minimized through measures such as excluding the use of certain substances, replacing them with less hazardous ones or changing the process to a safer one as far as reasonably practicable [46]. Risk assessment should help to decide the appropriate control,

Fig. 15.2 Sustainable and safe by design (SSbD) approach

taking account of necessity, practicability and cost. In all cases, selection of controls should as a minimum be based on national regulatory requirements and supplemented with additional controls, as appropriate [103].

Application of the precautionary principle does not imply that organizations should not use nanomaterials until H&S hazards are fully understood. Precautionary actions should be determined according to the assessment of possible consequences of the nanomaterials used, including the consideration of available hazard information and the concomitant uncertainties [65]. One way to incorporate precautionary principles from the design of product is through a sustainable and safe-by-design (SSbD) approach. SSbD consists on applying safety and sustainability principles and strategies on the process and products from the earlier stages of design and considering the full life cycle [100]. Particularly, the nano-specific SSbD approach is a risk management strategy in which the principal goal is to try to balance the safety of a nano-enable products, over its lifecycle, while achieving commercially viable performance and functionality [54]. There has been growing research into the knowledge and various methods and tools that could support the implementation of a safe innovation approach, specifically in the context of nano-enable products from the several industrial sector [62]. Some examples of recent European research projects focusing on SSbD aspects include ProSafe, NanoMile, EC4SafeNano, NANoREG and NANoREG II [93]. Particularly, the latter presents the most comprehensive approach to the safer development of nanomaterials. Using the Cooper's Stage-Gate innovation methodology as the basis, their SSbD process focuses on three pillars of development (safe product, safe production and safe use) and three elements of risk assessment (uncertainty, exposure and hazard) [102]. The scope of the SSbD is shown in Fig. 15.2.

Furthermore, precautionary actions should follow the established hierarchy of controls for protecting workers, that are in general, the main approaches to risk control of hazardous materials in the workplace, focused on prevention of exposure by: (a) elimination of the hazard, (b) substitution of the hazard, (c) engineering control techniques, (d) administrative control systems and (e) use of personal protective equipment (see Fig. 15.3).

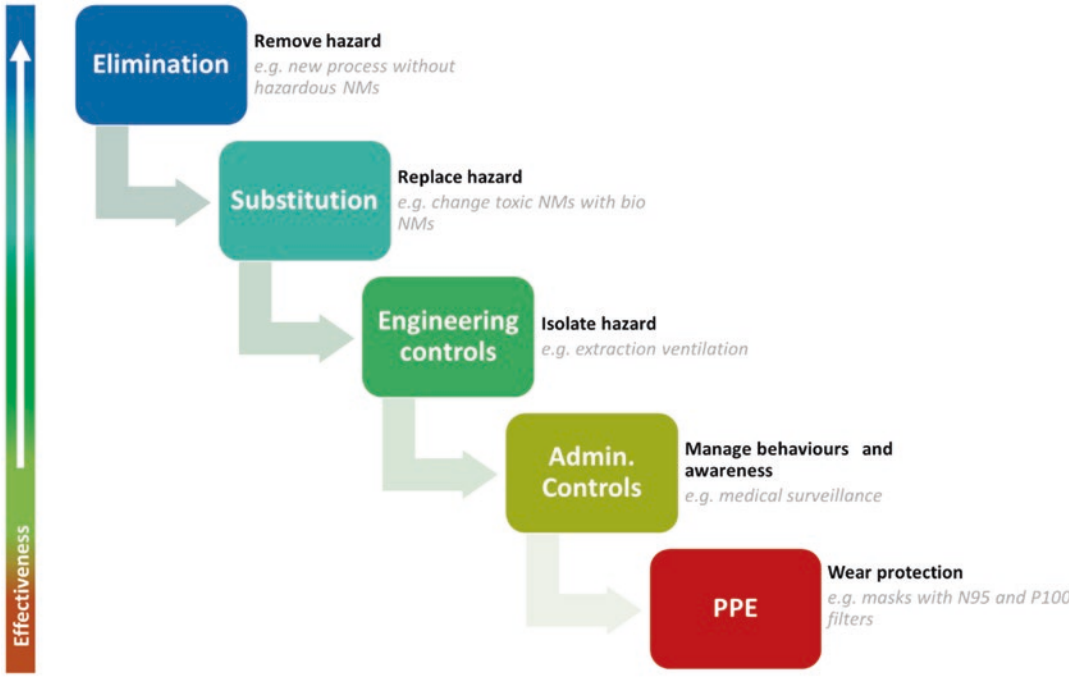

Fig. 15.3 Hierarchy of controls applied to Nanomaterials

In general, it is advisable to adopt a control as high in the control hierarchy as is technically and economically feasible. However, the decision of selecting a specific control should take into consideration the level of control required to provide a safe working environment and the efficacy of the control measures. These complementary approaches should be considered starting with the design stage of an industrial process [48]. The combination of all these control strategies should be a good approach to control the exposures. Changing the process to a less releaser of NMs, using matrices containing the NMs in order to minimize the release of NMs or modifying the NMs, for example, using coating to lower the hazardous characteristics of the NMs, are some of the measures that could be used.

15.4.1 Elimination and Substitution

The unique properties of commercial exploitation of nanoparticles are one of the reasons that hinder the application of the elimination control. The substitution is more applicable in reducing potential toxicity, by coating with a less hazardous substance but without changing the properties [98]. Changing the NMs physical form in order to reduce the possibility of inhalation or direct contact, like encapsulate or using suspensions (see Sect. 15.3.2.2) can be another way of substitution.

15.4.2 Engineering Controls

Another level of control that can be used when the first ones could not be implemented, or the implemented ones were not successful enough is the engineering controls. These engineering controls separate workers from the source that releases NMs, or capture NMs during their manipulation, through technics such as glove boxes, or fume hoods, or laminar flow cabinets, or custom fabricated enclosures. In general, the highest risks for nanomaterials are considered to be respiratory exposure, in view of the well-known lung toxicity of particulates [69]. Control

practices for the reduction of inhalable and respirable dust in the workplace are well-known and well stablished. The efficiency of these methods for nanomaterials has so far been only partially evaluated, but these measures seem useful as a starting point for the development of preventive measures. Some adjustments might be needed to prevent potential exposure to nanomaterials [48]. When applying the engineering controls, they should not interfere with the workers activities (passive measures), because in this case, and if they were not properly protected from the action of workers, the controls can be easily deactivated or stopped. The type of engineering control to apply depends on the location, duration of the task, the amount and characteristics of NMs that are manipulated. Without this information, the control may not prevent exposure and sometimes could increase it [72].

Operations involving easily dispersed dry nanomaterials, deserve more attention and more stringent controls (such as enclosure) than those involving nanomaterials that are suspended in a liquid matrix or embedded in a solid. When handled, liquid nanoparticle suspensions usually offer less risk of inhalation, but if they are aerosolized by sonication or dispersed in some way the likelihood of exposure can increase significantly [35].

Nanomaterials incorporated into bulk solids may pose some risk if the solid matrix is cut, sawed, drilled, sanded, or handled in any way that creates a dust or releases the nanomaterial [17].

For air velocities prevailing in workplaces, airborne nanoparticles can be considered as having no inertia and behave in a similar way to a gas and if not fully enclosed will diffuse rapidly and will remain airborne for a long time. Because of their high diffusion velocity, these particles will readily find leakage paths in systems in which the containment is not complete [2].

Most of the engineering controls already used to remove micro-scale powders and gases are adequate to minimize occupational exposure to NMs [73]. In any case, these systems should be effective in removing the released NMs taking into account the available information about their transport and behaviour in the air [69]. Some studies showed that that a biological safety cabinet was more effective than a custom fume hood to control airborne exposures resulting from sanding epoxy containing CNTs [12]. In the other hand other studies show that the performance of an air-curtain hood during nanoparticle use was outstanding for the various conditions tested and avoids the difficulties found when using traditional hoods [106]. To ensure the good performance of these systems, maintenance should be planned and performed.

At the design stage of engineering controls, observance with the requirements proposed by the local authorities must be taken into account. High-Efficiency Particulate Air (HEPA) filter, preferably H14, should be effective in removing nanoparticles from the airstream. HEPA filters have been recognized as one of the most effective filtration media that can be employed as the end-of-pipe treatment to capture and eliminate transport of nanomaterials (99.97%) [107].

In the precautionary approach, it is desirable to avoid any exposure to nanomaterials, and a number of containment approaches might be considered [30]. Operations can be performed by isolating the materials in separate, ventilated rooms equipped with a system that avoids any possibility of contaminating other workplaces. Other examples of isolation are the use of closed-circuit processes, use of robotics and equipment enclosure. In certain situations, where the process is too polluting, workers can be isolated in a controlled atmosphere workstation to operate the entire process by remote control. The workers are located in booths or rooms where the air quality conditions are controlled to protect their H&S [48]. It is worth mention that when NMs are released into the atmosphere, and as aforementioned, they have the potential to cause fire or explosion when subject to an ignition source. In this case, only elimination, substitution and engineering controls could reduce these associated risks.

15.4.3 Administrative Controls

Administrative means should not be a substitute for the type of controls discussed above but they should be implemented as a complementary

action to those solutions. When engineering solutions are not completely effective or are too expensive, administrative controls become a way to mitigate exposure. These solutions include changing working methods, minimizing the time workers are exposed to NMs, limiting contaminated spaces through door control and cleaning routines in the workplace.

15.4.4 Personnel Protective Equipment

Personnel Protective Equipment (PPE) should not be the primary control and should be used to supplement the other controls, when workers are in contact with nanomaterials during activities with nanomaterial-exposure potential. In general, PPE recommendations for nanoparticle handling will be the same as for exposures to other powders, fine dusts, or aerosols.

PPE must be selected based on many reflexions, such as the toxicological effects of the nanoparticle; quantity handled and physical form (physically bound/ encapsulated, in suspension in a liquid, in the form of powder), other exposure controls in place and PPE performance requirements and limitations. PPE is suggested for performing maintenance or opening a sealed enclosure or when having evidence that any residual exposures are under control, operators should wear PPE as a precautionary measure. The workers should be communicated about the decision of use PPE and a training plan where the reasons the limitations of that decision and the properly way to use, maintain and remove of the PPE will be explained. Research is still trying to validate methods to determine the efficacy of the PPEs as a real barrier to NMs. Inhalation is the preferred entry of NMs into the human body, so respirators should be employed when workers could inhale NMs because of the lack of effective engineering controls or during activities with higher potential NMs exposure (which is the case for maintenance or emergencies). The lack of OELs for many types of nanomaterials makes specific recommendations difficult.

N95 and P100 like the FFP2 and FFP3 filter cartridges are effective at capturing nanoparticles, but studies on the potential for face seal leakage (that is, leakage of particles through gaps between the respirator and the face) need more research addressing this issue [92]. However, the European Commission established that the level of protection of self-filtering masks against nanomaterials must be at least FFP3 with a nominal level of protection of 30 or higher [26].

Whenever exposure occurs during NMS handling tasks that provide skin contact, it is important to be aware that certain nanoparticles can cause adverse effects on the skin in specific circumstances, when crossing the skin barrier because it is compromised due to cracking or peeling. and entering the bloodstream potentially causing adverse health effects - local and systemic [60]. Workers should be informed about this ability of NMs to penetrate the skin and be stored in the skin's attachments, more so in damaged or flexed areas [59].

Protective clothing such as working clothes or disposable suits must be used and, at the end of the tasks, these must be removed and placed in specific containers, to avoid contamination of other places or workers. Polyethylene fabrics or similar are preferable [33].

Single-use gloves like disposable rubber gloves (e.g. latex), such as non-sterile medical examination gloves, should be used in order to avoid the NMs contact with the skin. Some chemicals (e.g. cleaning agents) may reduce the integrity of these kind of gloves, therefore, special care must be taken when handling these chemicals in such a way to avoid contact with them. Also, after use, these gloves should be taken off by pulling them inside out, so as to contain any raw powder or powder condensate that may have accumulated on the outside. For the same reasons eye protection must be worn in these situations (minimum of close-fitting safety glasses).

15.5 Conclusion

Due to their diversity of applications, nanotechnologies will experience an exponential expansion in the coming years and their uses promise great benefits for society. However, this growth brings additional exposure (of more workers) to a series of products with toxicological properties, in many cases unknown. In order to determine the benefits of using these advances and the risks that this entails, it is necessary to have a deeper understanding of these new materials. Many of these novel substances and elements could have the potential to be harmful for humans' health and the natural environment.

Specifically, in the H&S field and in order to adequately protect workers, it is necessary to continue the development of methods to assess the toxicity and other potentially source of hazards, as well as equipment of reasonable cost that allows monitoring exposure concentrations. Hazard identification of NMs among occupationally exposed workers in industries is one of the risk assessment, however, there is no conclusive data available on the effect of NMs in occupational contexts for many of the chemicals. The other step exposure assessment is based in air measurements that are taken in the vicinity of processes or operations using nanomaterials, either in companies or research laboratories, very little data have been published. In addition, no international consensus has been reached on any single measurement method for characterising occupational exposure. At the time there is no agreement in what testing strategies and methods of risk characterisation can be applied for nanomaterials. Precaution should be taken in controlling exposures when the extent of the hazard is not well known, as with many nanomaterials. The use of precautionary risk assessment approaches seems fairly reasonable especially considering the current lack of comprehensive and reliable toxicological and/or exposure information.

Finally, it is convenient for regulators as well as employers to strengthen research in this area and put in place processes for risk assessment. They also need to make more efforts to facilitate the data obtained from exposure assessment at different levels (national, EU, international), which would make possible to improve toxicological studies and would also help in establishing exposure limits and determining the right index for them.

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References

1. ACGIH (2008) TLVs and BEIs based on the documentation of the threshold limit values for chemical substances and physical agents & biological exposure indices. American Conference of Governmental Industrial Hygenists, Cincinnati
2. Aitken R, Creely K, Tran C (2004) Nanoparticles: an occupational hygiene review. HSE UK – Institute of Occupational Medicine, Edinburg
3. Albom A, Bridges J, De Jong W et al (2009) Risk assessment of products of nanotechnologies. Rep Sci Comm Emerg New Identified Health Risks–SCENIHR Eur Comm Health Consum DG Bruss
4. Aschberger K, Christensen FM, Rasmussen K, Jensen KA (2016) Feasibility and challenges of human health risk assessment for engineered nanomaterials. In: Engineered nanoparticles and the environment: biophysicochemical processes and toxicity. Wiley, Hoboken, pp 409–441
5. Boccuni F, Ferrante R, Tombolini F et al (2018) Workers' exposure to Nano-objects with different dimensionalities in R&D laboratories: measurement strategy and field studies. Int J Mol Sci 19:349
6. Bondarenko OM, Heinlaan M, Sihtmäe M et al (2016) Multilaboratory evaluation of 15 bioassays for (eco) toxicity screening and hazard ranking of engineered nanomaterials: FP7 project NANOVALID. Nanotoxicology 10:1229–1242
7. Bouillard J, Vignes A, Dufaud O et al (2010) Ignition and explosion risks of nanopowders. J Hazard Mater 181:873–880
8. Brouwer D, Boessen R, van Duuren-Stuurman B et al (2016) Evaluation of decision rules in a tiered assessment of inhalation exposure to nanomate-

rials. Ann Occup Hyg 60:949–959. https://doi.org/10.1093/annhyg/mew045
9. BSI (2007) PD 6699–2-2007 nanotechnologies – part 2: guide to safe handling and disposal of manufactured nanomaterials. British Standards Institution, London
10. CEN (2018) EN 17058 workplace exposure – assessment of exposure by inhalation of nano-objects and their aggregates and agglomerates. European Committee for Standardization, Brussels
11. CEN (2020) CEN/TC 352 – nanotechnologies. https://standards.cen.eu/dyn/www/f?p=204:7:0::::FSP_ORG_ID:508478&cs=1A6FDA13EC1F6859FD3F63B18B98492ED. Accessed 20 Feb 2020
12. Cena LG, Peters TM (2011) Characterization and control of airborne particles emitted during production of epoxy/carbon nanotube nanocomposites. J Occup Environ Hyg 8:86–92
13. Chaturvedi S, Dave PN (2018) Nanomaterials: environmental, human health risk. In: Handbook of nanomaterials for industrial applications. Elsevier, pp 1055–1062
14. Dahm MM, Evans DE, Schubauer-Berigan MK et al (2012) Occupational exposure assessment in carbon nanotube and nanofiber primary and secondary manufacturers. Ann Occup Hyg 56:542–556
15. Dekkers S, Oomen AG, Bleeker EAJ et al (2016) Towards a nanospecific approach for risk assessment. Regul Toxicol Pharmacol 80:46–59. https://doi.org/10.1016/j.yrtph.2016.05.037
16. Dimou K, Emond C (2017) Nanomaterials, and occupational health and safety – a literature review about control banding and a semi-quantitative method proposed for hazard assessment. J Phys Conf Ser 838:012020. https://doi.org/10.1088/1742-6596/838/1/012020
17. Duncan TV (2015) Release of engineered nanomaterials from polymer nanocomposites: the effect of matrix degradation. ACS Appl Mater Interfaces 7:20–39
18. Eastlake A, Hodson L, Geraci C, Crawford C (2012) A critical evaluation of material safety data sheets (MSDSs) for engineered nanomaterials. J Chem Health Saf 19:1–8
19. Eastlake AC, Beaucham C, Martinez KF et al (2016) Refinement of the nanoparticle emission assessment technique into the nanomaterial exposure assessment technique (NEAT 2.0). J Occup Environ Hyg 13:708–717
20. ECHA (2019a) Appendix for nanoforms applicable to the guidance on registration and substance identification draft (public) Version 1.0 September 2019. European Chemical Agency, Helsinki
21. ECHA (2019b) Appendix R6–1 for nanoforms applicable to the guidance on QSARs and grouping of chemicals, Version 2.0 December 2019. European Chemical Agency, Helsinki
22. EU Commission (2006) Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC
23. EU Commission (2011) Commission recommendation of 18 October 2011 on the definition of nanomaterial (2011/696/EU). Off J Eur Communities Legis 275:38–40
24. EU Commission (2012) Communication from the commission to the European parliament, the council, the economic and social committee and the committee of the regions: Second Regulatory Review on Nanomaterials {SWD(2012) 288 final}
25. EU Commission (2014a) Guidance on the protection of the health and safety of workers from the potential risks related to nanomaterials at work
26. EU Commission (2014b) Working safely with manufactured nanomaterials – guidance for workers. Employment, Social Affairs & Inclusion, European Commission, Brussels, Belgium
27. EU Parliament (2006) Regulation (EC) Nº 1907/2006 of the European Parliament and of the council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC
28. EU Parliament (2008) Regulation (EC) nº 1272/2008 of the European Parliament and of the council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) nº 1907/2006
29. EUON (2020) Regulation. https://euon.echa.europa.eu/regulation
30. EU-OSHA (2009) Workplace exposure to nanoparticles. European Agency for Safety and Health at Work, Bilbao, Spain
31. Fisher E, Selin C, Wetmore J (2008) Presenting futures. Springer, Dordrecht
32. Fransman W, Van Tongeren M, Cherrie JW et al (2011) Advanced Reach Tool (ART): development of the mechanistic model. Ann Occup Hyg 55:957–979
33. Freeland J, Hulme J, Kinnison D et al (2012) Working safely with nanomaterials in research & development. The UK NanoSafety Partnership Group, Edinburg
34. Froggett SJ, Clancy SF, Boverhof DR, Canady RA (2014) A review and perspective of existing research on the release of nanomaterials from solid nanocomposites. Part Fibre Toxicol 11:17

35. Geraci C, Heidel D, Sayes C et al (2015) Perspectives on the design of safer nanomaterials and manufacturing processes. J Nanopart Res 17:366
36. Godinho da Fonseca AS (2016) Exposure characterisation and sources of nanoparticles in workplace environments. PhD thesis, Universitat de Barcelona
37. Goede HA, McNally K, Gorce J-P et al (2019) Dermal advanced REACH tool (dART) – development of a dermal exposure model for low-volatile liquids. Ann Work Expo Health 63:624–636
38. Gottardo S, Alessandrelli M, Amenta V et al (2017) NANoREG framework for the safety assessment of nanomaterials. European Commission Joint Research Centre, Luxembourg
39. Hansen SF, Jensen KA, Baun A (2014) NanoRiskCat: a conceptual tool for categorization and communication of exposure potentials and hazards of nanomaterials in consumer products. J Nanopart Res 16:2195. https://doi.org/10.1007/s11051-013-2195-z
40. Hristozov D, Gottardo S, Semenzin E et al (2016) Frameworks and tools for risk assessment of manufactured nanomaterials. Environ Int 95:36–53. https://doi.org/10.1016/j.envint.2016.07.016
41. HSE UK (2020) Understanding the hazards of nanomaterials. In: Health Saf Exec. https://www.hse.gov.uk/nanotechnology/understanding-hazards-nanomaterials.htm. Accessed 25 May 2020
42. Iavicoli I, Fontana L, Pingue P et al (2018) Assessment of occupational exposure to engineered nanomaterials in research laboratories using personal monitors. Sci Total Environ 627:689–702. https://doi.org/10.1016/j.scitotenv.2018.01.260
43. ICBA (2004) Carbon black user's guide, safety, health, & environmental information. International Carbon Black Association, Louisiana
44. IOM SAFENANO (2020) Current nanotechnology standardisation activities. https://www.safenano.org/KnowledgeBase/Standards.aspx. Accessed 20 Feb 2020
45. ISO (2012a) ISO/TS 12901–2 2012 nanotechnologies – occupational risk management applied to engineered nanomaterials – part 2: Use of the control banding approach. International Organization for Standardization, Geneva, Switzerland
46. ISO (2012b) ISO/TS 12901–1 2012 nanotechnologies – occupational risk management applied to engineered nanomaterials – part 1: Principles and approaches. International Organization for Standardization, Geneva, Switzerland
47. ISO (2018a) ISO 31000: 2018 risk management–principles and guidelines. International Organization for Standardization, Geneva, Switzerland
48. ISO (2018b) ISO/TR 12885:2018 nanotechnologies – health and safety practices in occupational settings. International Organization for Standardization, Geneva, Switzerland
49. ISO (2020) Technical Committees: ISO/TC 229 nanotechnologies. https://www.iso.org/committee/381983.html. Accessed 20 Feb 2020
50. Jalonen H (2012) The uncertainty of innovation: a systematic review of the literature. J Manag Res 4:1
51. Jeevanandam J, Barhoum A, Chan YS et al (2018) Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol 9:1050–1074. https://doi.org/10.3762/bjnano.9.98
52. Jensen KA, Saber AT, Kristensen HV et al (2013) NanoSafer vs. 1.1 – nanomaterial risk assessment using first order modeling. In: 6th International symposium on nanotechnology, occupational and environmental health, p 120
53. Khan FH (2014) Chemical hazards of nanoparticles to human and environment (a review). Orient J Chem 29:1399–1408
54. Kraegeloh A, Suarez-Merino B, Sluijters T, Micheletti C (2018) Implementation of safe-by-design for nanomaterial development and safe innovation: why we need a comprehensive approach. Nano 8:239
55. Kuempel ED, Tran CL, Castranova V, Bailer AJ (2006) Lung dosimetry and risk assessment of nanoparticles: evaluating and extending current models in rats and humans. Inhal Toxicol 18:717–724. https://doi.org/10.1080/08958370600747887
56. Kuijpers E, Bekker C, Brouwer D, le Feber M, Fransman W (2017) Understanding workers' exposure: systematic review and data-analysis of emission potential for NOAA. J Occup Environ Hyg 14(5): 349–359. https://doi.org/10.1080/15459624.2016.1252843
57. Kumar A, Kumar P, Anandan A et al (2014) Engineered nanomaterials: knowledge gaps in fate, exposure, toxicity, and future directions. J Nanomater
58. Lamon L, Aschberger K, Asturiol D et al (2019) Grouping of nanomaterials to read-across hazard endpoints: a review. Nanotoxicology 13:100–118
59. Larese Filon F, Mauro M, Adami G et al (2015) Nanoparticles skin absorption: new aspects for a safety profile evaluation. Regul Toxicol Pharmacol 72:310–322. https://doi.org/10.1016/j.yrtph.2015.05.005
60. Larese Filon F, Bello D, Cherrie JW et al (2016) Occupational dermal exposure to nanoparticles and nano-enabled products: part I – factors affecting skin absorption. Int J Hyg Environ Health 219:536–544. https://doi.org/10.1016/j.ijheh.2016.05.009
61. Lee EG, Lamb J, Savic N et al (2019) Evaluation of exposure assessment tools under REACH: part I – tier 1 tools. Ann Work Expo Health 63:218–229. https://doi.org/10.1093/annweh/wxy091
62. Leszczynski J, Puzyn T (2012) Towards efficient designing of safe nanomaterials: innovative merge of computational approaches and experimental techniques. Royal Society of Chemistry
63. Liguori B, Hansen SF, Baun A, Jensen KA (2016) Control banding tools for occupational exposure assessment of nanomaterials – ready for use in a

regulatory context? NanoImpact 2:1–17. https://doi.org/10.1016/j.impact.2016.04.002
64. Malsch I, Subramanian V, Semenzin E et al (2015) Supporting decision-making for sustainable nanotechnology. Environ Syst Decis 35:54–75. https://doi.org/10.1007/s10669-015-9539-4
65. Marchant GE, Sylvester DJ, Abbott KW (2008) Risk management principles for nanotechnology. NanoEthics 2:43–60
66. Maynard AD, Aitken RJ (2007) Assessing exposure to airborne nanomaterials: current abilities and future requirements. Nanotoxicology 1:26–41. https://doi.org/10.1080/17435390701314720
67. Mihalache R, Verbeek J, Graczyk H et al (2017) Occupational exposure limits for manufactured nanomaterials, a systematic review. Nanotoxicology 11:7–19. https://doi.org/10.1080/17435390.2016.1262920
68. Nakanishi J, Morimoto Y, Ogura I et al (2015) Risk assessment of the carbon nanotube group: risk assessment of CNT. Risk Anal 35:1940–1956. https://doi.org/10.1111/risa.12394
69. NIOSH (2009) Approaches to safe nanotechnology – managing the health and safety concerns associated with engineered nanomaterials. National Institute for Occupational Safety and Health, Washington DC
70. NIOSH (2011) Occupational exposure to titanium dioxide. Centers for Disease Control and Prevention – National Institute for Occupational Safety and Health, Washington DC
71. NIOSH (2013) Occupational exposure to carbon nanotubes and nanofibers. Centers for Disease Control and Prevention – National Institute for Occupational Safety and Health, Washington DC
72. NIOSH (2014) Current strategies for engineering controls in nanomaterial production and downstream handling processes. National Institute for Occupational Safety and Health, Washington DC
73. NIOSH (2016) Building a safety program to protect the nanotechnology workforce: a guide for small to medium-sized enterprises. National Institute for Occupational Safety and Health, Washington DC
74. NIOSH (2017) NIOSH pocket guide to chemical hazards. National Institute for Occupational Safety and Health, Washington DC
75. NRC (2011) Prudent practices in the laboratory: handling and management of chemical hazards, updated version. National Academies Press - National Research Council, Washington DC
76. O'Shaughnessy PT (2013) Occupational health risk to nanoparticulate exposure. Environ Sci Process Impacts 15:49–62
77. OECD (2011) Nanosafety at the OECD: the first five years 2006–2010. Organisation for Economic Co-operation and Development, Paris
78. OECD (2015) Harmonized tiered approach to measure and assess the potential exposure to airborne emissions of engineered nano-objects and their agglomerates and aggregates at workplaces. Organisation for Economic Co-operation and Development, France, Paris
79. OECD (2017) Strategies, techniques and sampling protocols for determining the concentrations of manufactured nanomaterials in air at the workplace. Organisation for Economic Co-operation and Development, France, Paris
80. Osman EM (2019) Environmental and health safety considerations of nanotechnology: nano safety. Biomed J Sci Tech Res 19. https://doi.org/10.26717/BJSTR.2019.19.003346
81. Ostiguy C, Riediker M, Triolet J et al (2010) Development of a specific control banding tool for nanomaterials: report. ANSES. French agency for food, environmental and occupational health and safety
82. Ostrom LT, Wilhelmsen CA (2019) Risk assessment: tools, techniques, and their applications. Wiley, Cambridge
83. Park M, Wijnhoven S (2017) GUIDEnano: a web-based guidance tool for risk assessment and mitigation of nano-enabled products. TCDD 3
84. Pauluhn J (2010) Multi-walled carbon nanotubes (Baytubes®): approach for derivation of occupational exposure limit. Regul Toxicol Pharmacol 57:78–89. https://doi.org/10.1016/j.yrtph.2009.12.012
85. Pietroiusti A, Stockmann-Juvala H, Lucaroni F, Savolainen K (2018) Nanomaterial exposure, toxicity, and impact on human health. Wiley Interdiscip Rev Nanomed Nanobiotechnol 10:e1513. https://doi.org/10.1002/wnan.1513
86. Pośniak M (2020) Emerging chemical risks in the work environment. CRC Press, London
87. Ramos D, Almeida L, Gomes M (2019) Application of control banding to workplace exposure to nanomaterials in the textile industry. In: Arezes PM, Baptista JS, Barroso MP et al (eds) Occupational and environmental safety and health. Springer, Berlin, pp 105–113
88. Rasmussen K, Rauscher H, Mech A et al (2018) Physico-chemical properties of manufactured nanomaterials-characterisation and relevant methods. An outlook based on the OECD testing programme. Regul Toxicol Pharmacol 92:8–28
89. Rasmussen K, Rauscher H, Kearns P et al (2019) Developing OECD test guidelines for regulatory testing of nanomaterials to ensure mutual acceptance of test data. Regul Toxicol Pharmacol 104:74–83
90. Rauscher H, Mech A, Gibson N et al (2019a) Identification of nanomaterials through measurements, EUR 29942 EN. Publications Office of the European Union, Luxembourg
91. Rauscher H, Roebben G, Mech A et al (2019b) An overview of concepts and terms used in the European Commission's definition of nanomaterial, EUR 29647 EN. European Commission, JRC, Ispra

92. Rengasamy S, Eimer BC, Shaffer RE (2009) Comparison of nanoparticle filtration performance of NIOSH-approved and CE-marked particulate filtering Facepiece respirators. Ann Occup Hyg 53:117–128. https://doi.org/10.1093/annhyg/men086
93. Rose G, Pavlicek A, Gazsó A (2019) Safe-by-design – the early integration of safety aspects in innovation processes. NanoTrust Doss 50
94. Rothen-Rutishauser B, Clift MJ, Jud C et al (2012) Human epithelial cells in vitro–are they an advantageous tool to help understand the nanomaterial-biological barrier interaction? EURO NanoTox Lett 4:1–20
95. Sajid M, Ilyas M, Basheer C et al (2015) Impact of nanoparticles on human and environment: review of toxicity factors, exposures, control strategies, and future prospects. Environ Sci Pollut Res 22:4122–4143. https://doi.org/10.1007/s11356-014-3994-1
96. Sánchez Jiménez A, Varet J, Poland C et al (2016) A comparison of control banding tools for nanomaterials. J Occup Environ Hyg 13:936–949. https://doi.org/10.1080/15459624.2016.1200191
97. Schneider T, Brouwer DH, Koponen IK et al (2011) Conceptual model for assessment of inhalation exposure to manufactured nanoparticles. J Expo Sci Environ Epidemiol 21:450–463. https://doi.org/10.1038/jes.2011.4
98. Schulte P, Geraci C, Zumwalde R et al (2008) Occupational risk Management of Engineered Nanoparticles. J Occup Environ Hyg 5:239–249. https://doi.org/10.1080/15459620801907840
99. Sellers K, Deleebeeck NM, Messiean M et al (2015) Grouping nanomaterials: a strategy towards grouping and read-across. Rijksinstituut voor Volksgezondheid en Milieu RIVM
100. Semenzin E, Giubilato E, Badetti E et al (2019) Guiding the development of sustainable nano-enabled products for the conservation of works of art: proposal for a framework implementing the safe by design concept. Environ Sci Pollut Res 26:26146–26158
101. Silva GLE, Viana C, Domingues D, Vieira F (2019) Risk assessment and health, safety, and environmental Management of Carbon Nanomaterials. In: Clichici S, Filip A, do Nascimento GM (eds) Nanomaterials-toxicity, human health and environment. IntechOpen, London
102. Soeteman-Hernandez LG, Apostolova MD, Bekker C et al (2019) Safe innovation approach: towards an agile system for dealing with innovations. Mater Today Commun 20:100548. https://doi.org/10.1016/j.mtcomm.2019.100548
103. Sparrow MK (2011) The regulatory craft: controlling risks, solving problems, and managing compliance. Brookings Institution Press, Washington, DC
104. Stockmann-Juvala H, Taxell P, Santonen T (2014) Formulating occupational exposure limits values (OELs)(Inhalation & Dermal) – Scaffold Public Documents-SPD7. Finnish Institute of Occupational Health, Helsinki, Finland
105. Sweeney LM, MacCalman L, Haber LT et al (2015) Bayesian evaluation of a physiologically-based pharmacokinetic (PBPK) model of long-term kinetics of metal nanoparticles in rats. Regul Toxicol Pharmacol 73:151–163
106. Tsai S-J, Huang RF, Ellenbecker MJ (2010) Airborne nanoparticle exposures while using constant-flow, constant-velocity, and air-curtain-isolated fume hoods. Ann Occup Hyg 54:78–87
107. Tsai CS-J, Echevarría-Vega ME, Sotiriou GA et al (2012) Evaluation of environmental filtration control of engineered nanoparticles using the Harvard versatile engineered nanomaterial generation system (VENGES). J Nanopart Res 14:812. https://doi.org/10.1007/s11051-012-0812-x
108. TSI (2012) NanoScan SMPS nanoparticle sizer model 3910. TSI, Minnesota, US
109. van Broekhuizen P, van Veelen W, Streekstra W-H et al (2012) Exposure limits for nanoparticles: report of an International workshop on nano reference values. Ann Occup Hyg. https://doi.org/10.1093/annhyg/mes043
110. van Duuren-Stuurman B, Vink SR, Verbist KJM et al (2012) Stoffenmanager Nano Version 1.0: a web-based tool for risk prioritization of airborne manufactured nano objects. Ann Occup Hyg. https://doi.org/10.1093/annhyg/mer113
111. van Harmelen T, Zondervan-van den Beuken EK, Brouwer DH et al (2016) LICARA nanoSCAN-a tool for the self-assessment of benefits and risks of nanoproducts. Environ Int 91:150–160
112. van Teunenbroek T, Dijkzeul A, Baker J (2017) PROSAFE – promoting the implementation of safe by design: white paper. Dutch Ministry of Infrastructure and the Environment
113. Warheit DB (2018) Hazard and risk assessment strategies for nanoparticle exposures: how far have we come in the past 10 years? F1000Res 7
114. Yan X, Sedykh A, Wang W et al (2019) In silico profiling nanoparticles: predictive nanomodeling using universal nanodescriptors and various machine learning approaches. Nanoscale 11:8352–8362
115. Zalk DM, Paik SY, Swuste P (2009) Evaluating the control banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures. J Nanopart Res 11:1685–1704. https://doi.org/10.1007/s11051-009-9678-y
116. Kuijpers EC, Bekker D, Brouwer M, le Feber W, Fransman (2017) Understanding workers' exposure: Systematic review and data-analysis of emission potential for NOAA. Journal of Occupational and Environmental Hygiene 5:349-359 10.1080/15459624.2016.1252843