

DEVELOPMENT OF A SYSTEMATIC EVIDENCE REVIEW FOR THE
WHO GUIDELINE ON PROTECTING WORKERS FROM
POTENTIAL RISKS OF MANUFACTURED NANOMATERIALS

What training should be provided to workers who are at risk from exposure to the specific nanomaterials or groups of nanomaterials?

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1. Introduction

In 2010, the World Health Organization (WHO) initiated the development of a guideline entitled *Protecting workers from potential risks of manufactured nanomaterials* (http://www.who.int/occupational_health/topics/nanotechnologies/en/) using a systematic evidence review process (1). The guideline aims to improve occupational safety and to protect the health of workers handling nanomaterials in all countries, especially those of low- and medium-income.

The WHO Guideline Development Group (GDG) identified key questions to be addressed using the Delphi process of consensus seeking (2). For each question, guideline recommendations will be developed.

The Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA) has undertaken to answer Question (h), which asks: “What training should be provided to workers who are at risk from exposure to the specific nanomaterials or groups of nanomaterials?”

It is vitally important to train employees who may be exposed to hazardous chemicals, biological or physical agents. However, assessing the effectiveness of training is not straight forward as a systematic review by the Toronto-based Institute for Work & Health showed (3). The authors found it is of the utmost significance to define the study subject as precisely as possible to get a reliable answer to the question and to avoid inconsistency in the findings.

Burke et al. discussed how hazard and safety training influences workers’ learning about safety aspects and safety performance and contributed a whole chapter to *The Wiley Blackwell Handbook of the Psychology of Occupational Safety and Workplace Health* (4, 5). They found in 2011 that highly-engaging training was considerably more effective than less-engaging training when the hazardous event/exposure severity was high. However, this was not found when the hazardous event/exposure severity was not high or was unknown (6). In 2008 the same group had concluded that to avoid uncertainty may paradoxically lead to greater uncertainty and ineffective safety training as a result (7). This is important in relation to nanomaterials where the risk is still largely unknown. In summary, training is more effective when the hazardous exposure is well-defined and the training methods are highly engaging.

For this review, we have defined training as “planned efforts to learn or facilitate the learning of specific competencies for the safe use of nanomaterials at the workplace”.

In our review we considered active or passive training, given centrally or individually, with learning-centred or teaching-centred material. Evaluation of the training included timing, format and content of the programme and materials, and also guidance on occupational health and safety measures relating to nanomaterials. This included the use of engineering controls and appropriate personal protective equipment, guidance on dealing with spills and accidental releases, and guidance on appropriate handling of these materials during disposal. We also reviewed enhancements in learning that result from reaction, knowledge, dialogue, behaviour, results and reflections on the training (adopted from Kirkpatrick’s four-level model) (8).

2. Methods

To answer the question, a literature review was conducted in the year 2015 by searching scientific journal databases via the Internet, to find evidence for effective training regarding the handling of nanomaterials (NM) at the workplace.

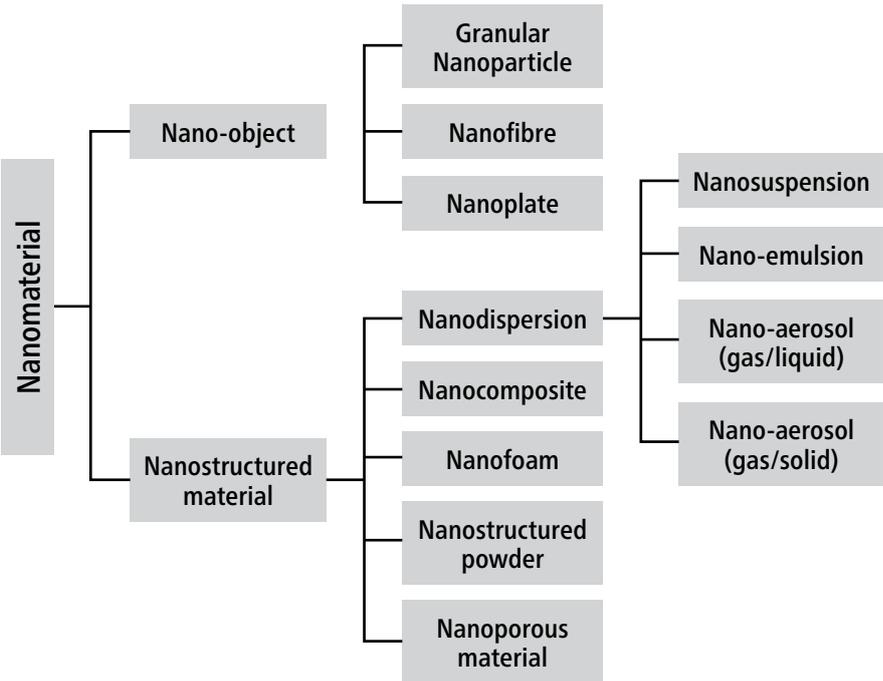
First, inclusion and exclusion criteria were defined to be able to determine a suitable search strategy. Second, a pilot study was conducted to see if it was possible to find any information about the topic on the Internet before focusing on the scientific literature. The pilot study was also helpful to indicate proper search terms and strings. Third, after the pilot study two researchers from IFA searched the selected databases with a certain set of terms in a certain order (strings) and recorded the results. We also evaluated the references in the papers that we read full-text and we evaluated the grey literature, such as reports not published by commercial or academic distribution channels. Finally, European Union and international research projects (such as Nanodiode, nanoInDex, NanoEIS, NanOpinion and QualityNano) were assessed.

The results were evaluated using the PICO approach. Finally, the selected studies were assessed for their methodological quality with a score that ranged from -12 to +12 (1, 9, 10).

2.1 Inclusion criteria for nanomaterials

The literature review included synthetically-manufactured nano-objects (nanoparticles, nanofibres and nanoplates) and agglomerates and aggregate forms of these materials, as well as nanostructured materials (Fig. 1) also known as engineered nanomaterials (ENM). The “form” of the ENMs referred to its physical form or the environment (matrix) where the ENM is contained (for instance powder, liquid, paste or solid). All studies relevant to the workplace, in all stages of the life-cycle of the material, including observational findings, were included in the systematic review. Studies in any language were considered, especially those from low- or middle-income countries.

Fig. 1. Classification of a nanomaterial included in the literature review



2.2 Exclusion criteria

We excluded studies that did not refer to occupational settings or exposure simulations (for instance, toxicity studies, material characterization studies), as well as studies on nanomaterial that did not fall under the International Standardization Organization (ISO) definition (material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale) (11).

Studies without concrete suggestions, recommendations or specifications for training, as well as studies that recommended unspecified “general” training were excluded. However, to assist readers we have summarized information found about general training in **Annex 1**.

Studies that suggest risk measurement measures, especially the use of personal protective equipment, but without indication of special training on their use were excluded.

2.3 Search strategy

The cut-off date for published papers was 15 December 2015. Papers found were published between 2005 and 2015.

2.4 Pilot study

The authors decided to check whether studies could be found that fell within the defined criteria, by conducting a preliminary search using Google, Google Scholar, MetaGer and PubMed.

The first set of search terms (in any language and including abbreviations) were:

- nanomaterial AND management measures (maximum 335 000 results on Google);
- nanomaterial AND operation instructions (maximum 306 000 results on Google);
- nanomaterial AND good work practices (maximum 182 000 results on Google);
- nanomaterial AND industrial workplace use or professional workplace use or disposal or recycling (maximum 371 000 results on Google);
- nanomaterial industrial use OR professional use OR worker use OR disposal OR recycling (maximum 519 000 results on Google).

For a second search, the search terms were rearranged to indicate: (i) the different stages of handling nanomaterials, and (ii) emission and exposure.

The second set of search terms used were:

- nanomaterial AND management measures AND industrial workplace use OR professional workplace use AND disposal OR recycling AND emission OR exposure;
- nanomaterial AND operation instructions AND industrial use OR professional use OR worker use AND disposal OR recycling AND emission or exposure;
- nanomaterial AND good work practices AND industrial use OR professional use OR worker use AND disposal OR recycling AND emission OR exposure.

The set of search terms were combined with terms like “training” or “schooling” to indicate if training on nanomaterials used at the workplace was mentioned (maximum 324 000 results on Google).

The pilot study indicated that it should be possible to conduct an evidence-based review with a certain set of search terms to answer Question (h).

2.5 Scientific literature study – search strings

2.5.1 Searched databases

1. Medline via PubMed (<https://www.pubmed.gov>).
2. ICON database (<http://cben.rice.edu/>); this site was not updated after 30 September 2014, so a third database was used.
3. LIVIVO – The Search Portal for Life Sciences (<https://www.livivo.de/app?LANGUAGE=en>).

A fourth database, the Directory of Open Access Journals (<https://doaj.org>) was considered but unfortunately had limitations, so was not used for the actual search: (i) the database was under maintenance in November and not working properly; (ii) there was limited availability of papers published (or entered in the database) before 2014. However, this database could be useful for future literature studies.

2.5.2 First search strategy

The following search terms were used one after another (seven strings) to filter those papers that met the inclusion criteria:

(nanostructures* OR nanostructure* OR nanomaterial* OR nanotechnology* OR nanocomposite* OR nanofiber* OR nanoparticle* OR nano particle* OR nanofill* OR nanopore* OR nanotube* OR nanowire* OR dendrimer* OR nanocapsule* OR nanoconjugate* OR nanodiamond* OR nanosphere* OR quantum dot* OR fullerene C60* OR carbon nanotube* OR carbon nanofiber* OR silver nanoparticle* OR iron nanoparticle* OR titanium dioxide nanoparticle* OR aluminium oxide nanoparticle* OR cerium oxide nanoparticle* OR zinc oxide nanoparticle* OR silicon dioxide nanoparticle* OR nanoclay* OR gold nanoparticle* OR nanocomposites* OR nanofibers* OR nanoparticles* OR nano particles* OR nanopores* OR nanotubes* OR nanowires* OR dendrimers* OR nanocapsules* OR nanoconjugates* OR nanodiamonds* OR nanospheres* OR quantum dots* OR fullerenes C60* OR carbon nanotubes* OR carbon nanofibers* OR silver nanoparticles* OR iron nanoparticles* OR titanium dioxide nanoparticles* OR aluminium oxide nanoparticles* OR cerium oxide nanoparticles* OR zinc oxide nanoparticles* OR silicon dioxide nanoparticles* OR nanoclays* OR gold nanoparticles*)

= **string 1**

AND (emission* OR emissions*) [All Fields]

= **string 2**

AND (exposure* OR exposures*) [All Fields]

= **string 3**

AND (work* OR occupational* OR worker* OR workers* OR employee* OR employees* OR industrial plant* OR industrial plants* OR factory* OR factories* OR industry* OR industries* OR facility* OR facilities* OR manufacture* OR manufacturing*) [All Fields]

= **string 4**

AND (measure* OR risk managing measure* OR measures* OR risk managing measures*) [All Fields]

= **string 5**

AND (training* OR professional training* OR schooling* OR training course* OR education* OR practice*) [All Fields]

= **string 6**

AND (practice* OR instruction* OR briefing* OR order* OR procedure* OR operational procedure* OR directive* OR guideline* OR guidance*) [All Fields]

= **string 7**

2.5.3 *Alternation of the first search strategy*

After an evaluation of the results by the first researcher, an alternation of the combination of search terms and strings was done:

(nanostructures* OR nanostructure* OR nanomaterial* OR nanotechnology* OR nanocomposite* OR nanofiber* OR nanoparticle* OR nano particle* OR nanofill* OR nanopore* OR nanotube* OR nanowire* OR dendrimer* OR nanocapsule* OR nanoconjugate* OR nanodiamond* OR nanosphere* OR quantum dot* OR fullerene C60* OR carbon nanotube* OR carbon nanofiber* OR silver nanoparticle* OR iron nanoparticle* OR titanium dioxide nanoparticle* OR aluminium oxide nanoparticle* OR cerium oxide nanoparticle* OR zinc oxide nanoparticle* OR silicon dioxide nanoparticle* OR nanoclay* OR gold nanoparticle* OR nanocomposites* OR nanofibers* OR nanoparticles* OR nano particles* OR nanopores* OR nanotubes* OR nanowires* OR dendrimers* OR nanocapsules* OR nanoconjugates* OR nanodiamonds* OR nanospheres* OR quantum dots* OR fullerenes C60* OR carbon nanotubes* OR carbon nanofibers* OR silver nanoparticles* OR iron nanoparticles* OR titanium dioxide nanoparticles* OR aluminium oxide nanoparticles* OR cerium oxide nanoparticles* OR zinc oxide nanoparticles* OR silicon dioxide nanoparticles* OR nanoclays* OR gold nanoparticles*)

= **string 1a**

AND (emission* OR emissions*) [All Fields]

= **string 2a**

AND (exposure* OR exposures*) [All Fields]

= **string 3a**

AND (work* OR occupational* OR worker* OR workers* OR employee* OR employees* OR industrial plant* OR industrial plants* OR factory* OR factories* OR industry* OR industries* OR facility* OR facilities* OR manufacture* OR manufacturing*) [All Fields]

= **string 4a**

AND (practice* OR instruction* OR briefing* OR order* OR procedure* OR operational procedure* OR directive* OR guideline* OR guidance*) [All Fields]

= **string 5a**

AND (training* OR professional training* OR schooling* OR training course* OR education* OR practice*) [All Fields]

= **string 6a**

2.5.4 *Second search strategy*

After a discussion of the first search results with the WHO GDG, the two researchers conducted a second search using the following terms:

(nanostructures* OR nanostructure* OR nanomaterial* OR nanotechnology* OR nanocomposite* OR nanofiber* OR nanoparticle* OR nano particle* OR nanofill* OR nanopore* OR nanotube* OR nanowire* OR dendrimer* OR nanocapsule* OR nanoconjugate* OR nanodiamond* OR nanosphere* OR quantum dot* OR fullerene C60* OR carbon nanotube* OR carbon nanofiber* OR silver nanoparticle* OR iron nanoparticle* OR titanium dioxide nanoparticle* OR aluminium oxide nanoparticle* OR cerium oxide nanoparticle* OR zinc

oxide nanoparticle* OR silicon dioxide nanoparticle* OR nanoclay* OR gold nanoparticle* OR nanocomposites* OR nanofibers* OR nanoparticles* OR nano particles* OR nanopores* OR nanotubes* OR nanowires* OR dendrimers* OR nanocapsules* OR nanoconjugates* OR nanodiamonds* OR nanospheres* OR quantum dots* OR fullerenes C60* OR carbon nanotubes* OR carbon nanofibers* OR silver nanoparticles* OR iron nanoparticles* OR titanium dioxide nanoparticles* OR aluminium oxide nanoparticles* OR cerium oxide nanoparticles* OR zinc oxide nanoparticles* OR silicon dioxide nanoparticles* OR nanoclays* OR gold nanoparticles*)

= **string 1**

AND (exposure* OR exposures*) [All Fields]

= **string 2**

AND (work* OR occupational* OR worker* OR workers* OR employee* OR employees* OR industrial plant* OR industrial plants* OR factory* OR factories* OR industry* OR industries* OR facility* OR facilities* OR manufacture* OR manufacturing*) [All Fields]

= **string 3**

AND (training* OR professional training* OR schooling* OR training course* OR education* OR practice*) [All Fields]

= **string 4**

AND (practice* OR instruction* OR briefing* OR order* OR procedure* OR operational procedure* OR directive* OR guideline* OR guidance*) [All Fields]

= **string 5**

AND (effect* OR benefit*) [All Fields]

= **string 6**

2.5.5 *Alternation of the second search strategy*

After an evaluation of the results by the two researchers, an alternation of the combination of search terms and strings was done:

(nanostructures* OR nanostructure* OR nanomaterial* OR nanotechnology* OR nanocomposite* OR nanofiber* OR nanoparticle* OR nano particle* OR nanofill* OR nanopore* OR nanotube* OR nanowire* OR dendrimer* OR nanocapsule* OR nanoconjugate* OR nanodiamond* OR nanosphere* OR quantum dot* OR fullerene C60* OR carbon nanotube* OR carbon nanofiber* OR silver nanoparticle* OR iron nanoparticle* OR titanium dioxide nanoparticle* OR aluminium oxide nanoparticle* OR cerium oxide nanoparticle* OR zinc oxide nanoparticle* OR silicon dioxide nanoparticle* OR nanoclay* OR gold nanoparticle* OR nanocomposites* OR nanofibers* OR nanoparticles* OR nano particles* OR nanopores* OR nanotubes* OR nanowires* OR dendrimers* OR nanocapsules* OR nanoconjugates* OR nanodiamonds* OR nanospheres* OR quantum dots* OR fullerenes C60* OR carbon nanotubes* OR carbon nanofibers* OR silver nanoparticles* OR iron nanoparticles* OR titanium dioxide nanoparticles* OR aluminium oxide nanoparticles* OR cerium oxide nanoparticles* OR zinc oxide nanoparticles* OR silicon dioxide nanoparticles* OR nanoclays* OR gold nanoparticles*)

= **string 1a**

AND (emission* OR emissions*) [All Fields]

= **string 2a**

AND (exposure* OR exposures*) [All Fields]

= **string 3a**

AND (work* OR occupational* OR worker* OR workers* OR employee* OR employees* OR industrial plant* OR industrial plants* OR factory* OR factories* OR industry* OR industries* OR facility* OR facilities* OR manufacture* OR manufacturing*) [All Fields]

= **string 4a**

AND (practice* OR instruction* OR briefing* OR order* OR procedure* OR operational procedure* OR directive* OR guideline* OR guidance*) [All Fields]

= **string 5a**

AND (training* OR professional training* OR schooling* OR training course* OR education* OR practice*) [All Fields]

= **string 6a**

AND (effect* OR benefit*) [All Fields]

= **string 7a**

2.6 PICO inclusion criteria

We used the PICO approach to evaluate the results with the following four elements as our inclusion criteria:

Population (P): Workers involved in the handling of nanomaterial, or products containing nanomaterial, across all the stages of the life-cycle (synthesis, manufacture, downstream use and disposal and recycling). Studies about the need for effective and specific training of workers that discuss the efficiency of suggested training materials.

Intervention (I): Specific worker training or contextual data or measurements so that the training needs can be identified. Studies should include:

- description of the work activity;
- description of the workers' profession;
- description of the nanomaterial used;
- description of emission or exposure.

Comparator (C): No training or only general occupational health and safety training.

Outcome (O): Information on the need, type, content and efficiency of (specific) training for workers handling nanomaterial, to avoid or reduce substance/product emission, exposure, transmission and contamination, including risk measurement measures (like using respiratory protection) that require training.

3. Quality criteria for individual studies

We assessed the quality of the seven full-text papers selected before deciding about inclusion (Table 1). Information for the following four items was assessed. The first item (AA) scored the precise specification of the nanomaterial application area and related tasks/workplaces. The second item (VS) scored the validation of the examination in field studies and/or other (transdisciplinary) studies. The third item (DQ) scored the quality of the description of (i) the assessment that was conducted, (ii) the suggested risk management measures and (iii) the standard operating procedures that workers' training should address. The fourth item (PC) was scored on the information given on the physicochemical characterization of the examined nanomaterial.

The following information was also extracted from the reviewed studies where available:

- ENM characteristics:
 - ENM name;
 - form of the pristine material and characterization method (nanoparticle, nanofibre, nanoplate).
- Exposure conditions:
 - form of ENM that workers are exposed to and characterization method used;
 - industrial or professional setting;
 - routes of exposure;
 - life-cycle and process/activity where exposure/release occurs, with the aim of developing life-cycle maps;
 - amount of ENM handled (small scale/laboratory scale, pilot plant, commercial/large-scale).
- Description of training:
 - consideration of the STOP-principle (substitution, technical, organizational and personal management measures) for OSH (occupational safety and health);
 - involvement of stakeholders/social partners in the development of documents;
 - user-friendliness for target group(s);
 - clear allocation of responsibilities;
 - inclusion of risk-related tiered solutions.
- Suggestions for – or evaluation of – effective training.

Information from the items above was applied to assess the overall quality of the papers (Table 2).

Table 1. Criteria for assessing the quality of evidence for Question (h)^a

CRITERIA	SCORE
Item 1: Precise specification of application area and related tasks/workplaces (AA)	
Item 2: Validation in field studies and/or transdisciplinary studies (VS)	
Item 3: Description (DQ) of: i. quality assessment ii. quality of risk management iii. standard operating procedures	
Item 4: Questionnaire included questions on physicochemical characterization of the nanomaterials (or at least bulk material) (PC)	
Total ^b	

^a Specific nanomaterials or groups of nanomaterials are identified in Question (a) of the WHO guideline.

^b High: 6-12; moderate: 0 to 5; low: -5 to 0; very low: -12 to -6.

Table 2. Methodological quality of studies selected for full-text assessment

ENM NAME	NO. OF STUDIES	QUALITY OF TRAINING	QUALITY CRITERIA	CONCLUSION
Various metal oxide NM Methner (12)	1	Only LEV and cleaning	AA: 12 VS: 6 DQ: i 10 ii 6 iii 10 PC: 10	Good quality but no indication of effective training; excluded
Various NM Iavicoli et al. (13)	1	No field studies	AA: 6 VS: 0 DQ: i 12 ii 10 iii 6 PC: 0	Good quality but no indication of effective training; excluded
Saline NM Cesard et al. (14)	1	—	AA: 10 VS: 5 DQ: i 10 ii 10 iii. 10 PC: 6	Good quality but no indication of effective training; excluded
TiO ₂ Koivisto et al. (15)	1	—	—	After contacting the author the paper was excluded
MWCNT Takaya et al. (16)	1	—	—	After contacting the author the paper was excluded
Carbonaceous NM Schubauer-Berigan et al. (17)	1	—	AA: 12 VS: 12 DQ: i 10 ii 12 iii. 10 PC: 6	Good quality but no indication of effective training; excluded
Various Ricaud et al. (18)	1	—	AA: 12 VS: 12 DQ: i 10 ii 12 iii 10 PC: 6	Good quality but no indication of effective training; excluded

AA: application area; DQ: description quality; ENM: engineered nanomaterials; LEV: local exhaust ventilation;

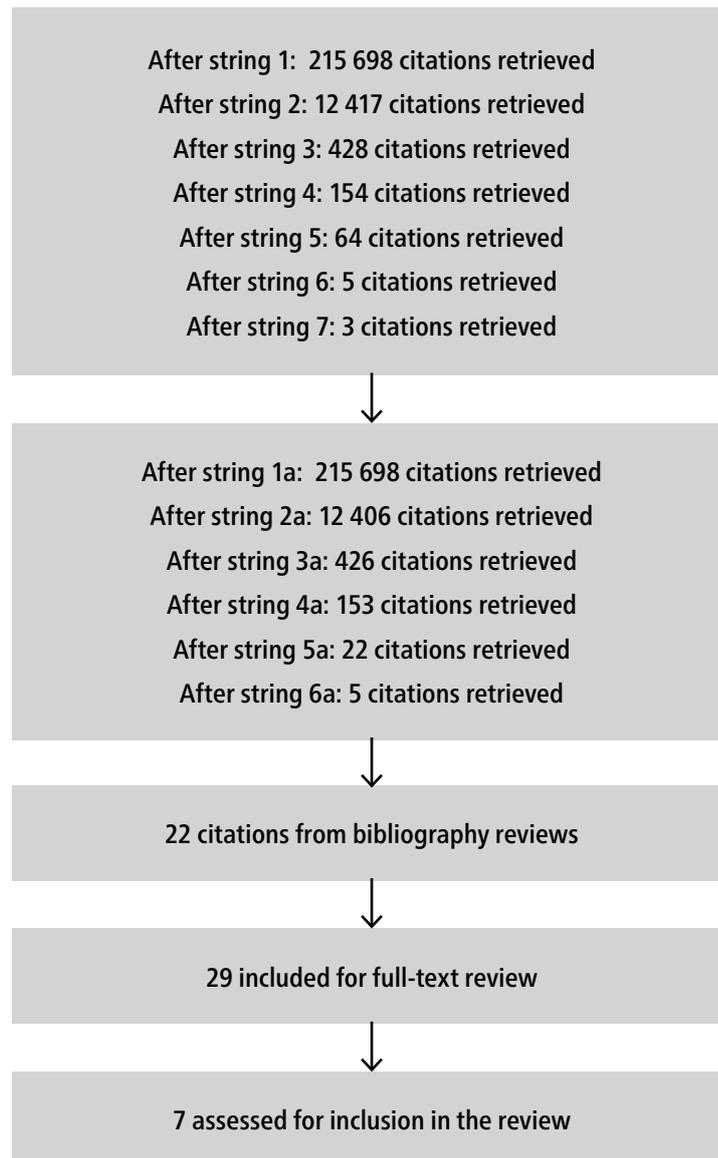
MWCNT: multi-walled carbon nanotubes; NM: nanomaterial; PC: physicochemical characterization; TiO₂: titanium dioxide; VS: validation study.

4. Results

4.1 Selection procedure

Fig. 2 below shows the first search using studies from PubMed and LIVIVO searches.

Fig. 2. Flow diagram of first search



All results after the sixth string of the first search were examined. Together with cross-referencing and grey literature review, 43 documents were checked for duplicates and relevance by title and abstract. As a result 29 papers were assessed full-text. The second search strategy led to 57 documents and, after alternation, to 13 final papers. They had all been included already in the first search. From the 29 fully-reviewed papers seven were scored by the procedure shown in Table 2.

None of the included literature gave quantifiable evidence of specific training for workers about handling nanomaterial.

4.2 Description of studies assessed in detail

Ricaud et al. (18) recommend that training and information must be provided to workers that meets the following objectives:

- understanding of the health and safety risks of nanomaterials;
- implementation of collective prevention measures;
- use of personal protective equipment (PPE).

and at the very least, this should include:

- definitions;
- regulatory context;
- organizational measures;
- best working practices;
- cleaning and waste management procedures;
- hygiene measures;
- measures in the event of incident or accident.

Methner et al. (12) recommend minimizing potential worker exposure. This should be done mainly through changes in work practices and the use of a control, such as a local exhaust ventilation (LEV) system, and also by changing the existing reactor cleanout practice, (vigorously brushing and scraping in multiple directions without the LEV), to a more targeted brushing and scraping (towards the flanged inlet duct of the LEV).

Cesard et al. (14) recommend that good practice rules, already generally defined for the use of fume hoods or other types of ventilated enclosures, must be respected as rigorously as possible when nanoparticles with unknown hazard values are handled or produced.

Iavicoli et al. (13) advise the following:

1. Plan and implement control measures (risk management) and communicate the plan.
2. Manage potential worker exposures by using the hierarchy of controls starting with elimination of the hazard, substitution with a non-hazardous or less hazardous alternative (such as modifying the molecule if possible), and introduction of engineering controls such as enclosed systems, LEV, engineering hoods or pressure differentials. These steps should be followed by administrative controls, including training programmes through which companies communicate sufficient information to workers to understand the nature and routes of potential NM workplace exposure, possible risks, adequate job procedures, preventive and protective measures and policies adopted.
3. Give workers training so that they can recognize and report symptoms of exposure to a given hazard.
4. Conduct epidemiological research to enhance the impact of occupational health surveillance through the periodic analysis of aggregated data in order to identify patterns of worker health that may be linked to work activities and practices. Exposure registries may be useful in setting the stage for this kind of research. Registries are important to enumerate and identify exposed individuals, to provide them with adequate information and guidance.
5. Make available complex technical and health information in language accessible and understandable to the occupational and general population.

Iavicoli et al. (13) also suggested that researchers, regulatory scientists, representatives of the workforce, industry and governmental authorities, should be actively engaged in proactive communication of the potential nanotechnology risks with the aim of forming accurate perceptions and attitudes. They found it extremely important to ensure the spread of appropriate information (including via the mass media) regarding the benefits and challenges of nanotechnology, to give a realistic picture to the public, and also to build and sustain a highly skilled workforce that can face emerging and known physicochemical risks and be trained to avoid accidents.

Schubauer-Berigan et al. (17) indicate that engineering control techniques (e.g. source enclosure, chemical hoods, and LEV) in conjunction with administrative controls (e.g. good work practices and training) are preferred over the use of PPE to protect workers.

5. Conclusion

Based on our experience of carrying out this literature study, we recommend contacting several experts and researchers directly, especially those that are active in relevant projects, to interview them about their experience of training and their estimates of the effects of training. The latter should be qualitative (based on their expert judgement) and quantitative, for instance data on the reduction in accidents and sick leave, reduction of emissions, prevention of exposure, etc. This should be done using one of the approaches outlined above to study the effectiveness of training.

Regarding the four elements of the PICO approach, the following conclusions can be drawn:

Population (P): Seven studies were found regarding the defined population. These are described in the results section of this paper.

The need for education features prominently in European policy texts such as the European Commission's *Towards a European Strategy for Nanotechnology* (19) and its report *Nanosciences and nanotechnologies: an action plan for Europe 2005–2009* (20), which aims to: "Promote networking and disseminate best practices for education and training in nanosciences and nanotechnologies". Since 2005, a number of documents have been published by governmental health research agencies, nongovernmental organizations, international standards organizations and academic groups to address best practices for managing occupational exposure to nanomaterials (for instance MARINA, QualityNano and nanoIndEx) (21, 22, 23). More specific information regarding occupational risk management applied to engineered nanomaterials is given by the ASTM International Committee E56 on Nanotechnology (24) as well as the ISO Technical Committee (TC) 229 on Nanotechnologies (25). However, most of these documents were not uploaded to the searched databases for this study, or address training only in general terms.

There are a range of further initiatives from the European Union as follows.

NanOpinion developed an educational programme during 2013 and 2014, in collaboration with scientists and teachers, which has been carried out in 15 countries in parallel with the European Commission's Public Consultation on Nanotechnologies and offers educational materials on its website (26).

NanoEIS (Nanotechnology Education for Industry and Society) investigates the European labour market for employees trained in nanotechnology and evaluates existing nanotechnology education and training in universities, vocational training institutes and secondary schools. By 2015 training modules were due to be made available online but were delayed and not ready by May 2016 (27).

NanoDiode is another ongoing project funded by the EU that will review and evaluate European nanotechnology education as part of its objective to define and assess best practices. Instead of reinventing the wheel, the project's Workpackage 4 aims to identify the most effective, useful elements within nanotechnology education and to roll out classes in Europe. NanoDiode provides a collection of links to online resources, reports and best practices on nanotechnology dialogue and engagement in Europe. Regarding training, material on the project can be found easily via the European Trade Union Institute (ETUI) website (28).

On a more general level of science education, the EU inGenious project aims to foster young people's interest in STEM (science, technology, engineering and mathematics) education and careers (29); it is a joint initiative launched by European Schoolnet and the European Roundtable of Industrialists (ERT). Registered users can find information on the EU Centre for the Development of Vocational Training website.

Intervention (I): Only a few studies could be found that gave contextual data or measurements on nanomaterial exposure at workplaces (30, 31). As mentioned in other areas of this WHO research, the different strategies and instruments used hamper the comparability of these studies. No study at all could be found that describes an effect of training in relation to nanomaterials at the workplace.

Unfortunately, no paper was found using the search strategy described that reported effectiveness of training for handling nanomaterials at the workplace. So no conclusion can be drawn either on the **comparator (C)** or the **outcome (O)**.

In future, we recommend that the effects of training could be studied and reported using different approaches (32, 33) such as:

- classical (emphasis on the aims and achievements);
- scientific (experimental approach, quantitative measures);
- comparative (ratio of costs and benefits between programmes);
- overall judgement (qualitative assessment of a programme);
- decision-making (production of information for decision-makers);
- systemic (relationships between inputs and outputs of a programme);
- user-centred (information useful for individuals, for instance the stakeholder);
- goal-free (emphasis on unexpected consequences);
- responsive (relationship between members being evaluated).

6. Annex 1: Summary of general training content

This annex summarizes some of the general training content for employees who are working with ENM or could be exposed to ENM. This was extracted from different papers, projects or websites that describe training materials for workers, regardless of whether they address handling and exposure of engineered nanomaterials and without quantifying the effectiveness of the training.

Based on our experience of carrying out this literature study, we recommend contacting several experts and researchers directly, especially those that are active in relevant projects, to interview them about their experience of training and their estimates of the effects of training. The latter should be qualitative (based on their expert judgement) and quantitative, for instance data on the reduction in accidents and sick leave, reduction of emissions, prevention of exposure, etc. before and after the application of a specific training programme.

First of all, the employee should be aware that they are handling nanomaterial. Training about risk assessment, risk management and risk communication is crucial for all types of workers and processes.

For the information gathering and hazard assessment, employees should know or understand how a safety data sheet is used as a source of information in the industrial and commercial supply chain. The following sections of the Material Safety Data Sheet (MSDS) should yield specific information on ENM:

- identification of the substance/mixture and of the producing company (Section 1);
- hazards identification (Section 2);
- composition/information on ingredients (Section 3);
- physical and chemical properties (Section 4).

Employees should be trained to recognize the potential release of ENM in relation to the source and the activity performed. Technical Data Sheets or additional product information (such as advertising brochures) may also contain references to the presence of manufactured nanomaterials in the substance or the mixture in question, especially regarding:

- classification of the nanoscale form;
- particle size distribution (such as granulometric findings);
- specific surface;
- form and structure (such as information on the applicability of the WHO fibre criteria);
- surface modification;
- solubility in water
- data on dustiness (such as characteristics of dust);
- combustion data (such as flammability and explosion limits).

For risk assessment, employees should know and understand the assessment criteria especially when measurements are used to indicate workplace exposure.

For risk management, employees should understand the hierarchy and efficacy of risk management measures and use them properly, especially:

- coveralls/uniforms supplied/laundered at the worksite;
- equipment maintenance standard operating procedures;

- housekeeping programme, high efficiency particulate air (HEPA) filter vacuums for clean-up;
- changing facilities, showers, hand washing.

For risk communication, employees should be trained in a language accessible and understandable to their work colleagues and the general population. It should be oriented to the target group because for example a laboratory technician needs different information (professional use, e.g. handling of small amounts of NM under a bench) than a production technician (industrial use e.g. upscaling of NM). The target group can be defined as workplace-oriented if it has similar tasks and exposure profiles (in so-called similar exposure groups), or product-oriented if they have the same life-cycle process. For example, employees can be categorized as product-oriented in:

- industrial settings, like manufacturing;
- professional settings, like a painter or construction worker;
- laboratory settings, like a scientist.

Training in an industrial setting, for example, should cover control measures to prevent or reduce dust, or aerosol formation, including the formation of a hazardous explosive atmosphere when:

- Handling nanopowders, especially in the gaseous phase synthesis and in top-down processes, when nano-objects are produced by mechanically crushing the original material in a milling process, especially weighing, mixing, dosing, pouring, packaging and mechanical finishing of nanopowders or nano-liquid suspensions.
- Processing of nanopowders or nano-liquid suspensions, especially filling, sampling, emptying and cleaning.
- Packaging and transporting dry nanopowders and nano-liquid suspensions.
- Incorporation of NMs into nano-enabled products.
- Recovering NMs from reactors, batches or filters.
- ENM is released unintentionally.
- Maintaining equipment and facilities to prevent or reduce dust or aerosol formation.
- Processing or treating solid articles containing manufactured nanomaterials bonded to a matrix such as the cutting or grinding of polymers or varnish layers with embedded nanomaterials.
- Processing of mixtures containing manufactured nanomaterials bonded in a liquid matrix (including paste or sludge).

Training in an industrial setting should also cover how to identify emissions and the probable presence of ignition sources, and how to apply risk management measures such as:

- Substitution with a non-hazardous or less hazardous alternative (such as modifying the molecule if possible).
- Applying or adopting local exhaust ventilation (LEV):
 - LEV ducted to the outside of the building;
 - LEV filtered and ducted back into the room with a HEPA filter or without a HEPA filter.
- Applying or adopting chemical fume hoods.
- Applying or adopting (bio)safety cabinets (BSC):
 - BSC ducted to outside;
 - BSC HEPA filtered and exhaust into the room.
- Applying or adopting ventilated enclosures:
 - Glove boxes.

- Applying or adopting separate ventilation for non-industrial areas like a laboratory or office.
- Spill control and storage.
- Administrative controls, including health and safety training programmes, so the worker can understand the nature and routes of potential NM workplace exposure, possible risks, adequate job procedures, preventive and protective measures and policies adopted.

Training in a professional setting should cover control measures to prevent or reduce dust or aerosol formation, including the formation of hazardous explosive atmospheres when:

- Handling, processing, packaging, storing and transporting NMs or nano-enabled products, especially machining, sanding, drilling or cutting.
- Assembly, application and maintenance of devices containing NMs.
- Processing or treating solid articles containing manufactured nanomaterials bonded to a matrix such as the cutting or grinding of polymers or varnish layers with embedded nanomaterials.
- Processing of mixtures containing manufactured nanomaterials bonded in a liquid matrix (including paste or sludge).
- Disposal of nano-enabled products.
- Recycling nano-enabled products.
- Maintaining equipment and facilities.
- Cleaning NM spills or waste.

Training in a professional setting should also cover how to identify emission and probable presence of ignition sources and how to apply risk management measures such as:

- Substitution with a non-hazardous or less hazardous alternative (such as modifying the molecule if possible).
- Applying or adopting LEV:
- LEV ducted to the outside of the building;
- LEV filtered and ducted back into the room with a HEPA filter or without a HEPA filter.
- Applying or adopting fume hoods.
- Applying or adopting ventilated enclosures.
- Applying or adopting separate ventilation for non-professional areas like a laboratory or office.
- Spill control & storage.
- Administrative controls, including health and safety training programmes that explain the nature and routes of potential NM workplace exposure, possible risks, adequate job procedures, preventive and protective measures and policies adopted.

Training in a laboratory setting can be very diverse – sometimes comparable to an industrial setting, sometimes comparable to a professional setting. Laboratory-specific protective measures (that should be part of training) can be found in the German DGUV Information sheet 213–851, *Working safely in laboratories – basic principles and guidelines* and DGUV Information sheet 213–854, *Nanomaterials in the laboratory – tips and handling information* (34, 35).

7. References

1. WHO handbook for guideline development, second edition. Geneva: World Health Organization; 2014.
2. Brown BB. Delphi process: a methodology used for the elicitation of opinions of experts: Rand Corp: Santa Monica, CA; 1968.
3. Robson LS, Stephenson CM, Schulte PA, Amick BC 3rd, Irvin EL, Eggerth DE et al. A systematic review of the effectiveness of occupational health and safety training. *Scand J Work Environ Health*. 2012;38(3):193–208.
4. Burke MJ, Holman D, Birdi K. A walk on the safe side: the implications of learning theory for developing effective safety and health training. *International review of industrial and organizational psychology*. 2006;21.
5. Burke MJ, Smith Sockbeson CE. Safety Training. In: Clarke S, Probst TM, Guldenmund FW, Passmore J, editors. *The Wiley Blackwell handbook of the psychology of occupational safety and workplace health*. Chichester, England: John Wiley & Sons Ltd; 2015. pp 327–356.
6. Burke MJ, Salvador RO, Smith-Crowe K, Chan-Serafin S, Smith A, Sonesh S. The dread factor: how hazards and safety training influence learning and performance. *Journal of Applied Psychology*, 2011;96(1):46–70. <http://dx.doi.org/10.1037/a0021838>
7. Burke MJ, Chan-Serafin S, Salvador R, Smith A, Sarpy Sue Ann. The role of national culture and organizational climate in safety training effectiveness. *European Journal of Work and Organizational Psychology*. 2008;17(1): 133–152.
8. Kirkpatrick DL. *Evaluating training programs: the four levels*. Oakland CA: Berrett-Koehler Publishers; 1994.
9. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P et al.; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336(7650):924–6.
10. GRADE working group [website]. The GRADE working group. 2014. Available from: <http://www.gradeworkinggroup.org/> [accessed 2017 Oct 18].
11. ISO/TS 12901-1:2012 Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 1: Principles and approaches. Geneva: ISO; 2016.
12. Methner MM. Effectiveness of a custom-fitted flange and local exhaust ventilation (LEV) system in controlling the release of nanoscale metal oxide particulates during reactor cleanout operations. *Int J Occup Environ Health*. 2010 Oct–Dec;16(4):475–87.
13. Iavicoli I, Leso V, Ricciardi W, Hodson LL, Hoover MD. Opportunities and challenges of nanotechnology in the green economy. *Environ Health*. 2014 Oct 7;13:78.
14. Cesard V, Belut E, Prevost C, Taniere A, Rimbert N. Assessing the containment efficiency of a microbiological safety cabinet during the simultaneous generation of a nanoaerosol and a tracer gas. *Ann Occup Hyg*. 2013 Apr;57(3):345–59.
15. Koivisto AJ, Lyyräinen J, Auvinen A, Vanhala E, Hämeri K, Tuomi T et al. Industrial worker exposure to airborne particles during the packing of pigment and nanoscale titanium dioxide. *Inhal Toxicol*. 2012 Oct;24(12):839–49.

16. Takaya M, Serita F, Ono-Ogasawara M, Shinohara Y, Saito H, Koda S. [Airborne particles in a multi-wall carbon nanotube production plant: observation of particle emission and personal exposure 1: Measurement in the packing process]. *Sangyo Eiseigaku Zasshi*. 2010;52(4):182–8. Japanese.
17. Schubauer-Berigan MK, Dahm MM, Schulte PA, Hodson L, Geraci CL. Characterizing adoption of precautionary risk management guidance for nanomaterials, an emerging occupational hazard. *J Occup Environ Hyg*. 2015;12(1):69–75.
18. Ricaud M, Witschger O. Nanomaterials – Definitions, toxicological risk, characterisation of occupational exposure and prevention measures [ED 6050]. Paris: INRS; 2012
19. Towards a European strategy for nanotechnology. Brussels: European Commission; 2004. Available from:
http://cordis.europa.eu/pub/nanotechnology/docs/nano_com_en_new.pdf [accessed 2017 Oct 18].
20. Nanosciences and nanotechnologies: an action plan for Europe 2005–2009. Brussels: European Commission; 2005. Available from:
http://cordis.europa.eu/pub/nanotechnology/docs/action_plan_brochure.pdf [accessed 2017 Oct 18].
21. MARINA [website]. Managing the risks of nanomaterials. Edinburgh: IOM. Available from: <http://www.marina-fp7.eu/> [accessed 2017 Oct 18].
22. QualityNano [website]. Available from: <http://www.qualitynano.eu> [accessed 2017 Oct 18].
23. nanoIndEx [website]. Available from: <http://www.nanoindex.eu> [accessed 2017 Oct 18].
24. ASTM E2996-15 Standard guide for workforce education in nanotechnology health and safety. West Conshohocken, PA: ASTM International.
25. ISO/TC 229 Nanotechnologies. Geneva: ISO. Available from:
<https://www.iso.org/committee/381983.html> [accessed 2017 Oct 18].
26. NanOpinion [website]. Available from: <http://nanopinion.eu> [accessed 2017 Oct 18].
27. Research & Innovation: key enabling technologies [website]. Brussels: European Commission. Available from:
http://ec.europa.eu/research/industrial_technologies/policy_en.html [accessed 2017 Oct 18].
28. NanoDiode Project. Training materials on nano and workers [website]. Brussels: ETUI. Available from: <https://www.etui.org/Topics/Health-Safety/Nanotechnologies/Nanodiode-project-training-materials-on-nano-and-workers> [accessed 2017 Oct 18].
29. inGenious [website]. Brussels: European Schoolnet. Available from:
<http://www.ingenious-science.eu/web/guest/about> [accessed 2017 Oct 18].
30. Gavin H, Lippy BE, Cooper MR, Marsick D, Burrelli LG, Griffin KN et al. Toward responsible development and effective risk management of nano-enabled products in the US construction industry. *Journal of Nanoparticle Research*. 2016;18:49.
31. Working safely with manufactured nanomaterials – Guidance for workers. Brussels: Employment, Social Affairs & Inclusion, European Commission; 2014. Available from:
<http://ec.europa.eu/social/BlobServlet?docId=13088&langId=en>
32. Robson LS, Stephenson C, Schulte P, Amick B, Chan S, Bielecky A et al. A systematic review of the effectiveness of training & education for the protection of workers. Toronto: Institute for Work & Health; 2010.

33. Vignoli M, Punnett L, Depolo M. How to measure safety training effectiveness? Towards a more reliable model to overcome evaluation issues in safety training. *Chemical Engineering Transactions*. 2014;36:67–72. doi: 10.3303/CET1436012
34. Nanomaterials in the laboratory – tips and handling information [DGUV 213-854]. Berlin: DGUV; 2015. Available from:
<http://publikationen.dguv.de/dguv/pdf/10002/213-854.pdf> [accessed 2017 Oct 18].
35. Working safely in laboratories – basic principles and guidelines [BGI/GUV-1850-0e]. Berlin: DGUV; 2014. Available from:
https://www.bgrci.de/fileadmin/BGRCI/Downloads/DL_Praevention/Fachwissen/Laboratorien/Included_changes_BGI-GUV-I_850-0e_070514.pdf [accessed 2017 Oct 18].

7.1 Websites and grey literature reviewed

(All accessed on 2017 Oct 18)

<http://www.baua.de/en/Topics-from-A-to-Z/Hazardous-Substances/Nanotechnology/Nanotechnology.html>

<http://www.cdc.gov/niosh/docs/2009-125/>

<http://www.dguv.de/ifa/Fachinfos/Nanopartikel-am-Arbeitsplatz/index-2.jsp>

<http://nano.dguv.de/nanorama/bgrci/en/>

http://bgi850-0.vur.jedermann.de/index.jsp?isbn=bgi850-0&alias=bgc_bi850_0_di213_851_1_

<https://www.etui.org/Topics/Health-Safety/Nanotechnologies/Nanodiode-project-training-materials-on-nano-and-workers>

<https://www.etui.org/News/Pilot-testing-of-capacity-building-tools-on-nanomaterials>

<https://www.etui.org/Events/Seminar-for-a-Trade-Union-strategy-on-nanotechnologies>

<http://www.futurenanoneeds.eu/>

<http://www.guidenano.eu/>

<http://www.nano.gov/node/135>

<http://www.nanodefine.eu/>

<http://www.nanodiode.eu/>

<https://nanohub.org/groups/gng>

<http://nanomile.eu-vri.eu/>

<http://www.nanosafetycluster.eu/>

<http://nanosolutionsfp7.com/>

<http://www.siinn.eu/>

<http://www.sun-fp7.eu/>