

# Use of Engineered Nanomaterials in Dutch Academic Research Settings

## Good Practices

### Part B

The Hague, January 2014



Title	Use of engineered nanomaterials in Dutch academic research settings – Part B
Authors	R.T.M. Cornelissen, M. Samwel-Luijt, M.B.H.J. Vervoort and D. Hoeneveld
<p>All opinions, conclusions and recommendations given in this report are those of the authors and do not necessarily reflect those of the employers in this sector (the Association of Dutch Universities VSNU and the employers' association of Dutch knowledge-intensive research organizations WVOI). An attempt has been made to sketch a picture of risk assessment concerning the use of engineered nanomaterials in a research environment on the basis of the literature available in 2013.</p> <p>In view of the many different types of engineered nanomaterials (as regards not only their chemistry but also their form and composition), evaluation of the potential risk involved in working with nanomaterials must be based on skilled assessment. The recommendations and conceptual frameworks given in this report can provide support, but no absolute certainty, in this connection.</p>	
<p>For further information about this report, please contact:  Mr. R.T.M. Cornelissen Tel: +31 30-3006012 or E-mail: <a href="mailto:ralf.cornelissen@fom.nl">ralf.cornelissen@fom.nl</a></p>	
<p>Data from this report may be used as long as the source is explicitly stated.  The authors and their employers accept no responsibility for any possibly damage arising from use of the results of this study or of the recommendations it contains.</p>	

## **Table of contents**

Good Practice 1	Definition of engineered nanomaterials
Good Practice 2	Working Conditions Act
Good Practice 3	Nanorelevance: am I dealing with a nanomaterial?
Good Practice 4	Risk assessment methods for nanomaterials
Good Practice 5	Research planning
Good Practice 6	Planning and implementation of a risk assessment
Good Practice 7	Secondary processes involving nanomaterials
Good Practice 7A	Safe transport of nanomaterials
Good Practice 7B	cleaning procedures in nanolaboratories
Good Practice 7C	Dealing with waste containing nanomaterial
Good Practice 7D	Maintenance procedure for equipment
Good Practice 8	Exposure measurement
Good Practice 9	Control measures
Good Practice 10	Standard Operating Procedure (SOP)
Good Practice 11	Information and training
Good Practice 12	Facilities for working with nanomaterials in newly built or renovated laboratories
Good Practice 13	Protocol for dealing with severe accidental exposure to nanomaterials

## GP 1 Definition of engineered nanomaterials

### *Introduction*

This Good Practice gives further details of the definition of synthetic nanomaterials, the classification of nanomaterials by form and current insights concerning the classification of nanomaterials by the health risks they entail.

### *Definition recommended by the European Commission*

The [European Commission](#) approved the following definition of nanomaterials in October 2011 (1).

“Nanomaterial” is defined as:

a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and which meets one of the following criteria:

- for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 – 100 nm;
- the specific surface area by volume of the material is greater than  $60 \text{ m}^2/\text{cm}^3$ , (this only applies to particles larger than 1 nm).

In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size threshold of 50 % may be replaced by a threshold between 1 and 50 %. Fullerenes, graphene flakes and single wall carbon nanotubes with one or more external dimensions should be considered as nanomaterials.

### *Comments on the definition*

It is theoretically possible that the definition of nanomaterials to be used in legislation may differ from that based for example on the health effect of these materials. A great deal of toxicological research is needed to test all the different compounds and physical forms of these materials for toxicity. It should be realized that each combination of chemical composition and form (with or without coating) can give rise to a different toxic or other effect. This makes it difficult to give an unambiguous definition of a synthetic nano-compound, especially because it is impossible to state with certainty whether a harmful effect will start to manifest itself at particle sizes below 100 nm, or whether the cut-off point is higher than this (2, 3, 4, 5, 6).

---

<sup>1</sup> Commission recommendation on the definition of nanomaterial, 2011/696/EU, 18 October 2011.

<sup>2</sup> ICRP publication 66 (1994) *Ann. ICRP* (UK), vol. 24, Nos. 1-3, Pergamon.

<sup>3</sup> Risk assessment of products of nanotechnology, SCENIHR, 2009.

<sup>4</sup> Geiser, M., Ultrafine Particles Cross Cellular Membranes by Nanophagocytosis Mechanisms in Lungs and in Cultured Cells, *Environmental Health Perspectives*, volume 113 (11), November 2005.

<sup>5</sup> E.A.J. Bleeker et al. (2012) Interpretation and implications of the European Commission Recommendation on the definition of nanomaterial RIVM Letter Report 601358001/2012.

<sup>6</sup> E.A.J. Bleeker et al. (2013) Considerations on the EU definition of a nanomaterial: Science to support policy making *Regulatory Toxicology and Pharmacology*, Volume 65, Issue 1, February 2013, Pages 119–125.

*Definition for use by research institutes*

It is clear from the above that the size range from 1 to 100 nm should be viewed in a wider context. This provides a basis for arguing that particles smaller than 1 nm or larger than 100 nm (up to 500 nm) should also be considered as nanomaterials.

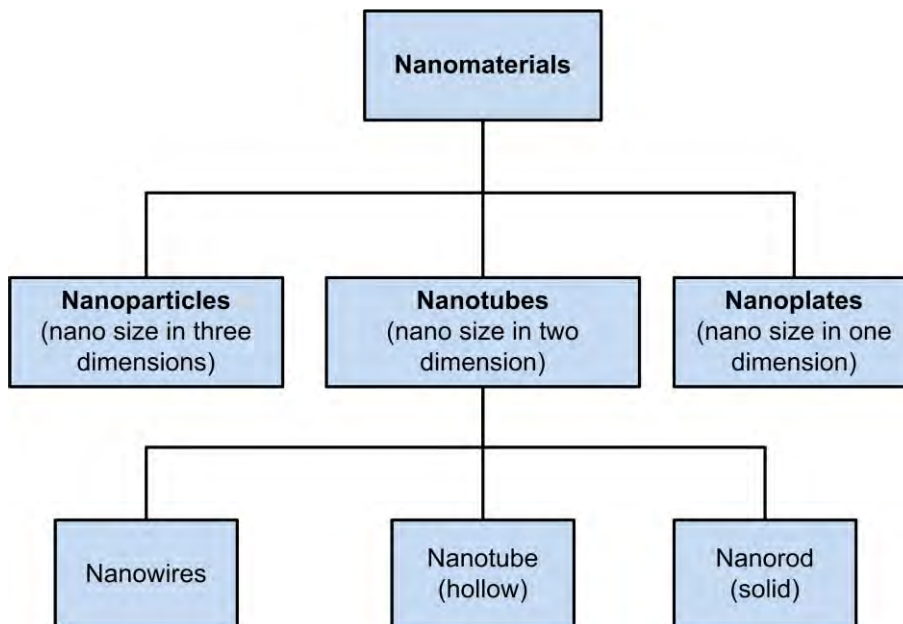
Since the risks associated with new nanomaterials made or existing nanomaterials modified in research are practically unknown, it should be considered whether the following definition should be used for these materials:

A **nanomaterial** is a simple substance or a product in which “engineered” nanomaterials are **intentionally** used in order to give the product specific properties and:

- where the primary particle size is between 1 and 500 nm;
- regardless of the concentration or amount used in a product.

*Classification of nanomaterial by form*

A definition of nanomaterials was given at the start of this Good Practice. It is also possible to classify these materials by form, as illustrated in the following figure (7).



**Figure 1.1** Classification of nanomaterials by form

<sup>7</sup> CEN-ISO/TS 27687:2008-08 en: Nanotechnologies -- Terminology and definitions for nano-objects - Nanoparticle, nanofibre and nanoplate (2008).

*Classification of hazards of engineered nanomaterials*

Exposure to nanomaterials can occur via the respiratory tract, the digestive tract and the skin. In addition, nanomaterials are often injected directly into the bloodstream for medical applications (imaging, diagnosis or therapy). Particles can also be released into the body due to wear of implants (8). It is to be expected that the main exposure route for employees among all those listed above will be that via respiration.

Working with and possible exposure to nanomaterials should thus have to be included in the risk assessment of hazardous substances for which the nature, extent and duration of possible exposure has to be mapped (see Good Practice 2 and 6). Exposure to nanomaterials does not differ essentially from exposure to chemical substances in bulk form. However, extra attention needs to be paid to mapping of the safety aspects specifically relevant to nanomaterials. The measure of exposure to nanomaterial used to estimate the risks associated with these materials can be different from the measure used when considering substances in bulk form.

While there are many uncertainties about the possible risks of nanomaterials, there are indications about possible ways of estimating the harm they can cause. A widely used classification of the potential hazard associated with such materials (listed in order from high to low), about which consensus exists at present, is as follows (9, 10):

- fibrous, rigid, insoluble forms;
- insoluble particles where the parent material is classified as a CMR substance;
- insoluble particles (non-fibrous and where mother material does not have CMR properties); and
- soluble particles.

CMR stands for carcinogenic, mutagenic or reprotoxic.

---

<sup>8</sup> Gezondheidsraad. (2006) Betekenis van nanotechnologieën voor de gezondheid. Den Haag: Gezondheidsraad. publicatie nr. 2006/06;

<sup>9</sup> PD 6699-2:2007 (2007) Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials. British Standards. ISBN 978 0 580 60832 2;

<sup>10</sup> S. Dekkers en C. de Heer (2010) [Provisional nano-reference values : Applicability of the concept and of published methods.](#)

## GP 2 Working Conditions Act

### *Introduction*

Since nanotechnology engages with many different disciplines, some of its products may not be covered by any national or European legislation. The Dutch Ministry of Social Affairs and Employment (SZW) has no plans at present to draft any separate legislation for nanotechnology in the Netherlands, since the Working Conditions Act (Arbowet) [offers sufficient scope](#) for regulation of work involving nanotechnology (1). This Good Practice gives a number of suggestions about how to fit working with nanomaterials into the current legislative and regulatory framework.

### *Dutch Working Conditions Act (Arbowet)*

The [Arbowet](#) states that the employer is responsible for assessing the risks run by employees at work and for taking the necessary precautions to guard against these risks. These activities should be included in the companies risk inventory and evaluation (RI&E), which also covers new risks about which little is as yet known.

According to the new Dutch system for establishing occupational exposure limits (OEL), the employer is also responsible for setting safe occupational exposure limits for the various substances used at work. In the absence of any legally binding OELs, the safe exposure limits at work must be health based, without reference to economic or technical feasibility.

The employer retains the final responsibility for a safe, healthy working environment, taking the latest advances in science and technology into account. The point of departure is that substances involving an uncertain or unknown risk – which includes nanomaterials – must be treated as if they were hazardous or very hazardous. This means that the policy for managing such substances and the precautions taken must be aimed at preventing or minimizing employees' exposure to them. [REACH](#), the EU's integrated system for the registration, evaluation, authorization and restriction of chemicals, should also be taken into account in this connection. When derived no-effect levels (DNELs) for nanomaterials become available, they should be used as a basis for setting occupational exposure limits.

The basis for the policy on hazardous substances as laid down in the Arbowet is Article 3 (employer's general duty of care). The following other portions of this Act are also of importance:

#### Working Conditions Act

- Article 5: obligation to produce a written inventory and assessment of the risks to which employees are exposed as a result of their work;
- Article 6: prevention of serious accidents involving hazardous substances;
- Article 8: information and training;
- Article 10: preventing hazards to third parties;
- Article 16: further obligations concerning inventory of hazardous substances and biological agents;

---

<sup>1</sup> Kabinetsvisie Nanotechnologieën. Van Klein Naar Groot, 2010.

Working Conditions Decree

- Chapter 4: further obligations concerning handling of dangerous substances.

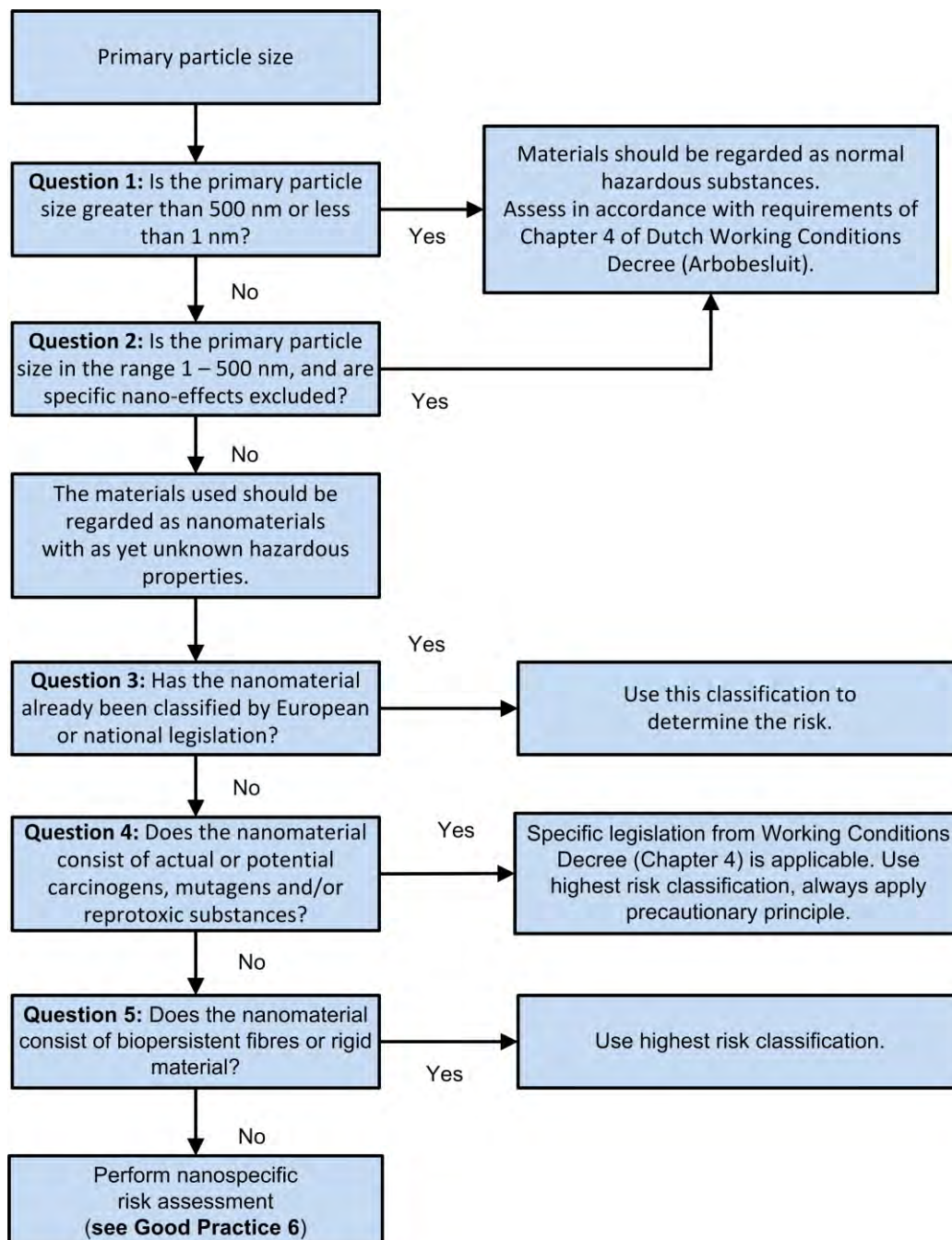
*It follows in concrete terms from these provisions that:*

- engineered nanomaterials should be included in the companies risk assessment;
- a plan of attack should be available containing measures for optimum management of exposure to engineered nanomaterials (trying to keep this exposure as low as possible);
- individual companies or organizations should set their own OELs if no official OELs are available.



**GP 3 Nanorelevance: am I dealing with a nanomaterial?***Introduction*

Before performing a risk assessment for the use of nanomaterials, it is important to check whether the material in question is indeed covered by the definition of engineered nanomaterials, and whether risks are associated with its use (see Good Practice 1). The decision diagram shown below can be used to determine whether the substance is a nanomaterial whose use might possibly be associated with health risks, and what steps need to be taken to estimate the risk of the relevant work operations accurately. The diagram will be followed by a brief explanation of each question.



**Figure 3.1 Decision diagram for determining nanorelevance of materials used**

*Explanation of decision diagram*

Question 1 concerns the size of the nanomaterials used. In order to judge whether the substance in question really is a nanomaterial, use the wider definition given in Good Practice 1. If the material is found not to be covered by this definition, it is advisable to use the normal methods (as employed with bulk chemicals) to determine the nature, degree and duration of exposure. Chapter 4 of the Dutch Working Conditions Decree (Arbobesluit) should be used as frame of reference here.

If the substance used is found to be covered by the definition of nanomaterials, it is advisable to check or determine its pyrophoric properties – that is, its tendency to ignite spontaneously in air. Nanopowders are often pyrophoric, even if the material does not have this property in bulk form. If the amounts used exceed a few milligrams, as small a sample as possible should be taken to determine the pyrophoricity. If the material is found to be pyrophoric, special precautions should be taken such as use in a low-oxygen environment.

Question 2 refers to studies that have already been performed on the type of nanomaterials used in the research institute. When scientific research has incontrovertibly shown that the nanomaterials used can be regarded as not harmful for humans (on the basis of both their chemical composition and their form), then the nanomaterials used can be evaluated as indicated in Question 1.

Question 3 involves checking whether the nanomaterial in question has already been classified with reference to European regulations (such as [SCOEL](#), [REACH](#), [Globally Harmonised System of Classification and Labelling of Chemicals](#)) or by national legislation (such as recommended or binding exposure limits). If the material has been classified, it is recommended that this hazard classification should be used.

Question 4 deals with the issue of whether it is known if the nanomaterials in question (or the parent material) could have carcinogenic, mutagenic or reprotoxic (CMR) properties. If this is the case, it is recommended that the requirements and measures mentioned in section 2 of Chapter 4 of the [Working Conditions Decree](#) are acted on. These measures go so far that there is little scope for supplementary risk management measures.

The risk assessment should consider the nanospecific properties of the materials in question as well as their CMR properties.

Question 5 concerns the fibrous properties of various nanomaterials. A number of studies have pointed out the possible carcinogenic properties of tubular nanomaterials that are comparable with asbestos fibres (Fibre Paradigm) (1, 2). As a precaution, materials with a tubular structure (fibres, rods and wires) should be placed in the highest hazard category (Good Practice 1).

It is recommended that a nanospecific risk assessment should be carried out for the use of other nanomaterials (Good Practice 6).

---

<sup>1</sup> Takagi, A., et al. (2008) Induction of mesothelioma in p53+/- mouse by intra peritoneal application of multi-wall carbon nanotubes, *The Journal of Toxicological Sciences*, 33, 2008, 105-116.

<sup>2</sup> Poland, C.A. et al. (2008) Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study, *Nature Nanotechnology*, 3, 2008, 423-428.

## GP 4 Risk assessment methods for nanomaterials

### *Introduction*

Various methods of evaluating the risks associated with the use of nanomaterials have been developed. Vervoort and Cornelissen (1) subjected thirteen such methods to theoretical investigation in their study. In addition, ten methods were tested in practice by applying them to various laboratory processes where nanomaterials were used. It may be concluded from their results that three of the thirteen methods are most suitable for use in an academic research environment. These are the Control Banding Nanotool (2, 3, 4), the EPFL method (5) and the Nanotoolkit (6). All three methods were specifically developed by research institutes.

### *Further explanation of the three methods*

All three methods have pros and cons. Users will have to take the specific features of each method into account when using it. Despite the fact that most risk assessment methods make use of a hazard classification (severity) and probability of exposures, assessment of a given process can lead to different risk classes, when using different methods. One method may classify a process as safe, while another method classifies the same process as unsafe. This difference is partly due to the use of different variables for determining the hazard and exposure band, the target group and the structure of the method. Apart from the differences in approach, differences can also arise because different users make different choices concerning the instruments they employ, and some may estimate certain variables conservatively while others estimate them progressively.

When deciding which method is the best take in consideration if the method is suitable for the process, the control measures that have already been taken and renovation or construction of a new building is planned. A brief description of the three above-mentioned methods is given in the following pages. The Control Banding Nanotool, the EPFL method and the Nanotoolkit will be discussed in that order. A schematic representation of the procedures used in these three methods is given in the appendices to this Good Practice.

---

<sup>1</sup> Vervoort, M.B.H.J. et al, Risk Assessment of Occupational used Nanomaterials – A comparison of risk assessment methods in order to determine the risk of occupational used nanomaterials in a research environment- master thesis Netherland School of Public and Occupational Health, September 2012.

<sup>2</sup> David M. Zalk, Samuel Y. Paik and Paul Swuste. Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures. J Nanopart Res 11:1685–1704 (2009).

<sup>3</sup> Paik, S.Y., et al, Application of a pilot Control Banding tool for risk level assessment and control of nanoparticle exposure, Ann. Occ. Hyg., vol 52, no 6, pp 419 - 428, 2008.

<sup>4</sup> Zalk, D.M., et al, Control Banding and Nanotechnology. The Synergist, volume 21, issue 3, 2010, pp 26 – 29.

<sup>5</sup> Groso, A. et al. (2010) Management of nanomaterials safety in research environment. Particle and Fibre Toxicology 2010 7:40.

<sup>6</sup> California Nanosafety Consortium of Higher Education (2012) Nanotoolkit. Working safely with engineered nanomaterials in academic research settings.

### Control Banding Nanotool

One of the first methods used to assess the risks of occupational exposure to nanomaterials is the Control Banding Nanotool (CBN). This method was originally developed for characterization of the health hazards of working with nanomaterials in two departments of a research institute. It is thus ideally suited for use in the assessment of research activities, and less suitable for assessment of the risks to end-users and those engaged in the processing of nanoproducts.

The CBN assesses the possible risks of working with nanomaterials with reference to one score for the severity of exposure to these materials and another score for the probability of exposure. The maximum severity score is 100, where 70 points are derived from the characteristics of the nanomaterial and 30 points from those of the parent material. Fifteen variables are used to determine the severity score. The maximum probability score is also 100 points; this is divided over five variables relating to the extent to which employees are exposed to the nanomaterials (for example, amounts used, number of employees exposed, frequency and duration of exposure). When the score for a given variable is unknown, a value equal to 75 per cent of the maximum possible score for that variable is assigned. Combining the two scores gives the overall risk of the activities in question, as represented in the decision matrix of Figure 4.1.

		Probability (risk of exposure)			
		Extremely unlikely (0-25)	Less likely (26-50)	Likely (51-75)	Probable (76-100)
Severity	Very high (76-100)	RL 3	RL 3	RL 4	RL 4
	High (51-75)	RL 2	RL 2	RL 3	RL 4
	Medium (26-50)	RL 1	RL 1	RL 2	RL 3
	Low (0-25)	RL 1	RL 1	RL 1	RL 2

**Figure 4.1** Decision matrix for taking of control measures according to the Control Banding Nanotool

This model distinguishes a total of four risk categories or risk levels (RL), ranging from RL1 (low) to RL4 (high). There is a direct relationship between the risk level and the control measure to be taken.

- RL 1: Use general ventilation
- RL 2: Use fume hoods or local exhaust ventilation
- RL 3: Containment
- RL 4: Seek specialist advice

The safety measures described above, corresponding to risk levels RL1 - RL4, are not in line with the occupational hygiene strategy, also known as the STOP-approach<sup>7</sup>, but are mainly limited to ensuring the appropriate exhaust or ventilation level. Users of the CBN should bear in mind that this method was developed for a research environment, where most activities take place in a fume cupboard.

#### *Pros and cons*

##### Pros:

- the risk analysis is performed in a systematic, convertible way;
- the method is suitable for use in an MS-Excel environment, which can then be used to perform the necessary calculations;
- the risk analysis takes the number of persons exposed into account (not every method does this);
- each research step is analysed separately, so that it immediately becomes apparent which activities are susceptible to risks;
- if a new nanomaterial is used in a given process, it is only necessary to change the hazardous properties of the material in MS-Excel to generate a new risk analysis;
- new insights (and new risk scores for each variable) can easily be processed.

##### Cons:

- the toxicological properties of nanomaterials and exotic parent materials are often unknown;
- only a limited number of safety measures have been described, and these are all technical measures;
- the variable “number of employees exposed” has a lower limit of six. This is quite high for a research environment, where only one or two researchers generally work on a given experiment in practice;
- the risk assessment is relatively time-consuming;
- it is not always clear what significance the author attaches to the variables used, since concrete explanation is not given;
- the tool is only suitable for assessment of the use of pure materials, not for mixtures or processing of nanoproducts.

---

<sup>7</sup> The STOP approach describes the hierarchy in which control measures have to be taken into account: (Source – Technical – Organisational – Personal)

### The EPFL method

This method is named after the Ecole Polytechnique Fédérale de Lausanne (EPFL), which developed a method for 'Management of Nanomaterials Safety in Research Environment'. It differs from other instruments in not making use of risk classes. The authors justify this approach on the basis of the argument that sufficient data on exposure and the likely effects of exposure on health is not yet available. They therefore only use hazard classes (1, 2 and 3). The higher the class, the greater the hazard involved.

The point of departure of the EPFL method is that the materials in question have one or more dimensions between 1 and 100 nm. The method makes use of a decision tree (see Figure 4.2), which is applied to activities that may be used when handling nanomaterials. These activities may involve handling nanofibres, nanomaterials in suspension, nanopowders and nanomaterials in a matrix or composite material. The activities are assigned to hazard classes on the basis of the intended application, the amount used and the agglomeration status. Three hazard classes (1, 2 and 3) are distinguished. The higher the class, the more hazardous the activity. There is a direct relationship between the hazard class and the safety measures to be taken in this method. The higher the class, the more stringent the safety measures to be taken in the laboratory. This is comparable with the classification (ML-I, ML-II and ML-III) of laboratories working with GMO (genetically modified organisms) (8), and the A, B, C and D classification of laboratories working with radioactive substances.

#### *Activities to be distinguished*

The activities involving fibrous nanomaterials may be divided into three categories:

1. working with dry materials;
2. working with suspensions;
3. working with composites (nanomaterials in a matrix).

Activities with nanomaterials in powder form (dry materials):

1. use (for example weighing out purchased or self-produced nanomaterials);
2. production (synthesis) of materials.

In the case of production, the hazard class depends on the amount of material produced per batch and its agglomeration status. Large batch sizes (> 100 mg), absence of agglomeration or no knowledge of agglomeration status leads to a higher hazard class. A similar classification is employed for the use of nanomaterials in powder form, but the amounts involved are smaller: the minimum amount of material is less than or equal to 1 mg.

Activities with nanomaterials in suspension:

1. the nanomaterial remains in suspension;
2. aerosols are formed in at least one process step;
3. dry material is formed in at least one process step.

---

<sup>8</sup> Schellekens, H., Veilig werken met micro-organismen, parasieten en cellen in laboratoria en andere werkrumten, 4<sup>e</sup> druk 2010.

The classification of nanomaterials used in suspension depends on the likelihood of exposure (risk of release of material) and the amount of material used.

Activities with nanomaterials in a matrix:

Nanomaterials used in a matrix (enclosed in a solid material) are assigned to the lowest hazard class, unless the use of the material can cause dust to be formed. In this case, the precautions for nanomaterials in powder form must be followed.

Risk classification and safety measures

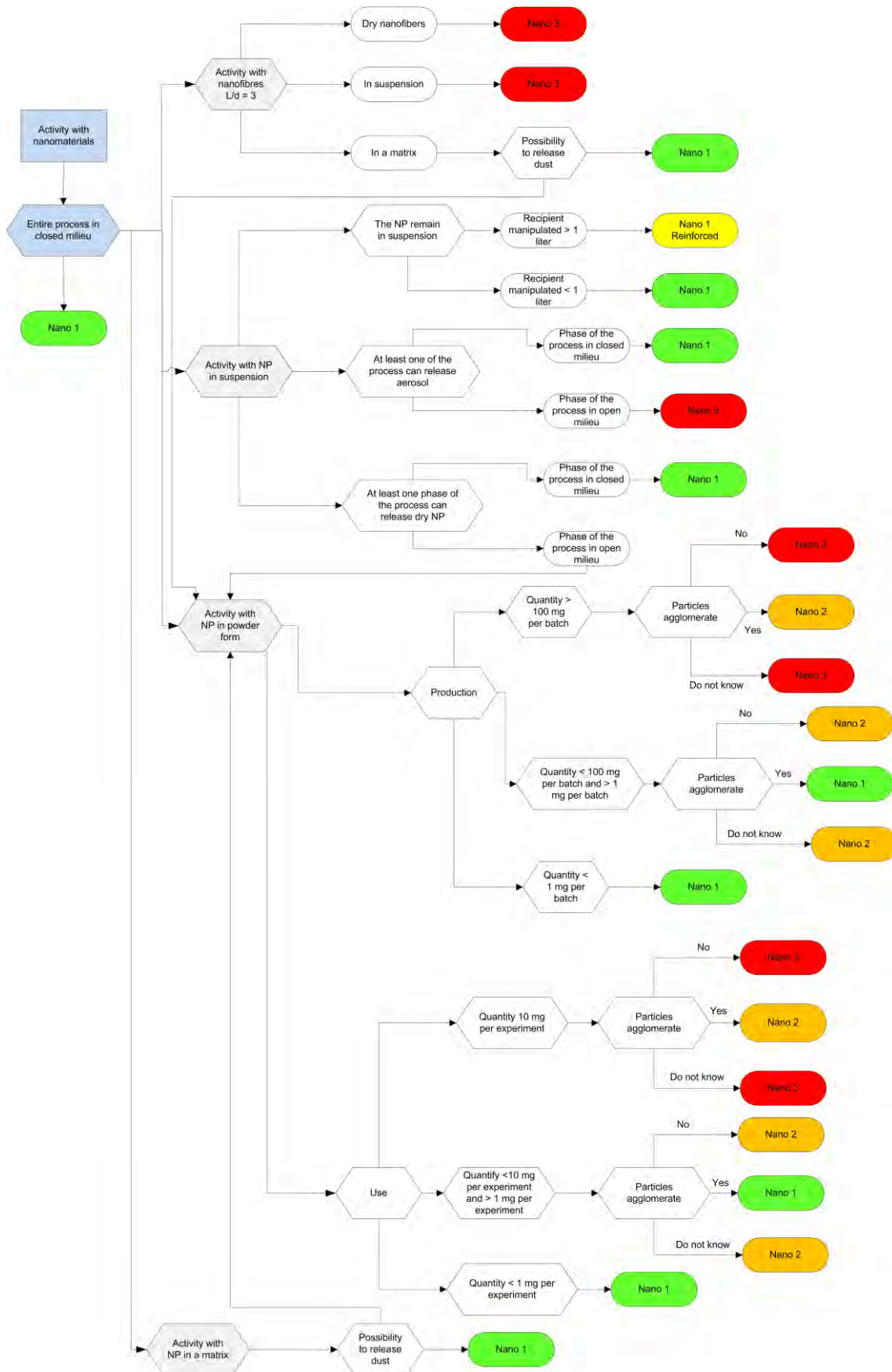
There is a direct relationship between the hazard class (1, 2 or 3) and the safety measures to be taken. Tables (such as Table 4.1) are used to indicate the kind of measures to be taken. These measures may be divided into four groups:

- technical measures (ventilation, properties of the floor, access to lab etc.);
- organizational measures (information and training, waste management etc.);
- use of personal protective equipment;
- cleaning the laboratories.

**Table 4.1** Example of technical safety measures used in the different hazard classes

Technical safety measures		Laboratory (hazard class)		
		Nano 1	Nano 2	Nano 3
Ventilation	Chemistry lab type (renewal without recycling 5-10 X /hour)	X	X	X
	With at least sealed F7 filter for exiting air			X
	Low pressure in the room	X	X	>20 mPa
	Capture at source		X	X
Floor	Flooring	Tiling or linoleum		resin
Manipulation under fume hood	Optional	X (1)		
	Compulsory		X	X
Access restriction	Restricted (magnetic card access control system)		X	X
	Regular lab access control (laboratory key)	X		
	Evidence about exposed people + board to record presence			X
SAS entrance and exit	Double SAS (if >100 g ultrafine particles)			X
	Simple SAS (if <100 g ultrafine particles)		Light SAS	X
	Safety shower			X
Use of vacuum cleaners	Asbestos type	X	X	X
	Domestic type		Forbidden	

(1) Reinforced type 1 = type1 plus obligatory manipulation under fume hood.



**Figure 4.2** Decision tree for determination of nano hazard class according to EPFL method. NP = nanoparticles; L/d = length-diameter aspect ratio; Nano1 reinforced = Nano1 with extra safety measures.



This method of laboratory design with different management levels is particularly suitable for use when the laboratories are being newly constructed (Good Practice 12).

*Pros and cons*

Pros:

- direct relationship between hazard class and safety measures;
- easy to use;
- type of activity and physical properties of material (fibre, powder, agglomeration etc.) play a key role in determining hazard class;
- the risk classification is conservative, in other words the activity is often classified as nano2 or nano3 if there is a risk of exposure.

Cons:

- the proposed safety measures (especially the technical safety measures) may be difficult or impossible to implement in a given situation;
- the method is based on an occupational exposure limit of  $0.1 \text{ mg/m}^3$ , which means that activities using 10 mg or more of powder often lead to a hazard class of nano3 and hence to the need to implement costly safety measures;
- like the CBN, this tool is also based on the assumption that the material used is pure.

### Nanotoolkit

The Nanotoolkit is a document produced by the joint activity of a number of research institutes from California, USA. It is basically a summary of scientific publications and existing recommendations on how to work safely with nanomaterials. The Nanotoolkit gives a brief description of the main nanomaterials, the possible exposure routes and current knowledge concerning possible health risks. Readers are also given a number of practical tips on how to plan their own research and ensure their working conditions are safe. These tips are briefly explained below with reference to each step of the process involved in the use of the toolkit.

#### *Step 1 Gather information*

First of all, as much information as possible is collected on the nanomaterial to be used, on the basis of the Material Safety Data Sheet (MSDS), the Technical Data Sheet (TDS) and local agreements on laboratory safety. During this step, the possibility of substitution (replacing hazardous materials by less hazardous ones) and of using materials so as to reduce the risk of exposure at the source should be examined.

#### *Step 2 Determine potential risks and recommended control measures*

Here the potential risk is determined as described in the Quick Guide that forms part of the Nanotoolkit. This risk depends on the probability that material will be released into the air, which in its turn depends on the type of use (the Quick Guide gives examples of types of use). The chemical and toxicological properties of the material do not play a role here. Three risk categories are distinguished:

- category 1: no risk that material will be released into air when used as specified;
- category 2: moderate risk that material will be released into air when used as specified;
- category 3: high risk that material will be released into air when used as specified.

The Nanotoolkit establishes a direct relationship between the risk category and the control measures to be taken. These measures are divided into technical and organizational control measures and the use of personal protective equipment (PPE). If the risk category is found to be 2 or 3, then all control measures from lower risk categories also apply. The Nanotoolkit includes a standard set of control measures that may be applied.

#### *Step 3 Develop a standard operating procedure (SOP)*

The SOP covers six aspects of the investigation to be performed, which have to be specified in detail. The SOP must be approved by the principal investigator or laboratory supervisor. An example of such a standard operating procedure is given in Good Practice 10.

The aspects dealt with are:

1. general information about the experiment such as the process description, name of the principal investigator and an estimate of the nature, extent and duration of the exposure;
2. identification of the hazard represented by the compounds used, including the known potential chemical risks;
3. the control measures to be taken;
4. action to be taken during incidents (spillage, accidents etc.);
5. the information and training to be provided;
6. finally, details of how wastes are to be handled and disposed of (Good Practice 7C).

#### *Step 4 Information and training*

The final step in the process of working safely with nanomaterials consists in giving and receiving the necessary information and training. The information should include both explanation of the general rules concerning laboratory safety and details of the specific nanomaterials and technical aids to be used for the investigation in question.

Further details of information and training are given in Good Practice 11.

#### *Pros and cons of the Nanotoolkit*

Pros:

- easy to use; the risk level can be determined quickly with the aid of clearly formulated reference tables;
- there is a direct relationship between the risk assessment of the experiment and the control measures to be taken;
- the control measures described include all elements of the occupational hygiene strategy, also known as the STOP-approach<sup>9</sup>;
- the risk analysis and the SOP to be developed inform the user about the risks involved and the control measures to be taken;
- all steps of the experiment (from production up to and including waste generation and disposal) are covered by the SOP.

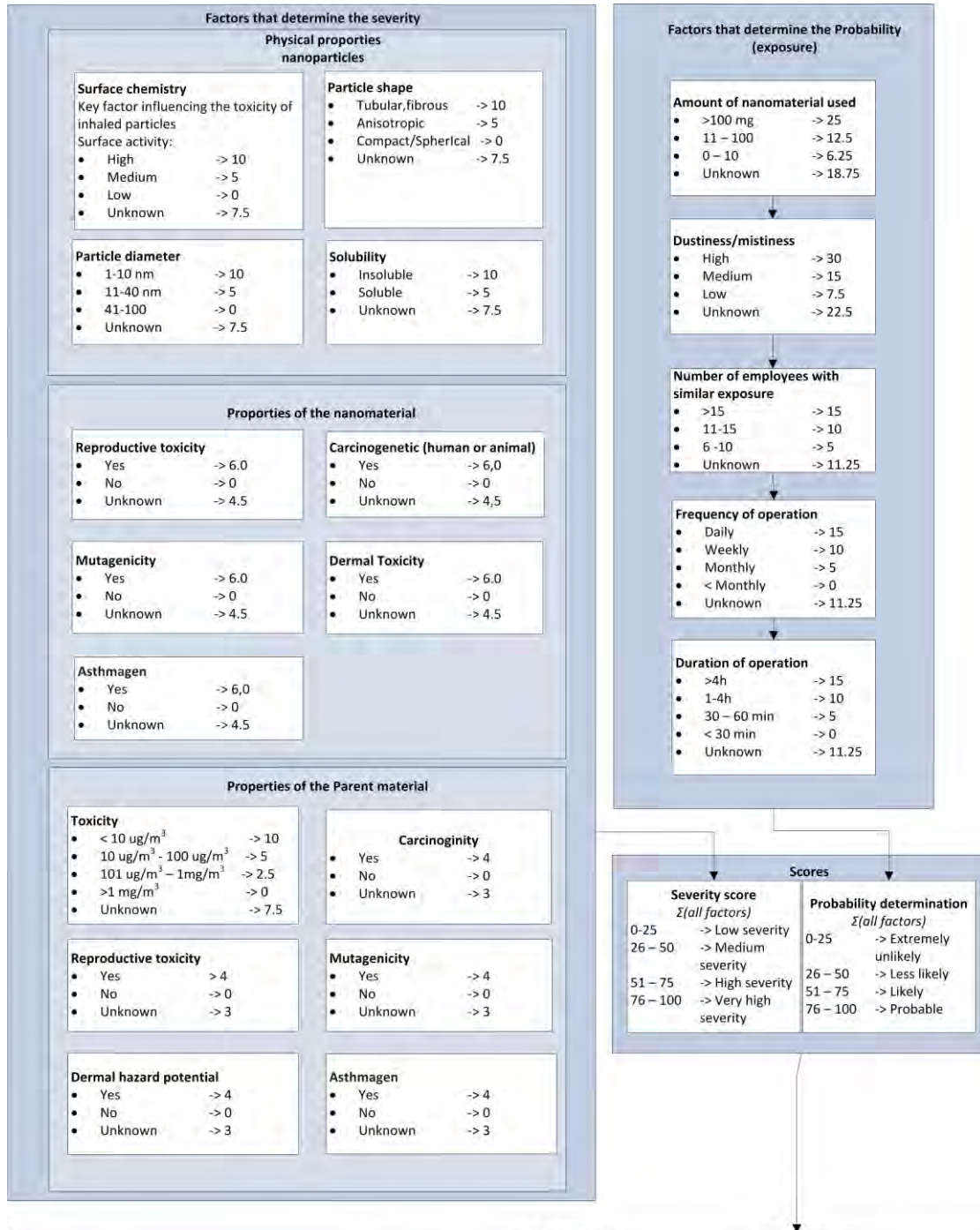
Cons:

- the method does not always give a clear description of the way nanomaterials are used. As a result, the risk associated with certain types of use may be underestimated;
- developing the SOP is a time-consuming business, and there is no Management of Change procedure that specifies how the SOP should be modified in response to changes in the way the nanomaterial is used.

---

<sup>9</sup> The STOP approach describes the hierarchy in which control measures have to be taken into account: (Source – Technical – Organisational – Personal)

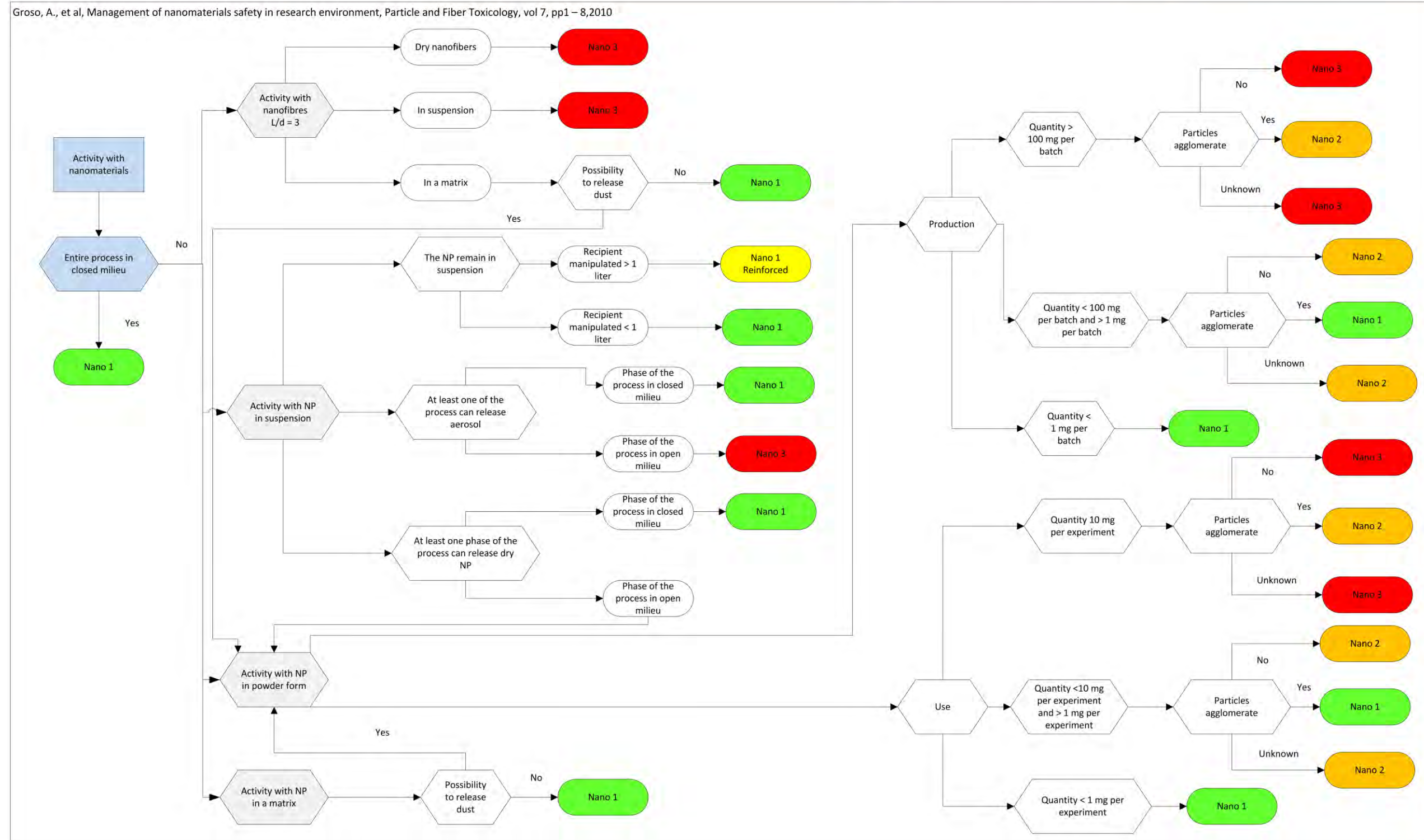
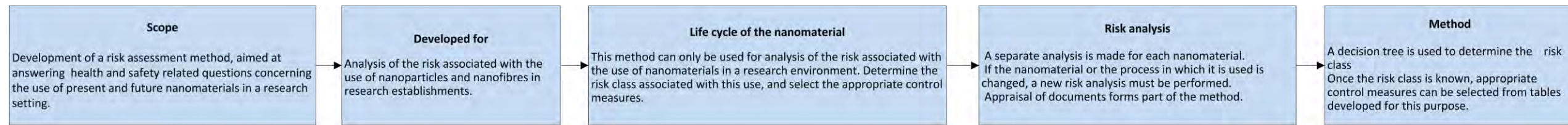
**Appendix 1 Schematic representation of the Control Banding Nanotool**



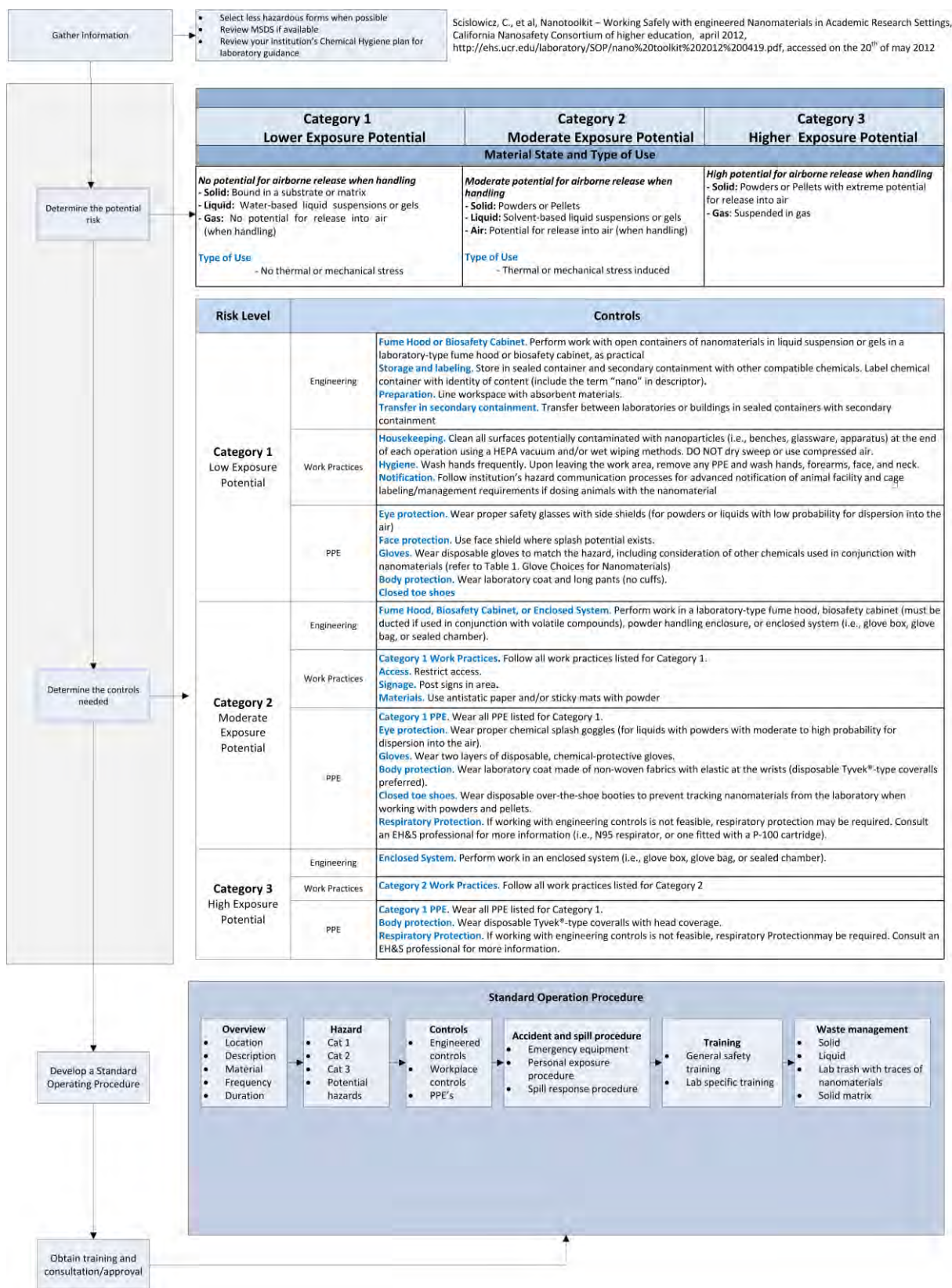
		Probability			
		Extremely Unlikely (0-25)	Less Likely (26-50)	Likely (51-75)	Probable (76-100)
Severity	Very High (76-100)	RL3	RL3	RL4	RL4
	High (51-75)	RL2	RL2	RL3	RL4
	Medium (26-50)	RL1	RL1	RL2	RL3
	Low (0-25)	RL1	RL1	RL1	RL2

RL = Risk Level  
 RL 1: General ventilation  
 RL 2: Fume hood or local exhaust ventilation  
 RL 3: Containment  
 RL 4: Seek specialist advice

Appendix 2 Schematic representation of the EPFL method for management of nanomaterials in a research environment



Appendix 3 Schematic representation of Nanotoolkit



## GP 5 Research planning

### *Introduction*

Planning an investigation is the point where many researchers start to consider whether the intended research is “*nano relevant*” (see Good Practice 3), and if so which control measures need to be taken when working with the nanomaterials in question.

This Good Practice contains information about the various steps involved in the planning of research in which nanomaterials are used. The process to be followed is illustrated in Figure 5.1. Other Good Practices are referred to where appropriate.

### *Step 1 Gathering information*

Determine whether you are dealing with a nanomaterial with reference to data from the safety or technical information sheet (if available), the literature and/or product information.

### *Step 2 Mapping potential risks*

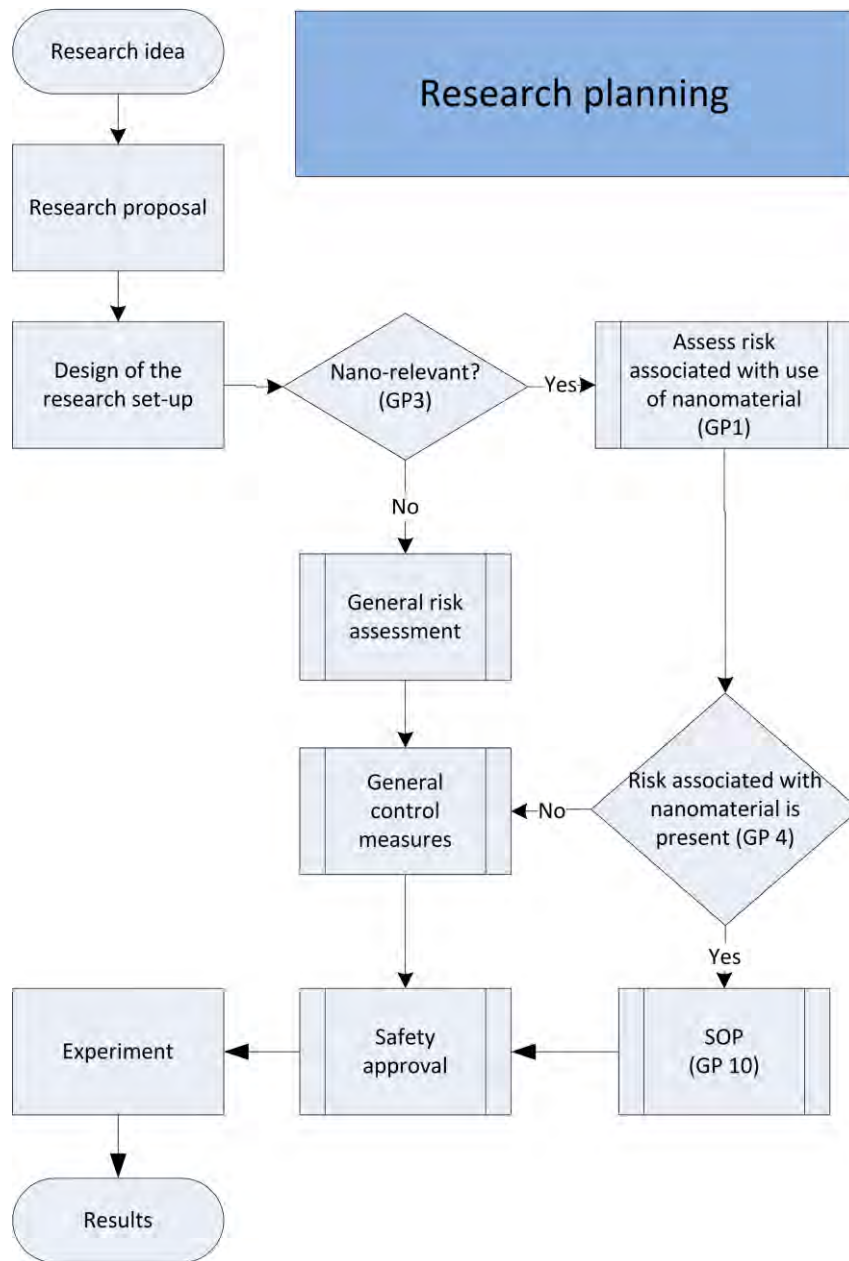
Determine the nature of the risks associated with the use of the nanomaterial with the aid of Good Practice 1, one of the available risk assessment methods or control banding tools. If the risk assessment shows that there is no risk, or the risk is completely managed, there is no need to take any further safety measures.

### *Step 3 Using a standard operating procedure (SOP)*

A standard operating procedure (SOP) is a set of detailed written instructions that provide a basis for performing a laboratory process and safe and effective research. An example of such an SOP is given in Good Practice 10. Education and training is part of the standard risk management measures.

### *Step 4 Getting safety approval*

Make sure that your principal investigator or laboratory supervisor has been informed of the research, and has signed the necessary approval form.



**Figure 5.1** Schematic representation of planning and authorization of research involving the use of nanomaterial.



## GP 6 Planning and implementation of a risk assessment for engineered nanomaterials

### *Introduction*

This Good Practice deals with the implementation of a risk assessment (RA) for work with nanomaterials. The flow diagram of Figure 6.1 shows how an RA for engineered nanomaterials can be planned and implemented. The diagram is followed by a stepwise explanation of the procedure involved.

### *Procedure*

In Step 1 research groups are asked whether they work with nanomaterials. This can be done with the aid of the sector analysis questionnaire drawn up for the purposes of this project, which is given in Appendix 1 of Part A. If this information is already available, skip Step 1 and proceed to Step 2, the inventory of the research projects where nanomaterials are used. Steps 3 – 9 are then carried out for each of these projects, with due regard to the “nanorelevance” (see Good Practice 3): in some cases, for the specific nanomaterials used a full risk assessment may not be necessary.

This procedure is independent of the risk assessment method used, but is based on process- and material-related parameters that are employed in most of these methods. In a given case, more or fewer parameters may be needed to evaluate the risk of the operations, depending on the risk assessment method selected from those listed in Good Practice 4.

### *Concrete example*

This Good Practice concludes with an example of an RA for a nanomaterial, performed in the Faculty of Science at Leiden University. The process analysed was split into unit operations as laid down in the Guidance on working safely with nanomaterials and nanoproducts (1), and the risk assessment method known as the Control Banding Nanotool (CBN)(2, 3) was applied to each unit operation.

Figure 6.1 makes use of two tables. For properties of the nanomaterial under consideration, Table 6.1 (which is a generic table) can be used. One can also use the guidelines given for the risk assessment method chosen, like in the last table where the CBN method was used. Example results of a risk assessment on unit operation level are shown in Table 6.2.

---

<sup>1</sup> Cornelissen, R.T.M., Jongeneelen, F and Van Broekhuizen, J.C. (2010) Guidance on working safely with nanomaterials and nanoproducts. The Guide for employers and employees. Executed on behalf of the Dutch Social Partners FNV, VNO-NCV and CNV and was financed by the Dutch Ministry of Social Affairs and Employment.

<sup>2</sup> D.M. Zalk, S.Y. Paik and P. Swuste. Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures. J Nanopart Res 11:1685–1704 (2009).

<sup>3</sup> D.M. Zalk and S.Y. Paik Control Banding and Nanotechnology. The Synergist Volume 21 No. 3 (2010).

**Table 6.1** Overview of properties of parent material and nanomaterial used in most risk assessment methods

<b>Properties</b>	
<i>Parent material</i>	
Commercial name	
Name of bulk material	amorphous silica
CAS number	112945-52-5
Chemical name	SiO <sub>2</sub>
CMR toxicity?	No
Hazard code and EU-GHS classification	
Density (kg/m <sup>3</sup> )	2.2
Soluble in water?	Yes
<i>Nanomaterial</i>	
Particle size	200 nm
Particle form	spherical
Dustiness	great
Density (kg/m <sup>3</sup> )	unknown

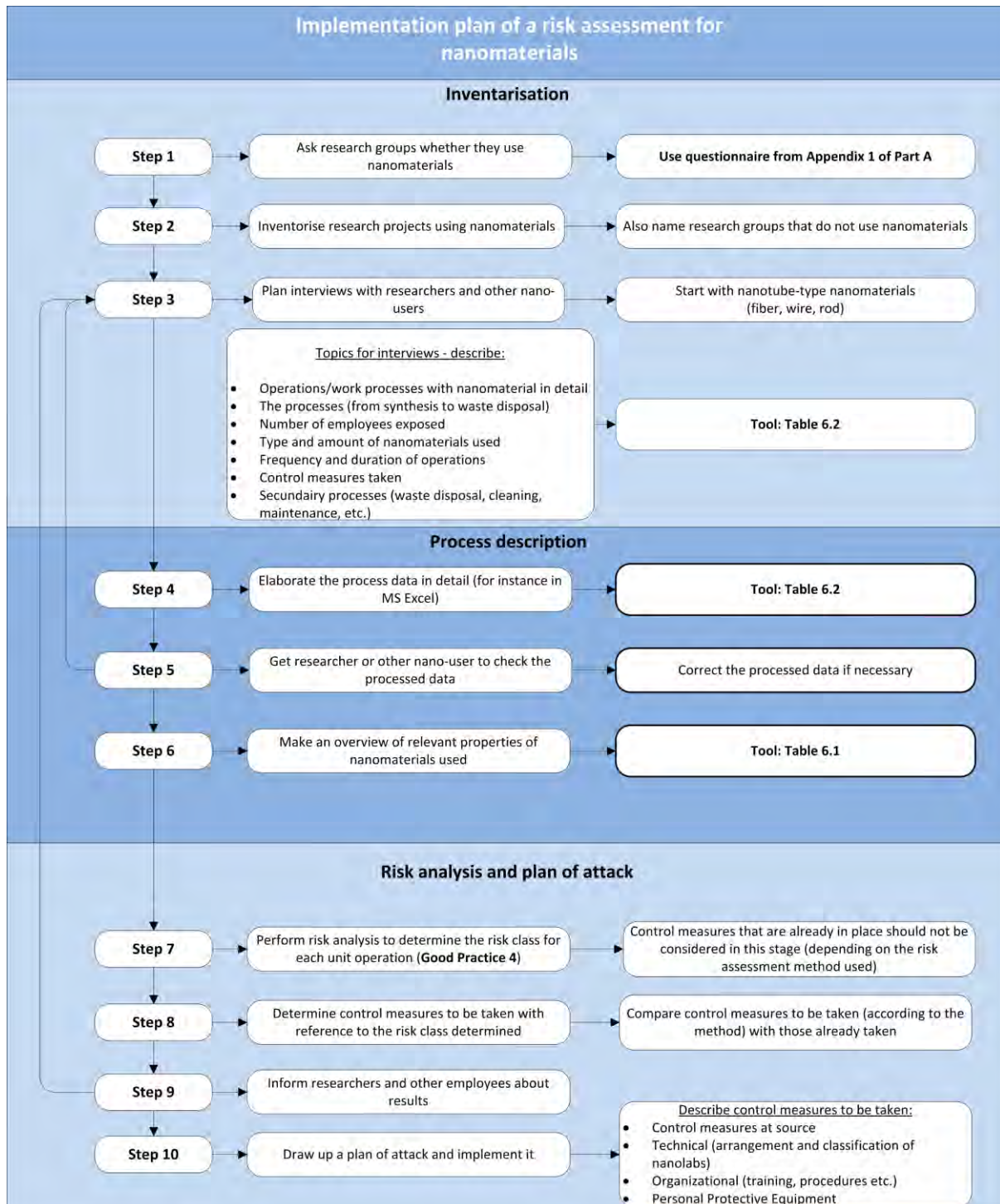


Figure 6.1 Flow diagram to perform a risk assessment for work with nanomaterials

*Concrete example*

Details of a risk assessment for nanomaterials performed at Leiden University are given below. The numbers refer to the steps in the flow diagram of Figure 6.1.

- 1 Ask all research groups whether they use nanomaterials in their research. Use the questionnaire from Appendix 1 of Part A for this purpose. Even if they answer No, record this in the overview of research performed.
- 2 Record the number of *research projects in each research group* that answer Yes. Remember that cooperation between research groups can lead to duplication of researchers and processes.
- 3 Plan interviews with the researcher or researchers in each research project who work with nanomaterials. Allow at least 2 hours for each interview. Start with the research groups where nanotube-type nanomaterials (fibres, wires or rods) are used.  
Request full details of all operations involving nanomaterials, from work preparation to synthesis, further treatment and analysis. Do not overlook secondary activities such as handling and disposal of wastes, cleaning and repairs. Request details of number of employees exposed, type of nanomaterial, frequency and duration of operations, and control measures that have already been taken. The Guidance on working safely with nanomaterials (see footnote 1) and details of the Control Banding Nanotool (see footnotes 2 and 3) were used at Leiden University.
- 4 Record the results of the interviews in MS-Excel (in a language that the researchers understand), with the various unit operations (work processes) arranged one under the other as shown in Table 6.2. If a given operation is performed several times, add up the different occurrences (for example, purification involves filtering and washing the material three times, so the frequency of filtration and washing has to be increased accordingly). Failure to do this can lead to underestimation of the risk of exposure.
- 5 Get the researcher or researchers to check the results, to make sure that all operations have been noted correctly.
- 6 Look up or estimate conservatively the parameters of the nanomaterial and parent material needed for the chosen risk assessment method, and record them in tabular form (thus creating your own table 6.1: for Leiden University this became table 6.3). NB: different nanomaterials may be used in different steps of the same project. Make sure the right material parameters are recorded for each step!
- 7 Use the Control Banding Nanotool to determine the severity and probability scores, neglecting control measures that have already been taken.
- 8 The risk class found on the basis of this risk analysis is linked with certain recommended control measures. Note which control measures have already been taken for each unit operation. Are these in agreement with the recommended measures, or do more stringent measures need to be followed?
- 9 Inform the researchers and principal investigator of each research group of the results of the risk analysis.  
Repeat steps 3 - 10 for each project.
- 10 List all operations on nanomaterials where the appropriate control measures are not yet taken, and draw up an overall plan of attack for the whole research establishment to improve the situation.

Merging all of the plans of attack of all research projects can reveal the need for organisation-wide policies and measures, such as the need to classify nanolabs, the setting up of training courses to be made compulsory throughout the establishment, a protocol for handling nanowaste, an appropriate emergency response plan etc.

**Table 6.2 Example of a completed table for the inventarisation and assessment of operations involving nanomaterials**

	Work process	Description of process step	Location (room)	used amount	release of material possible?	duration of process step (min)	frequency of process step	number of exposed people	remarks	Precautions already taken
Synthesis										
1	Preparation of mesoporous silica suspension	With a glass pipet, bring 9 ml into reaction flask with water and surfactant. Stirr for 2 h.	room x	1 l in total	yes, as aerosols or when spilling	120	1-2 x a month	1		in fumehood
2	Filtering	Filter the suspension trough a Buchner funnel / filter paper	room x	1 l in total	yes, when spilling		1-2 x a month	1	wet particles (not dusty)	in fumehood
3	Drying	Leave the paste on the filter to dry overnight	room x	800-900 mg yield	no. (moist)	720	1-2 x a month	0	wet particles	in fumehood
4	Collecting	Collect the particles from the filter: put on aluminium foil and transfer to previously tared vial. Close the vial.	room x	800-900 mg yield	yes	5	1-2 x a month	1		in fumehood, window as low as possible, I used also a mask
5	Washing	Add methanol to the vial and reflux overnight. Afterwards remove surfactant. Using a pipette and close the vial	room x	800-900 mg yield	no	720	1-2 x a month	1		in fumehood
6	Modification	Weigh 100 mg of silica and add chemicals to modify the silica surface; reflux overnight	room x	100 mg	yes, when spilling		1-2 x a month	1		in fumehood

The parameters collected for the various work processes are then used to determine the CBN likelihood score for each operation, and the material properties are used to determine the severity score.

As at Leiden University the CBN was chosen as risk assessment method, the table with material properties (Table 6.1 as meant in figure 6.1), looks like table 6.3. Table 6.3 shows the calculation of the CBN severity score for the nanomaterial used in the process in Table 6.2., silica.. The results for carbon nanotubes (CNT), which gives a higher severity score, are also presented by way of comparison.

Combination of the probability score and the severity score in the CBN decision matrix allows the risk class for the operation to be determined. This provides a basis for deciding whether the control measures already taken are adequate.

Table 6.3 Example of a table with (nano)material properties , using CBN at Leiden University

Severity factors	Research project		a	b
	Material		CNT (< 10 nm) fibres	SiO <sub>2</sub> (200 nm) spherical
	Surface chemistry	High (10) Medium (5) Low (0) Unknown (7.5)	7.5	7.5
	Particle shape	Tubular, fibrous (10) Anisotropic (5) Compact/spherical (0) Unknown (7.5)	10	0
	Particle diameter	1 – 10 nm (10) 11 – 40 nm (5) 41-100 nm (0) Unknown (7.5)	10	0
	Solubility	Insoluble (10) Soluble (5) Unknown (7.5)	10	10
	Carcinogenicity of nanomaterial	Yes (6) No (0) Unknown (4.5)	6	4.5
	Reprotoxicity of nanomaterial	Yes (6) No (0) Unknown (4.5)	4.5	4.5
	Mutagenicity of nanomaterial	Yes (6) No (0) Unknown (4.5)	4.5	4.5
	Dermal toxicity of nanomaterial	Yes (6) No (0) Unknown (4.5)	4.5	4.5
	Asthmagen nanomaterial	Yes (6) No (0) Unknown (4.5)	0	0
	Toxicity of parent material	< 10 µg/m <sup>3</sup> (10) 10-100 µg/m <sup>3</sup> (5) 101 µg/m <sup>3</sup> – 1 mg/m <sup>3</sup> (2.5) > 1 mg/m <sup>3</sup> (0) Unknown (7.5)	0	0
	Carcinogenicity of parent material	Yes (4) No (0) Unknown (3)	0	0
	Reprotoxicity of parent material	Yes (4) No (0) Unknown (3)	0	0
	Mutagenicity of parent material	Yes (4) No (0) Unknown (3)	0	0
	Dermal toxicity of parent material	Yes (4) No (0) Unknown (3)	0	0
	Asthmagen parent material	Yes (4) No (0) Unknown (3)	0	0
	<b>Severity score</b>		<b>61.5</b>	<b>40</b>

## **GP 7 Secondary processes involving nanomaterials**

### *Introduction*

Apart from the primary research process and the work with nanomaterials this involves, there are secondary processes that need to be taken into consideration to ensure safe handling of nanomaterials. These are at least equally important, since the researchers are not the only people in the laboratory who run the risk of exposure to nanomaterials. Incidental visitors, cleaners, maintenance workers, members of the in-house emergency response team and (outside the laboratory) employees of the waste management company are also at risk. These people often know little or nothing about nanomaterials, so it is important to give them all the information they need about the risks associated with the handling of nanomaterials and/or to offer them adequate protection against these risks.

### *Marking*

Rooms where nanomaterials are used must be clearly recognizable as such; this is one of the essential means of protecting third parties against the risks these materials can cause. Such rooms must be clearly marked as out of bounds for unauthorized persons, as is the case for example for laboratories working with genetically modified organisms. See also Good Practice 12, where a laboratory classification system is explained.

### *Information*

Older research laboratories will not always contain a dedicated nanolab, and it may not always be possible to set one up there. Care should therefore be taken to ensure that all other researchers and students who are not working with nanomaterials in the same laboratory, are fully informed about the risks associated with nanomaterials and the current nano-procedures. If new building work is planned, it may be possible to address some issues more effectively (see Good Practice 12).

This Good Practice on secondary processes is divided into the following four documents:

- GP 7A Safe transport of nanomaterials;
- GP 7B Cleaning procedures in nanolaboratories;
- GP 7C Dealing with waste containing nanomaterial;
- GP 7D Maintenance procedure for equipment.

**GP 7A Safe transport of nanomaterials***Internal Transport*

Nanomaterials may be transported within a building for example from the synthesis lab to the analytical facility. Make sure that the sample, which is often mounted on a sample holder, is covered and packed. It should then be packed once more in a secondary containment (1,2) in such a way that the nanomaterial remains within the packaging at all times, even when the person carrying it trips, knocks it against something or the like. This prevents contamination of the environment.

*Orders*

In addition, nanomaterials may be ordered from a chemicals supplier and delivered to goods reception. While chemicals are always well packed, it can do no harm to give staff there instructions about what to do if the packaging happens to break (Good Practice 7B).

*Transport of waste*

Containments with liquid nano-waste must be transported on trolleys with adequate spill capacity, by trained personnel. Use the goods lift for all vertical transport of nanomaterials.

*Shipment between research laboratories*

Make sure that the nanomaterial is packed in strong double packaging, and that all current requirements for transport of chemicals by road (ADR), sea (IMDG) or air (IATA) are met. Absorbent or shock-absorbing material may be placed between the two packaging layers (3). Use a carrier specialized in chemicals for shipment, and preferably never send by normal post.

---

<sup>1</sup> California Nanosafety Consortium of Higher Education (2012) Nanotoolkit. Working safely with engineered nanomaterials in academic research settings.

<sup>2</sup> Groso, A. et al. (2010) Management of nanomaterials safety in research environment. Particle and Fibre Toxicology.

<sup>3</sup> OECD (2010) Series on the Safety of Manufactured Nanomaterials No. 28. Compilation of nanomaterial exposure mitigation guidelines relating to laboratories. ENV/JM/MONO(2010)47.



**GP 7B Secondary processes - cleaning procedures in nanolaboratories***Introduction*

This Good Practice gives practical tips about the cleaning of laboratories. The original sources of these recommendations are referred to wherever possible.

*Routine and incidental cleaning*

Decide whether it is appropriate for regular cleaning staff to enter a 'nanolaboratory' (a laboratory where nanomaterials are used). This will depend on the risk class of the nanomaterial or materials in question (1). Cleaning personnel may also be required for incidental work such as window cleaning. If nanolabs are already part of the facility's laboratory classification system, permitted activities of third parties can be described per risk class

Draw up working instructions in each case, specifying which surfaces the cleaners are allowed to clean and which should be left to the researchers themselves. State which personal protective equipment (PPE) the cleaners should wear when working in a nanolab. If the risk analysis indicates that there is a high risk level – for example when working with carbon nanotubes (CNTs) or gold nanorods – the researchers should clean the entire laboratory themselves (1). Make sure in any case that both third-party cleaners and cleaning personnel employed by the research establishment are provided with comprehensive, clear instructions. When cleaners are not allowed to enter a lab, the reason for this should be clearly explained (2).

Cleaning work that should be given extra thought, regardless of who is doing it, includes:

- cleaning of floors;
- cleaning of work benches and laboratory equipment;
- incidental cleaning such as window cleaning, spring cleaning or cleaning before building maintenance.

*Cleaning floors and used equipment*

- wet cleaning is preferred. Floors can be cleaned with a damp mop, in which case the mop should be well rinsed out after use (1); alternatively, a vacuum cleaner fitted with a HEPA filter, used only for this purpose, may be employed;
- the vacuum cleaner may not be fitted with an emergency blow-off valve that bypasses a blocked HEPA filter;
- the amount of nanoparticles in the exhaust air downstream from the HEPA filter should be regularly monitored. A filter that does not work well simply serves to disseminate nanomaterial (3). The filter should be regularly replaced under controlled conditions, and the equipment should be disposed of as chemical waste at the end of its life (4);

---

<sup>1</sup> Groso, A. et al. (2010) Management of nanomaterials safety in research environment. Particle and Fibre Toxicology.

<sup>2</sup> The EFPL method (Groso et al.) assumes the availability of specially trained cleaning personnel for labs with an EFPL risk class of nano2. Caution should be used in adopting this recommendation. Cleaning is an activity that is often outsourced, and the training of third-party personnel is a complicating factor. It may be more appropriate to train cleaners if they are employed permanently by the research establishment.

<sup>3</sup> Delft University of Technology (2010), Nanosafety working group of the Faculty of Applied Sciences. Nanosafety Guidelines.

<sup>4</sup> UK NanoSafety Partnership Group (2012) Working Safely with Nanomaterials in Research & Development.

- normal vacuum cleaners or brooms should not be used in a nanolab (1), and surfaces should not be cleaned with compressed air (4)!
- if the nanomaterial can form a combustible or explosive mixture with air, only explosion-proof vacuum cleaners (with an EX marking) may be used in areas where such material may occur (5).

Used equipment and materials should in principle only be cleaned by the researcher involved.

- wear gloves and a lab coat (or other prescribed protective clothing), and depending on the outcome of the risk assessment, suitable respiratory protection (see Good Practice 9);
- used glassware, spatulas and the like should be rinsed with water or a suitable solvent, preferably in the fume hood, and the fume hood should also be cleaned afterwards (3);
- work benches and other work surfaces should be cleaned at the end of each operation, working day and/or working week with a cloth moistened in water/suitable solvent. Rinse the cloth out well after use, or use disposable cloths that should be treated as solid nano-waste after use;
- some literature sources also recommend using cloths moistened with solvent to wipe down surfaces (3); however, other sources advise against this because the solvent might react with the nanomaterial (5, 6);
- also clean the inside of equipment (such as drying ovens) with a damp cloth immediately after use. If there are seams in the equipment, it may be advisable to use a HEPA vacuum cleaner before wiping it with a damp cloth;
- equipment that is sensitive to water may in some cases be wiped clean with an electrostatic microfibre cloth (5); Cleaning of equipment not only ensures that the following user will not be exposed to nanomaterials but also prevents contamination of research material used later;
- when sending samples for analysis, always let the manager of the analytical facility know in advance that the sample contains nanomaterial. You can then consider together whether contamination is an issue, how the material can be fixed if necessary, and whether (and if so, how) cleaning can occur after analysis.

#### *Cleaning after a spillage or calamity*

In the first place, every possible care should be taken to avoid spillage through good preparation and careful working practices. If nanomaterial is spilled or disseminated into the air, the greatest risks are inhalation or uptake via the skin (1, 3).

- The effect of liquids spillage in chemical or biological work can be reduced by working on an absorbent surface with an impenetrable bottom layer; this can simply be thrown away with the solid nano-wastes after a spillage (5, 6, 7).
- If an absorbent layer is not available or the spillage is too extensive to be contained by it, do not allow the spilt liquid to dry to avoid dry nanoparticles to become airborne.
- Absorb the spilt liquid (for example with tissues, which are disposed of as solid nano-waste after use, as described in Good Practice 7C) and then clean the work surface thoroughly.

---

<sup>5</sup> OECD (2010) Series on the Safety of Manufactured Nanomaterials No. 28. Compilation of nanomaterial exposure mitigation guidelines relating to laboratories. ENV/JM/MONO(2010)47.

<sup>6</sup> California Nanosafety Consortium of Higher Education (2012) Nanotoolkit. Working safely with engineered nanomaterials in academic research settings.

<sup>7</sup> Fluttert, M.F.J and Samwel-Luijt, M., RI&E Werken met synthetische nanomaterialen, intern rapport Faculteit W&N Universiteit Leiden, September 2011.

- Cleaning after spillage of nanopowder can be made easy by working on a sticky mat or antistatic paper (6), or the powder can be sprayed with water to reduce dustiness and then absorbed (5).

The action to be taken in response to a major spillage depends on the location. Some research facilities have their own fire service, others only have an in-house emergency response team or something of that kind. In general, the following procedure, similar to that used to respond to radioactive contamination, can be used.

- In the case of major spillages of liquid (5, 8), release of large amounts of nanopowder into the air outside a fume hood or breakage of packaging containing nanomaterial during transport, call for expert backup (for example from a health & safety officer, a safety expert or an occupational hygienist) *by phone*;
- Further spread of nanomaterials through the building can be avoided by not walking outside the contaminated area while wearing contaminated shoes and/or clothing;
- Do not allow other persons to enter or pass through the contaminated area. Do not allow those present in the room at the time of the contamination to leave – but do allow (and help) them to take all possible protective measures;
- If powders are released, switch off all possible sources of ignition immediately, in connection with the risk of explosion posed by some finely divided nanomaterial;
- Make sure that a general emergency and clear-up procedure (6) has been drawn up and is available, and fill in the details in consultation with the safety officer (see Good Practice 10). The latter can call in the help of the in-house emergency team in a controlled fashion, to ensure that this team does not enter the contaminated area without taking due precautions after an emergency call;
- In any case, possible decontamination procedures for contaminated persons and/or areas must be thought out in advance;
- Special 'spill kits' (5) can be prepared; these may contain:
  - water spray bottles and disposable tissues for labs where carbon nanomaterial is used;
  - barricade tape, latex or nitrile gloves, FFP3 disposable safety masks, absorbent material, disposable tissues, sealable plastic bags, sticky mats, Tyvek disposable overalls and overshoes to deal with spills of nanomaterials in general;
- In any case, train the in-house emergency team in how to deal with calamities, teach them about the possible risks involved and how to use the spill kit.

---

<sup>8</sup> A major spill may be defined as one that takes more than 5 minutes to clear up.

## GP 7C Dealing with waste containing nanomaterial

### *Introduction*

A range of nanomaterials in different states are used on a small scale in Dutch universities, university medical centres and research organisations. All these materials need to be collected and disposed of safely.

### *Waste collection*

The main risk of the release of nanomaterial from waste containers coming from the above-mentioned organisations is not at the organisations themselves, but occurs outside the premises of these organisations. The research organisations have the obligation to properly inform the waste management companies, whose operations include sampling (to determine the calorific value of the waste) and shredding – both of which have the potential of releasing nanomaterial into the environment (1). It follows that nanowaste must be kept separate from normal industrial waste (2), and must thus be classified and marked as such in the research organisation and further on in the waste disposal chain in order to limit the potential of exposure. In addition, it is assumed that some nanomaterials (metals and metal oxides, such as quantum dots and zinc oxide) have a biocidal effect, so care should be taken to ensure that they do not get into the environment (3). A number of sources in the literature describe how nanowaste can be divided into various waste streams. However, they disagree about how this should be done. The classification is influenced by the way waste disposal is organized in the countries in question, and by the provisions of the national legislation on this point.

### *Waste disposal*

Dutch waste management companies do not process nanowastes separately. They receive wastes for processing in closed containers. Disposal of combustible wastes in landfill sites is forbidden in the Netherlands (4). Waste is incinerated at temperatures > 700 °C. A study by the UK Health and Safety Executive claims that heating above 500 °C [oxidizes carbon nanotubes completely](#) (3). According to the [Dutch Health Council \(Gezondheidsraad\)](#) however, it is not yet known how effective incineration plants are in removing nanomaterials from domestic waste (5). In this Good Practice, the decision has therefore been taken to classify all waste generated by activities involving nanomaterials as hazardous waste. This also ensures that cleaning personnel will not be unintentionally exposed to such materials, for example through the release of nanopowder into the air during the changing of rubbish bags. It should be noted, however, that some literature sources recommend that certain types of nanowaste can be disposed of in the normal industrial waste (= domestic waste) stream.

---

<sup>1</sup> [http://www.inspectieszw.nl/Images/Arbeidsomstandigheden-in-de-wastedisposal\\_tcm335-312358.pdf](http://www.inspectieszw.nl/Images/Arbeidsomstandigheden-in-de-wastedisposal_tcm335-312358.pdf).

<sup>2</sup> Groso, A. et al. (2010) Management of nanomaterials safety in research environment. Particle and Fibre Toxicology 2010 7:40.

<sup>3</sup> [OECD \(2010\) Series on the Safety of Manufactured Nanomaterials No. 28. Compilation of nanomaterial exposure mitigation guidelines relating to laboratories. ENV/JM/MONO\(2010\)47.](#)

<sup>4</sup> <http://rwsenvironment.eu/subjects/from-waste-resources/> accessed 23 September 2013.

<sup>5</sup> Gezondheidsraad (2011) Nanomaterials in waste. Rapport nr. 2011/14.

It is recommended that the following waste streams should be distinguished in research institutes:

1) Solid hazardous nanowaste

For example solid chemicals such as carbon nanotubes (CNTs) and nanopowders, also nanomaterial in a solid composite (6, 7, 8) – for example, embedded in a resin, a nanolayer on a metal support or nanomaterial on a carrier that is liable to fracture or pulverization. Objects that have been contaminated with nanomaterial such as tissues, filter paper, gloves, pipette tips, Eppendorf tubes, cellulose pads used to contain spillage etc. also belong in this waste stream. Place a waste bin (plastic bucket) with a strong plastic bag in it in the fume hood where all work with nanomaterials is performed, and put all solid nanowaste in it. Keep this bin and the plastic bag in it closed as much as possible. When the bin is full, seal the bag and put the lid on the bin, and make sure that the outside of the bin is clean (6). Mark this: "Nanowaste (type) – Do not reopen", together with your name and location (lab X in building Y), so that the local waste depot will be aware of the contents. Do not keep waste of this type in a local storage, but bring it straight to the central depot.

2) Nanomaterials in solution or dispersion

Put dilute (colloidal) solutions in the appropriate liquid waste container (7), irrespective of the amount. Remember to place a leakage tray under the container, and do not over-fill it. Make sure that the outside of the container is clean (6). Mark this: "Nanowaste (type) – Do not reopen", together with your name and location (lab X in building Y), so that the local waste depot will be aware of the contents. Do not keep waste of this type in a local storage, but bring it straight to the central depot.

3) Rinsing water from cleaning operations

This can go down the sink. Rinse well afterwards. (7)

4) Contaminated HEPA filters from nanolabs

Filters that do not fit in the solid waste bin must be disposed of separately (Good Practice 7D).

5) Discarded equipment from nanolabs

This equipment must first be cleaned with a HEPA vacuum cleaner and then wiped down with a wet cloth. After that, it can be released. Follow the same release procedure as for other equipment (for example that where radiation or genetically modified organisms are involved).

In addition, please note the following points:

- Instruct researchers (including students), waste depot personnel and maintenance personnel how to handle nanowaste.
- Give the persons concerned instructions about the right way of removing contaminated gloves without shaking them (which might release hazardous material).
- Know the proper response in case the contents of a solid or liquid waste container escape, or in the event of other calamities (Good Practice 7B).

---

<sup>6</sup> California Nanosafety Consortium of Higher Education (2012) Nanotoolkit. Working safely with engineered nanomaterials in academic research settings.

<sup>7</sup> Delft University of Technology, workgroup Nanosafety of the Faculty of Applied Sciences. Nanosafety Guidelines. Version 2 – September 2010.

<sup>8</sup> The UK NanoSafety Partnership Group (2012) Working Safely with Nanomaterials in Research & Development.

## GP 7D Maintenance procedure for equipment

### *Introduction*

Equipment used for the synthesis or analysis of nanomaterials will have to be maintained from time to time, as will safety devices such as fume hoods or laminar flow cabinets. Similarly, HEPA filters will have to be replaced at regular intervals, and other maintenance work may be required in a nanolab. This Good Practice gives some general recommendations concerning all such maintenance activities.

### *General remarks*

Make sure that all maintenance personnel – those employed by the research facility and those working for external companies – are fully informed about the nature of the materials used and the possible risks associated with their activities, and consult to determine the right working procedure. Establish a release procedure for the laboratory or the equipment prior to maintenance, to ensure that the proper cleaning procedure is followed (Good Practice 7B).

### *Analytical equipment*

The following comments apply to analytical equipment used occasionally for nanomaterials:

- inform the facility manager in advance that the equipment will be used for nanomaterials;
- determine whether the equipment needs to be cleaned after use, and if so how (Good Practice 7B);
- as long as the equipment has been properly cleaned and this has been noted in the logbook, it can be serviced in the normal way without the need for any special measures.

### *Synthesis equipment*

A very wide range of equipment can be used for the purposes of synthesis, so only very general comments can be made here:

- keep a logbook, so that there is a clear record of what nanomaterials and other materials are used in the equipment;
- clean all freely accessible parts of the equipment after use;
- if the equipment is specifically intended for to be used with nanomaterials, follow the manufacturer's instructions concerning cleaning before maintenance;
- if a maintenance contract has been signed with the supplier, inform the maintenance engineer that nanomaterials have been used and/or synthesized in the equipment, and give details of the type of nanomaterial involved. Consider where nanomaterials may have ended up within the equipment, and decide in advance – in consultation with the maintenance staff – which measures need to be taken. Follow the predetermined release procedure, if there is one;
- if the maintenance is carried out in-house, draw up working instructions in consultation with the local health & safety officer or other appropriate official, and make sure that these instructions also cover unplanned or unexpected situations.

*Maintenance of fume hoods*

A fume hood, biological safety cabinet or laminar flow cabinet that has been used for work with nanomaterials must be cleaned three times with soap and water and must go through a release procedure before repair or maintenance (1), to ensure that the service engineer is not exposed to nanomaterials.

*Replacement of HEPA filters*

HEPA filters in fume hood ducts, biological safety cabinets and laboratory vacuum cleaners need to be replaced periodically. The engineering staff responsible for this task must be informed what kinds of materials may be present in these filters, how these materials should be handled and what safety measures and personal protective equipment (PPE) should be used.

---

<sup>1</sup> OECD (2010) Series on the Safety of Manufactured Nanomaterials No. 28. Compilation of nanomaterial exposure mitigation guidelines relating to laboratories. ENV/JM/MONO(2010)47.

## GP 8 Exposure measurement

### *Introduction*

The measurement and evaluation of exposure to nanomaterials at the workplace is still in its infancy. There are at present no Dutch standards for assessment of the exposure to nanomaterials (comparable for example with standard EN 689 "Workplace atmospheres. Guidance for the assessment of exposure by inhalation to chemical agents for comparison with limit values and measurement strategy"), nor for the determination of factors relevant to exposure or for the statistical analysis of measured data.

Exposure to larger particles in air is usually expressed as a concentration in milligrams per cubic metre of air ( $\text{mg}/\text{m}^3$ ). There are indications that mass is not always the best measure for expressing the risk of exposure to nanomaterials, though there is not yet a single unambiguous physical or chemical parameter that would provide a better measure. Various parameters in addition to the mass are however known that should be determined as the minimum information required for investigation of the toxicity of nanomaterials (1, 2). Typical factors determining the properties (and the potential toxicity) of nanomaterials include:

- particle size and particle size distribution;
- surface area;
- crystalline structure;
- fibrous or rigid structure;
- surface reactivity;
- composition of surface (chemical and physical);
- possible contaminations;
- composite particle;<sup>3</sup>
- aggregation or agglomeration of particles in the relevant medium.

Workplace-related exposure to nanoparticles will in practice be a combination of exposure to (I) naturally occurring nanomaterials (natural background exposure), (II) nanomaterials induced by human activity (interfering factors) and (III) man-made synthetic nanomaterials (the exposure to which it is wished to measure). The challenge is to identify and quantify the exposure to synthetic nanomaterials apart from the overall exposure to particles in the nano range at the workplace.

---

<sup>1</sup> Warheit, D.B., 'How meaningful are the results of nanotoxicity studies in the absence of adequate material characterization?', *Toxicol. Sci.*, 101, 2008, 183-185

<sup>2</sup> Murdock, R.C., Braydich-Stolle, L., Schrand, A.M., Schlager, J.J., Hussain, S.M., 'Characterization of nanomaterial dispersion in solution prior to in vitro exposure using dynamic light scattering technique', *Toxicol. Sci.*, 2007

<sup>3</sup> For example, a coated particle or a particle where the core is of a different material than the surface.



### *Variables*

The parameters of importance for the characterization of exposure to nanomaterials are:

- number of particles;
- particle size distribution;
- surface area of particles;
- chemical composition;
- form;
- mass.

### *Measuring instruments*

A combination of instruments is often used for measuring exposure to nanomaterials, for example a particle counter (often a CPC – condensation particle counter) and an instrument that can measure the particle size distribution (such as an SMPS – scanning mobility particle sizer). Besides the use of direct reading instruments, it is common to collect samples on filter media that can be analysed in the laboratory in order to analyse size, shape and chemical composition of the material.

The lack of a good, standard measurement strategy, proven quality and reproducibility of the various measuring instruments and a standardized model for recording workplace-related factors makes it difficult to come to solid conclusions about the exact level of exposure to nanomaterials at the workplace and comparison of the various activities involving the handling of nanomaterials. It should also be borne in mind that a single measurement is not enough to give a reliable estimate of the exposure to nanomaterials, since the concentration in the air can vary widely from day to day as the result of changes in the humidity of the air, the weather and the background concentration of nanomaterials from external sources at the workplace.

Synthetic nanomaterials are normally only used to a limited extent in a research environment (see Part A of this report). As a result, the concentration of synthetic nanomaterials in air in laboratories is likely to be so low in practice that it may be asked whether it is possible to measure such low levels accurately enough to provide enough measurement points (with real-time measure instruments) or to ensure that measured values are above the detection limit of the measuring method (e.g. sampling on filters for offline analysis). It may also be asked whether the concentration of synthetic nanoparticles in air is high enough to be distinguished from the background level. It may be concluded that measurement of the concentration in air will not usually be of value in a research environment.

### *Measurement strategy*

Brouwer et al. have suggested, with reference to the results of an international workshop on the measurement and assessment of exposure to nanomaterials, that the measurement strategies used to provide a basis for such assessment should be harmonized (4). They make a number of recommendations in this publication concerning the procedure to be used to assess exposure to nanomaterials on the basis of measurements. A number of their conclusions are summarized below.

---

<sup>4</sup> Brouwer, D et al. (2012) Harmonization of measurement strategies for exposure to manufactured nano-objects: report of a workshop. Ann. Occup. Hyg. vol. 56, no.1;

Points to be taken into account in measuring strategy

- the measurements should as far as possible be task-related. The contribution of a given task to the daily exposure can easily be calculated, and facilitates the comparison of control measures;
- determine how often a given task is performed per day;
- identify the contribution of other potential sources of nanomaterials (synthetic, natural or man-made) to the measured values;
- identify the peak exposure and take this into account in the assessment;
- if possible, perform repeated measurements;
- make use of observations of the activities performed, and include a description of the relevant workplace factors in the report;
- particle size and particle size distribution are key exposure parameters. Other parameters of importance for health, such as the particle surface area, can be calculated in particular from the particle size distribution when certain assumptions are made.

Points relating to analysis, evaluation and reporting of measured data

- correct the measured data for background exposure;
- calculate basic statistical parameters such as the arithmetic and geometric mean, standard deviation, minimum and maximum values and 95 per cent confidence interval;
- check whether the data has a normal or log-normal distribution;
- check for the existence of partial or full autocorrelation if the measurements were performed by means of continuous recording. An ARIMA time series approach (5, 6) may be used for this purpose.

Harmonization of measuring strategies and methods, and of statistical analysis, will help to improve the assessment of the exposure data becoming available in coming years and may also contribute to better insights into the nature of exposure to nanomaterials. Better and more reliable data will also help to improve the comparison of differences in exposure between various sectors and may facilitate better use of nano reference values, DNELs (7) and occupational exposure limits (OEL) in the search for a safer workplace.

*Nano reference values*

Apart from monitoring and evaluating the effect of exposure to nanomaterials on health, it is also useful to assess the effect of the control measures used. One way of doing this is to measure the exposure level before and after implementation of the control measures selected. Threshold Limit values, benchmark exposure levels or DNELs can be used to check whether the exposure is low enough. Under normal conditions, the limit values for occupational exposure will be the maximum level at which employees are expected to be able to work safely (the TLV of the DNEL). Few limit values have yet been determined for nanomaterials, however.

---

<sup>5</sup> ARIMA = autoregressive integrated moving average.

<sup>6</sup> Klein Entink et al (2011) How to statistically analyze nano exposure measurement results: using an ARIMA time series approach. J Nanopart Res.

<sup>7</sup> DNEL = derived no-effect level.

Nano reference values may provide a solution as long as no limit values for occupational exposure are available. In the absence of health based recommended exposure limits, they provide a provisional generic limit value for various types of nanomaterials, determined on the basis of the precautionary principle.

Nano reference values for use in the Netherlands have been determined by the National Institute for Public Health and the Environment (RIVM) (8) and updated in 2012 on the basis of new insights by the Social and Economic Council of the Netherlands (SER) (9). It should be stressed that these are still *provisional* nano reference values.

**A provisional nano reference value (NRV)** is a warning level, to be used until effective exposure control for nanomaterials at the workplace has been established. An NRV is defined as an eight-hour time-weighted average (TWA) concentration corrected for the background concentration of ultrafine particles.

NRVs for a number of common nanomaterials are given in Table 8.1, which also indicates which category they belong to.

Table 8.2 gives an overview of limit values and DNELs described in the literature (based on the review article by Van Broekhuizen et al. (10)). This overview shows that there are still wide differences between the various derived limit values.

---

<sup>8</sup> S.Dekkers and C. de Heer (2010) Tijdelijke nano-referentiewaarden – Bruikbaarheid van het concept en van de gepubliceerde methoden. RIVM report 6010440001/2010,

<sup>9</sup> Sociaal Economische Raad (2012) Voorlopige nanoreferentiewaarden voor synthetische nanomaterialen. Advies nr. 2012/01, maart 2012;

<sup>10</sup> Van Broekhuizen et al. (2012) Exposure Limits for Nanoparticles: Report of an International Workshop on Nano Reference Values. Ann. Occup. Hyg. vol. 56 no. 5.

**Table 8.1 Temporary nano reference values for exposure to nanomaterials at the workplace**

Description of category	Density	Nano reference values (NRV <sub>8hr-TWA</sub> )	Type
1 carbon nanotubes (CNT)(length/diameter ratio > 3:1 and length > 5µm) whose asbestos-like effects have not been tested		0.01 fibres /cm <sup>3</sup> 10,000 fibres/m <sup>3</sup>	CNT where asbestos-like complaints are not excluded (i.e. without an explicit statement to this effect by the manufacturer).
2 biopersistent granular nanomaterials with a primary particle size in the 1 - 100 nm range	> 6,000 kg/m <sup>3</sup>	20,000 particles/cm <sup>3</sup>	Ag, Au, CeO <sub>2</sub> , CoO, Fe, Fe <sub>x</sub> O <sub>y</sub> , La, Pb, Sb <sub>2</sub> O <sub>5</sub> , SnO <sub>2</sub> ,
3 biopersistent granular nanomaterials with a primary particle size in the 1 - 100 nm range	< 6,000 kg/m <sup>3</sup>	40,000 particles/cm <sup>3</sup>	Al <sub>2</sub> O <sub>3</sub> , SiO <sub>2</sub> , TiN, TiO <sub>2</sub> , ZnO, nanoclay carbon black, C <sub>60</sub> , dendrimeres, polystyrene CNT without demonstrable asbestos-like effects
4 ultrafine liquid and soluble particles	corresponding limit value for parent material		fats, hydrocarbons, siloxanes, NaCl etc.

**Table 8.2 Proposed limiting values and DNELs for a number of specific nanomaterials**

Nanomaterial	Limiting value (mg/m <sup>3</sup> )	DNEL (mg/m <sup>3</sup> )
MWCNT (BayTubes)	8-hour TWA	0.05
MWCNT (10–20 nm/5–15 µm)	Short term exposure	201
	Chronic exposure	33.5
MWCNT (10–20 nm/5–15 µm)	Short term exposure	4
	Chronic exposure	0.67
MWCNT (Nanocyl)	8-hour TWA	0.0025
carbon nanotubes (MWCNT & SWCNT)	8-hour TWA	0.007
fullerenes	Short term exposure	44.4
	Chronic exposure	0.27
fullerenes		0.8
silver (18–19 nm)	DNEL - pulmonary scenario 1	0.33
	DNEL - pulmonary scenario 2	0.098
	DNEL - liver	0.67
titanium dioxide (21 nm)	Chronic exposure	17
titanium dioxide (10–100 nm)	10 hr day <sup>-1</sup> , 40 hr week <sup>-1</sup>	0.3
titanium dioxide ( 21 nm)	8-hour TWA	1.2

MWCNT: multi-wall carbon nanotubes, SWCNT: single-wall carbon nanotubes

## GP 9 Control measures

### *Introduction*

After a nanomaterial risk-inventory and evaluation has been performed, risks should be reduced by taking control measures. This Good Practice surveys control measures described in the literature. The overview is not exhaustive. The control measures are not described in full, but reference is made to the original article from which they were taken. The control measures are organised in line with the occupational hygiene strategy, also known as the STOP-approach<sup>1</sup>. The quality of the control measures mentioned is not discussed in this Good Practice. Readers are referred to descriptions of the methods in question, user guides and other literature on this topic for such a discussion.

### *Occupational hygiene strategy*

Employers must follow a predetermined occupational hygiene strategy in order to protect the health and safety of employees. Such a strategy must be based on investigation of the sources of the risks involved, followed by consideration of the collective, technical or organizational measures needed to reduce these risks. Only if these measures do not (yet) offer a complete solution to all the health and safety problems at issue will it be necessary to take individual measures such as the use of personal protective equipment (PPE). It goes without saying that this approach also applies to nanomaterials. Implementation of these measures is not a matter of personal choice. Only if convincing proof can be given that a measure addressing a higher-level risk cannot be implemented may use be made of a measure dealing with a lower-level risk. In cases concerning the use of certain substances (such as carcinogenic substances for which no threshold value is available), the choice of control measure may not be made dependent on economic considerations.

### *Measures taken at the source*

Risks associated with the use of nanomaterials can sometimes be reduced or eliminated by control measures taken at the source – for example by changing the properties of the nanomaterial in question, by using less hazardous nanomaterials or by reducing the amount of nanomaterial used. Studies have shown, however, that this approach is often impossible because use of a particular nanomaterial in particular amounts is necessary for the application in question. Nevertheless, it was considered appropriate to include measures taken at the source in this survey. Table 9.1 gives an overview of measures taken at the source that are often used in research, together with a reference to the article or articles given in the Reference list at the end of this Good Practice that describe each measure.

---

<sup>1</sup> The STOP approach describes the hierarchy in which control measures have to be taken into account: (Source – Technical – Organisational – Personal)

**Table 9.1 Measures taken at the source in nanomaterial research**

Measure	Reference
<a href="#">Safe design of nanomaterials</a> (for example by taking the properties of the material into account or by applying less hazardous or non-hazardous coatings)	11, 18
Eliminate use of the nanomaterial	1, 2, 3
Replace the material by a substance that poses a lower risk	2, 3, 6
Modify the material (for example coat it) so as to reduce the risk	1, 4
Don't use more nanomaterial than is strictly necessary	6
Buy ready-to-use material (thus avoiding extra processing steps)	6
Use nanomaterial in a matrix or dispersion. Avoid use in powder form	2, 3, 4, 6
Avoid working methods that avoid aerosol or dust formation (for example, moisten powders)	1,6
Reduce number of steps involving use of nanomaterial, or change these steps (for example, by use of automation)	1

*Technical control measures*

Technical control measures do not remove the risk, but limit the exposure (for example by diluting the nanomaterial) or may even eliminate it (for example by screening). Table 9.2 gives an overview of technical measures described in the literature.

**Table 9.2 Technical measures**

Measure	Reference
Use completely enclosed systems (such as a glovebox or other sealed container)	1, 2, 3, 5, 6, 8, 9, 10
Transport nanomaterials in enclosed systems	1, 2, 3, 6, 8
Use cleanroom ventilation	1, 2, 3, 4, 5, 6, 8, 10
Maintain underpressure in spaces where nanomaterials are used	8
Use airlocks at entrance to laboratory	8
Fume hood or exhaust cabinet (such as a laminar flow cabinet)	2, 3, 5, 6, 8, 9, 10, 13
Use local exhaust ventilation	1, 3, 4, 5, 6, 8, 10, 13
Use spraying booth	1
Use a work booth (with or without ventilation)	1
Make use of natural ventilation	1, 10, 13
Avoid recirculation of contaminated exhaust air	6, 13
Use HEPA filters in combination with ventilation systems	6, 2, 8, 3, 13
Make sure floor has a smooth finish	8
Use asbestos-type vacuum cleaners with HEPA filters	8
Install an emergency shower	3, 8

The ventilation in fume hoods may have the unintended consequence of disseminating finely divided nanomaterial. It might be worth considering performing the operations in question in a glovebox or a fume hood with little ventilation (for example used in a night setting) and introducing additional cleaning procedures. See the section on fume hoods below and Good Practice 7b for further information.

The following further comments may be made about technical control measures:

- the use of closed systems is recommended if the nanomaterials are very dusty or have a low level of agglomeration or aggregation, and when reactors or ovens in which nanomaterials are produced or processed have to be cleaned (11);
- underpressure should be maintained in such a closed system, and the outlet of the ventilation system should be provided with a HEPA filter. The latter requirement also applies to ovens and reactors used for production and processing of nanomaterials (11);
- if reactors or ovens are too big to fit in a walk-in or drive-in fume hood during the cleaning activities, the use of local exhaust ventilation (possibly in combination with a HEPA filter) might be worth consideration.

The most common technical control measure in research institutes is the use of ventilation in the form of general mechanical room ventilation or the use of a fume hood. A number of recommendations concerning the use of fume hoods are given below<sup>2</sup>.

#### *Fume hoods*

Sources in the literature indicate that the use of nanopowders in a fume hood can lead to significant exposure to nanoparticles in the air breathed by employees outside the fume hood. The following recommendations have been made in an attempt to avoid such exposure:

- fume hoods should have an air intake velocity between 0.4 and 0.6 m/s. At velocities below 0.4 m/s, movements in and outside the fume hood have too much influence on the air flow, and nanomaterials can escape from the fume hood. An intake velocity of more than 0.6 m/s can lead to turbulence, which can also cause nanomaterials to escape from the fume hood. It should be noted in this connection that the location of the fume hood in the laboratory is also important for avoiding undesired turbulence;
- when work involving the use of nanomaterial takes place in the fume hood, the sash window in front must be lowered as far as possible, preferably to arm height;
- fume hoods with a constant air flow rate work better than compensating fume hoods, which in their turn work better than standard fume hoods. The air flow rate in compensating fume hoods changes when the fume hood opens. Such changes can cause nanomaterials to escape from the fume hood;
- Draughts near the fume hood should be reduced and if possible eliminated because they can interfere with the air flow in the fume hood, causing nanoparticles to escape from the fume hood.

---

<sup>2</sup> The text in this section is a modified version of the summary of the article cited in reference 12, which was produced by [www.nanocentre.nl](http://www.nanocentre.nl)

It goes without saying that it is advisable to use nanopowders as little as possible, and when they must be used to minimize the use of operations that could cause the nanopowder to be dispersed into the air of the laboratory (12).

It may be noted in addition that fume hoods are often fitted with HEPA filters, which can remove up to 98 per cent of the particles from the air passing through them, depending on the type of filter used. The frequency with which the HEPA filters are replaced depends on the use made of the fume hood, but regular checks are to be recommended. Recirculation of filtered air should be avoided (see also Good Practice 7D).

#### *Organizational control measures*

Organizational measures in this field are aimed at minimizing exposure to nanomaterials. Such measures include reducing the number of employees exposed to nanomaterials, giving employees specific tasks, powers and responsibilities, setting up laboratory rules and procedures and training employees in their use, among other things. Table 9.3 gives an overview of organizational measures used in practice when working with nanomaterials.

**Table 9.3**      **Organizational measures**

Measure	Reference
Appoint and train an internal consultant on nanomaterials and the associated occupational risks	6, 8
Ask suppliers to indicate whether their products contain nanomaterials	6
Limit the number and/or amount of nanomaterials used	3, 6
Place appropriate danger or warning signs at the entrance to laboratories where nanomaterials are used	6
Restrict the access to nanolaboratories	3, 6, 8, 9
Give employees appropriate information and training (see also Good Practice 11)	3, 6, 8, 9, 13
Draw up general instructions to make employees aware of the possible risks	3
Draw up procedures for such activities as cleaning, maintenance, waste disposal and transport in situations involving nanomaterials (see also Good Practice 7)	2, 3, 8, 9
Clean the laboratory regularly	2, 3, 6, 8, 9
Draw up procedures for handling waste containing nanomaterials (see also Good Practice 7C)	2, 3, 6, 8
Maintain installations (such as local exhaust ventilation systems, fume hoods and gloveboxes) in accordance with maintenance instructions taking the presence of nanomaterials into account	1, 6, 9, 3
Label packages and preparations clearly to show that they contain nanomaterials	3, 6, 8, 13
Seek expert advice from someone with thorough knowledge of the scientific aspects of the handling of nanomaterials	2, 3, 4, 5, 10

The following comments may be made in connection with these organizational control measures:

- Appoint someone (for example a project manager, research manager or laboratory supervisor) with day-to-day responsibility for cleaning and working safely with nanomaterials;
- It might be appropriate to consider providing special changing rooms where employees can change into work clothing and PPE, if necessary, and where these articles can be kept. Work clothing must be treated properly and cleaned (or in many cases discarded properly after use) to prevent the spread of nanomaterials.



*Personal protective equipment (PPE)*

The final way to reduce risks is to provide personal protective equipment (PPE) including gloves, respiratory protection and protective clothing such as disposable coveralls, and to make sure that employees use it. PPE must never be used as the only control measure. Table 9.4 gives an overview of personal protective equipment that is used in practice.

**Table 9.4 Personal protective equipment**

Measure	Reference
<i>Skin protection</i>	
Disposable gloves (nitrile, latex, neoprene)	2, 3, 6, 8, 9, 13
<i>Eye and face protection</i>	
Safety glasses with side shields	3, 6, 8, 9
Face shield	13
Wide-vision safety goggles	13
<i>Respiratory protection</i>	
FFP3 SL face masks	1, 2, 3, 6, 8, 9, 13
<i>Other body protection</i>	
Non-woven protective clothing, such as Tyvek-type coveralls	2, 3, 6, 8, 9, 13

If personal protective equipment is used, it is normally assumed either that work is being performed in a potentially hazardous environment or that additional protection is required (13). It is possible, however, that PPE is worn to protect not humans but the nanomaterial, which could be “contaminated” by contact with humans.

*Respiratory protection*

It is important that respiratory protective equipment should fit properly (this can be checked with the aid of a test fitting), that it is well maintained and that the filters are changed regularly (the supplier can tell you how often this should be done).

Specific recommendations about the use of respiratory protective equipment when working with nanoparticles are rarely found in safety sheets and the like. The main reason for this is the lack of occupational exposure limits for such materials (15).

*Dermal exposure and protection*

A recent review of current view concerning the uptake of nanomaterials through the skin (19) showed that the results of different studies are often contradictory and that measures need to be taken to harmonize skin penetration or skin uptake tests. The authors further concluded that while various nanomaterials can penetrate the skin, they only do so to a slight extent. The degree of skin penetration depends even more than in the case of bulk chemicals on chemical bonding and the experimental conditions used.

The effectiveness of commercial latex gloves in resisting penetration by nanoparticles of about 40 nm in size was tested in 2009. No penetration of the gloves by nanoparticles was observed in this very limited study. The results of more extensive tests in current investigations will show how much credence can be given to this conclusion. The same study showed that airtight protective clothing made of non-woven material offered the best protection against nanoparticles (16). It was further concluded that protective work clothing should preferably not be reused, and that it should be stored separately after use to prevent contamination of the environment.

## References

1. Duuren-Stuurman, van, B., et al, Substancesmanager Nano version 1.0: A web-based tool for risk prioritization of airborne manufactured nano objects, *Ann. Occup. Hyg.*, pp 1 – 17, 2011.
2. Schmidt-Ott, A., et al, Nanosafety Guidelines, Delft University of Technology, version 2, September 2010.
3. Scislowicz, C., et al, Nanotoolkit – Working Safely with engineered Nanomaterials in Academic Research Settings, California Nanosafety Consortium of higher education, April 2012.
4. Schulte, P., et al, Occupational Risk Management of Engineered Nanoparticles, *Journal of Occupational and Environmental Hygiene*, vol 5, pp 239 – 249, April 2008.
5. Zalk, D.M., et al, Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposure, *J. Nanoparts*, 2009.
6. Cornelissen, R., et al, Guidance working safely with nanomaterials and nanoproducts 'the guide for employers and employees', FNV, VNO-NCW & CNV, version 1.0, May 2011.
7. ISO/TR 13121, Nanotechnologies – Nanomaterials risk evaluation, 15 May 2011.
8. Groso, A., et al, Management of nanomaterials safety in research environment, *Particle and Fibre Toxicology*, vol 7, pp1 – 8,2010.
9. Giacobbe, F., Monica, L., and Geraci, D. (2009). Risk assessment model of occupational exposure to nanomaterials. *Human & Experimental Toxicology* 28, 401-406.
10. Ostiguy, C., et al, Development of a specific control banding tool for nanomaterials, ANSES, report, December 2010.
11. Compilation of the safety of nanomaterial exposure mitigation guidelines relating to laboratories, Organisation for Economic Co-operation and development, 1 December 2010.
12. Tsai et al. 2008. Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods. *Journal of Nanoparticle Research*, Volume 11, Number 1, pp 147-161.
13. General safety practices for working with engineered nanomaterials in research laboratories, National Institute for Occupational Safety and Health (NIOSH), publication number 2012-147, May 2012.
14. Rengasamy et al. 2011. Total inward leakage of nanoparticles through filtering facepiece respirators. *The Annals of Occupational Hygiene*, Volume 55. Number 3, pp 253-263.
15. Schaffer et al. 2009. Respiratory protection against airborne nanoparticles: a review. *Journal of Nanoparticle Research*, Volume 11, pp 1661 – 1672.
16. Golanski et al. 2009. Experimental evaluation of personal protection devices against graphite nanoaerosols: fibrous filter media, masks, protective clothing, and gloves. *Human and Experimental Toxicology* volume 28, pp 353-359.
17. Park et al. 2011. Efficiency of protective dermal equipment against silver nanoparticles with water aerosol. *Journal of Nanoparticle Research*, volume 13, pp 3043-3049.
18. NanoNextNL. Safe Design of Nanomaterials – Paving the way for innovation (2012); Action plan and green paper.
19. Poland, C.A. et al. (2013) Dermal absorption of nanomaterials. Danish EPA. Environmental Project no. 1504.

**GP 10 Standard Operating Procedure (SOP)**

It might that standard work instructions (Standard Operating Procedure (SOP)) in research laboratories is used, on which research is conducted. An example of a SOP which can be used for the handling of engineered nanomaterials in a research environment is discussed in this Good Practice. These can be customized for each individual workplace/experiment. The example below is based on the SOP that is included in Annex A of the Nanotoolkit (1)

<b>Overview</b>	<b>Procedure Title:</b>		
	<b>Date of Creation/Revision:</b>		<b>Version nr.</b>
	<b>Location:</b> (e.g. Building, Lab, Room)		
	<b>Principle Investigator:</b>		
	<b>Laboratory Responsible Person / Laboratory Supervisor:</b>	<b>Phone:</b>	<b>Email:</b>
	<b>Description of the process:</b> Briefly describe the process. Indicate if aerosols are likely to be created.		
	<b>Material State and Conditions of Use</b> <input type="checkbox"/> dry particles (powders / pellets) <input type="checkbox"/> dispersion <input type="checkbox"/> gaseous phase <input type="checkbox"/> matrix <input type="checkbox"/> product containing nanoparticles	<b>Frequency of Use:</b> <input type="checkbox"/> one time <input type="checkbox"/> daily <input type="checkbox"/> weekly <input type="checkbox"/> monthly <input type="checkbox"/> other: .....	<b>Duration per Experiment</b> .....minutes or .....hours

<sup>1</sup> Nanotoolkit. (2012) Working Safely With Engineered Nanomaterials in Academic Research Settings. California Nanosafety Consortium of Higher Education.

<b>Hazard identification</b>	<b>Potential Hazard:</b> <input type="checkbox"/> fibrous / rigid / rod / plate <input type="checkbox"/> insoluble <input type="checkbox"/> soluble <input type="checkbox"/> nanomaterial with CMR potential <input type="checkbox"/> parent material with CMR potential	<b>Quantity Used:</b> <input type="checkbox"/> $\mu\text{g} / \mu\text{l}$ <input type="checkbox"/> mg / ml <input type="checkbox"/> gram / litre <input type="checkbox"/> > 1 kg / litre <input type="checkbox"/> other:.....
	<p>Identify potential and safety hazards for the nanomaterial or parent material using the material safety data sheet (MSDS), the technical data sheet (TDS) or other sources of information. The toxicity of the nanomaterial may be greater than the parent material. Special consideration should be given to the high reactivity of some nanopowders with regard to potential fire and explosion (ATEX), particular if scaling up the process. Consider the hazards of any precursor material in evaluating the process.</p>	

Indicate the necessary and prescribed control measures. A choice can be made from the examples listed in Good Practice 9.

<b>Control Measures</b>	<b>Technical Control Measures</b>	
	<input type="checkbox"/> fume hood (laboratory type) <input type="checkbox"/> biosafety cabinet (must be ducted if used in conjunction with volatile compounds) <input type="checkbox"/> enclosed system (e.g. glove box, sealed chamber) <input type="checkbox"/> other:	
	<b>Organisational Controls / Work Practices</b>	<b>How to Apply?</b>
	<input type="checkbox"/> storage <input type="checkbox"/> labelling <input type="checkbox"/> transport <input type="checkbox"/> preparation <input type="checkbox"/> cleaning <input type="checkbox"/> personal hygiene <input type="checkbox"/> absorbent (o.a. Whatman benchkote) <input type="checkbox"/> restrict access <input type="checkbox"/> post signs <input type="checkbox"/> use of nanomaterials in animals (management requirements)	
	<b>Approvals required?</b>	Yes <input type="checkbox"/> No <input type="checkbox"/>
	Identify tasks that require prior approval by the principal investigator before performing the described experiment.	
	<b>Other additional work practices?</b> Describe any additional work practices specific to the experiment / process.	
	<b>Personal Protective Equipment (PPE)</b>	Check all that apply
	Body Protection	<input type="checkbox"/> long pants (no cuffs) <input type="checkbox"/> laboratory coat made of standard materials <input type="checkbox"/> laboratory coat made of non-woven fabrics with elastics at wrists (i.e., Tyvek®) <input type="checkbox"/> coveralls (disposable) with head coverage (i.e., Tyvek®)
	Eye / face protection	<input type="checkbox"/> safety glasses with side shields <input type="checkbox"/> chemical splash goggles <input type="checkbox"/> face shield
Hand Protection	<input type="checkbox"/> latex (powder-free) <input type="checkbox"/> nitrile <input type="checkbox"/> neoprene <input type="checkbox"/> vinyl <input type="checkbox"/> other:.....	
Foot Protection	<input type="checkbox"/> closed toe shoes <input type="checkbox"/> over-the-shoe booties	
Respiratory Protective Equipment (RPE)	<input type="checkbox"/> facepiece, type ..... <input type="checkbox"/> full face mask, type... <input type="checkbox"/> powered respirators <input type="checkbox"/> other:.....	
Other	<input type="checkbox"/>	

<b>Accident and Spill Procedures</b>	<b>Location of Nearest Emergency Equipment</b>	
	<b>Item:</b>	<b>Location:</b>
	Telephone : Eyewash / Safety Shower : First Aid Kit : Fire Extinguisher : Fire Alarm: Spill clean-up materials :	
	<b>Personnel Exposure Procedures</b> 1. Flush contamination from eyes/skin and remove any contaminated clothing. 2. Alert the Emergency Response Team and (depending on local arrangements) the occupational physician and occupational hygienist. 3. Report potential exposures to your Principal Investigator/Laboratory Supervisor. 4. File an incident report with your institution. 5. File the protocol for dealing with severe accidental exposure to nanomaterials (Good Practice 13).	
<b>Spill Response Procedure (also see Good Practice 7B)</b> 1. <u>Alert</u> workers near spill to avoid entering the area and if necessary evacuate. 2. <u>Assess</u> . Are you able to cleanup spill yourself or is assistance of specialised personal needed? 3. <u>Cleanup Spill</u> . Wear existing PPE.  <i>For Powders:</i> – Use a dedicated, approved HEPA vacuum whose filtration effectiveness has been verified. – Do not sweep dry nanoparticles or use compressed air. – Consider possible pyrophoric hazards associated with vacuuming up nanoparticles. – Wet wipe using damp cloths with soaps or cleaning oils, or commercially available wet or electrostatic microfiber cleaning cloths. Consider possible reactivity of nanoparticles with the wipe solvent.  <i>For Liquid Dispersions</i> – Apply absorbent material (appropriate for the solvent in the dispersion) to liquid spill.  4. <u>Dispose</u> . Dispose of used cleaning materials and wastes as hazardous waste (Good Practice 7C). 5. <u>Report</u> . File incident report with your institution.		

<b>Training</b>	<p><b>General Safety Training</b></p> <p>Describe your institution's general laboratory safety training. (guidance: Good Practice 11)</p>
	<p><b>Laboratory / Experiment Specific Training</b></p> <p>Describe the (mandatory) laboratory / experiment specific safety training.</p>

	Waste Stream	Procedure
<b>Waste Disposal</b>	<input type="checkbox"/> Solid <ul style="list-style-type: none"> <li>– Dry nanomaterials</li> <li>– filter media containing nanomaterials</li> <li>– Debris / dust from nanomaterials bound in a matrix</li> </ul>	
	<input type="checkbox"/> Liquid <ul style="list-style-type: none"> <li>– Suspensions containing nanomaterials</li> <li>– Rinsing water from cleaning (spills)</li> </ul>	
	<input type="checkbox"/> Laboratory trash with trace nanomaterials <ul style="list-style-type: none"> <li>– PPE</li> <li>– sticky mats</li> <li>– absorbent materials</li> <li>– spill clean up materials</li> </ul>	
	<input type="checkbox"/> embedded in a solid matrix	
	<input type="checkbox"/> discarded laboratory equipment containing nanomaterials	
	<p>Describe (or refer to) the institution's waste management procedures here.</p> <p>More information on handling waste containing nanomaterials is described in Good Practice 7C.</p>	

## GP 11 Information and training

In view of the widespread lack of awareness of the risks people run when working with nanomaterials, it is advisable to give employees good, clear information about possible ways of working safely with these materials and the problems that may arise in this connection. The workshops and interviews discussed in Chapter 4 of Part A show that employees need clear instruction in this field, presented to them through formal procedures. Employees do not want to spend much time and effort collecting and accessing the necessary information themselves. They want support in this process. This Good Practice contains a number of suggestions about the best way of informing employees about ways of working safely with nanomaterials.

### *Information*

Employees need to be given adequate information and instruction about ways of working safely with nanomaterials. Before providing this information, you have to decide which topics are interesting and relevant for a given target group. For example, researchers will not need the same kind of information as support staff. Some of the main topics to be borne in mind are:

- What are nanomaterials?
- What is special about nanomaterials? (general introduction)
- Why do we pay extra attention to the health & safety aspects of nanomaterials?
  - How do they differ from “normal” chemicals?
  - How do they differ from ultrafine particles (UFP) in the environment, diesel emissions, particles produced by burning candles etc., for example?
  - See Good Practice 1 for further information;
- How to recognize the nanomaterials used.
- Where might you come across nanomaterials in your own organization?
  - Which nanomaterials and/or nanoproducts might be encountered?
  - What do we do with them? (Which operations and processes may be involved?)
  - See Good Practice 6 for further information.
- What is known about the risks associated with the use of nanomaterials and what is uncertain?
- What has our organization already done to control the risks of working with nanomaterials?
- How can nanomaterials be used and stored safely, and how can wastes containing nanomaterials be disposed of safely?
  - See Good Practice 7C for further information.
- Are any occupational exposure limits (OEL) known for nanomaterials?
  - See Good Practice 8 for further information.
- How to use and maintain the recommended personal protective equipment (PPE).
  - See Good Practice 9 for further information.
- How to use and maintain the recommended technical equipment.
  - See Good Practice 7D for further information.
- Action to be taken in case of spillage and other incidents.
  - See Good Practice 7B for further information.



*Training in the selected risk assessment methods*

Various guidelines and risk assessment methods for assessing the risk associated with exposure to nanomaterials have appeared in recent years. Most of these are based on Control Banding. A study by Vervoort (1) showed that about 32 risk assessment methods for nanomaterials were freely available for use in 2012. The most suitable instruments for use in a research environment have already been discussed in Good Practice 4.

While most risk assessment methods involve the determination of a risk level or risk category based on a calculated exposure score and a calculated severity score reflecting the severity of the exposure in question, different assessments of a given process or situation can lead to widely differing estimates of the risk level. One instrument may characterize a given process as safe, while another may characterize it as unsafe. These differences may be due to the use of different variables for the determination of the severity and exposure band, different target groups and different structures of the assessment method, among other things. Another important factor is that different users may make different choices when using the risk assessment methods and may estimate some variables conservatively and others more progressively.

All the above considerations provide a strong argument for training the users of risk assessment methods so as to arrive at greater uniformity of results, and stimulating discussion between users to reduce differences of interpretation of the various issues involved. Such measures will help to improve the effectiveness of the risk assessment methods used.

---

<sup>1</sup> M.B.H.J. Vervoort. (2012) Risk assessment of occupational used nanomaterials: A comparison of risk assessment methods in order to determine the risk of occupational used nanomaterials in a research environment. Master's thesis. Netherlands School of Public and Occupational Health (NSPOH).

**GP12 Facilities for working with nanomaterials in newly built or renovated laboratories***Introduction*

Certain facilities for working with nanomaterials can be introduced in newly built or renovated laboratories that would be impossible (or only possible at great expense) in existing premises. This Good Practice gives recommendations about how to plan nanolaboratories before the actual construction work begins.

*Examples*

First of all, assign existing operations on nanomaterials into hazard classes, with the aid of a tool such as the EPFL method (1) or the Nanotoolkit (2) (see Good Practice 4). These methods make use of three hazard classes, 1, 2 and 3. The higher the class, the greater the hazard involved. There is a direct relationship between the hazard class determined by these methods and the control measures to be taken. The higher the class, the more stringent the control measures to be taken in the laboratory. This is comparable with the classification (ML-I, ML-II and ML-III) of laboratories working with GMO (genetically modified organisms) (3) and the A, B, C and D classification of laboratories working with open radioactive substances (4). It is advisable not to define a hazard class 0, corresponding to situations or operations that are entirely without risk, since this might give a false sense of safety. The highest hazard class should be reserved for work with nanotubes such as carbon nanotubes (CNTs) and rod-shaped or wire-shaped nanoparticles. This distinction should be incorporated into the laboratory classification system, if such a system already exists – and if it doesn't, it should be introduced.

Different hazard classes normally lead to different technical and organizational control measures and use of different personal protective equipment (PPE).

---

<sup>1</sup> Groso, A. et al. (2010) Management of nanomaterials safety in research environment. Particle and Fibre Toxicology.

<sup>2</sup> California Nanosafety Consortium of Higher Education (2012) Nanotoolkit. Working safely with engineered nanomaterials in academic research settings.

<sup>3</sup> Schellekens, H., Veilig werken met micro-organismen, parasieten en cellen in laboratoria en andere werkrumten, 4<sup>de</sup> druk 2010.

<sup>4</sup> Richtlijn Radionuclidenlaboratoria, Hoofinspectie milieuhygiene publicatie 94-02, September 1994.

*Implementation*

Technical design specifications can be formulated as part of the planning process for new buildings or for renovation work. Appropriate control measures should be defined for each hazard class, with special reference to the following points:

- installation of a cleanroom for the highest hazard class;
- a changing room with a clean and a dirty section;
- an access airlock with emergency shower;
- demands to be made on ventilation capacity;
- number of fume hoods and/or laminar flow cabinets required, including spare capacity for the future;
- installation of local exhaust ventilation, now or in the future;
- decision on whether HEPA filters (type F7) are required;
- underpressure in laboratory;
- floors, walls and furniture should be cleanable (for example with a cloth or sponge moistened in water);
- magnetic card access control;
- separate room with restricted air flow for weighing out samples;
- possibility of regulating air flow in case of calamities;
- decision on whether windows should be openable ;
- other calamity response facilities especially for nanomaterials.

A number of these issues have been worked out in detail in the EPFL method (see Table 12.1).

**Table 12.1** Examples of technical safety measures used in the different hazard classes according to the EPFL method

Technical safety measures		Laboratory (hazard class)		
		Nano 1	Nano 2	Nano 3
Ventilation	Chemistry lab type (renewal without recycling)	X	X	X
	5-10 X /hour)			
	With at least sealed F7 filter for exiting air			X
	Low pressure in the room	X	X	>20 mPa
	Capture at source		X	X
Floor	Flooring	Tiling or linoleum		resin
Manipulation in fume hood	Optional	X		
	Compulsory		X	X
Access to lab	Restricted (magnetic card access control system)		X	X
	Regular lab access control (laboratory key)	X		
	Evidence about exposed people + board to record presence			X
Safety access system (SAS)	Double SAS (if >100 g ultrafine particles)			X
	Simple SAS (if <100 g ultrafine particles)		Light SAS	X
	Safety shower			X
Use of vacuum cleaners	Asbestos type	X	X	X
	Domestic type		Forbidden	

Special organizational measures can also be considered when new building work is being planned. Care should be taken to plan as many nanolaboratories as possible so that the need to work on nanomaterials (especially high-risk materials) in rooms where other activities are performed can be minimized. This may entail a need to plan shared facilities for research groups working on nanomaterials or the clustering of nanolabs (including the facilities they require) in a given wing. Is it not too far to walk from the nanolab to the analytical facilities, and are both on the same floor so that there is no need to use the stairs or lift for internal transport? Reserve a space just inside the entrance in the plan for each nanolab where lab coats (which should not be removed from the laboratory) can be hung on the wall.

Thought should also be devoted to secondary processes. Relevant topics here include the following, among others: How about the maintenance of nanolabs? What kind of technical devices and procedures are needed to ensure that maintenance personnel can change HEPA filters easily and safely? Can the lamps in the fume hood be changed without the need to enter the fume hood? Can the work of the cleaners be facilitated by such measures as making floors without seams, smooth work surfaces etc., so that the laboratory is easily cleanable with a wet cloth?

**GP 13 Protocol for dealing with severe accidental exposure to nanomaterials***Introduction and policy*

It has already been mentioned in other Good Practices that relatively little is known about the effects of exposure to nanomaterials. It may happen that employees are accidentally exposed to high, uncontrolled levels of nanomaterials at work. Since no cases of acute exposure to nanomaterial – as opposed to exposure to various kinds of bulk chemicals – have yet occurred and the incubation time for the effects of such exposure may be long, we do not as yet have any experience of nanomaterial-related illness, of dealing with questions of liability for such accidents or of the payment of compensation. Nevertheless, people who have suffered nanomaterial-related accidents are naturally very worried about the possible effects of exposure to harmful nanomaterials, and may be preparing claims for compensation in the future.

The policy of Dutch research institutes is in general aimed at dealing with such situations in a responsible way. The main focus is on the employees or students who think that they may have been exposed to nanomaterials, and making sure that they will be treated well and fairly.

This Good Practice concerns the registration of employees and students (not third parties) who believe they may have been exposed to nanomaterials at work in a Dutch research institutes. The registration meant in this Good Practice is focussed on registration after an incident and thus differs from the mandatory registration due to work with carcinogenic, mutagenic or reprotoxic substances, as regulated in the Dutch Working Conditions Decree (Arbobesluit) Art. 4.13 and 4.15.

The Director of the institute or faculty in question is regarded as the “owner” of the protocol proposed here and is responsible for its maintenance, the periodic coordination and evaluation of the related activities and ensuring – in consultation with stakeholders – that it is periodically updated and improved.

*Investigation of exposure and registration*

As soon as employees and/or students believe that they may have been exposed to nanomaterials, they can report this fact to their supervisor, who must in turn report it to the relevant health & safety officer. The latter will then investigate the nature, the estimated severity and the likelihood of the exposure. If the investigation shows that it is likely that exposure has actually taken place, the supervisor will fill in and sign a registration form, a copy of which will be kept in the medical and personnel files of an employee in question. In the case of a student, the copy of the registration form will be sent to the Education & Student Affairs department and kept in the student’s file.

In connection with the long possible incubation time of nanomaterial-related illnesses, such records must be kept in the relevant files for 30 years after the end of employment or graduation. The general procedure for reporting, investigation and registration of alleged accidental exposure to nanomaterials is illustrated in Figure 13.1.

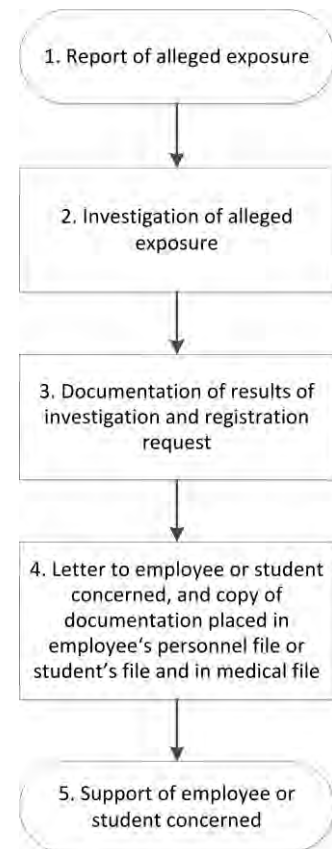
*Letter to employee or student involved*

The director of the research institute will send a letter to the person concerned, stating the results of the investigation and the registration of the alleged exposure. The letter will also mention that the research institute offers care and support to all those who may have been involved in exposure to nanomaterials (see section on *Care and support* below), and may add that the institute places no time limit on claims for damage in such cases (see final section).

*Registration data*

At least the following data will be included in each record of possible exposure to nanomaterials:

- name and data of birth of person concerned;
- time or period of incident;
- location of incident;
- chemical name or product name of nanomaterial;
- physical form of nanomaterial (particles, fibre, tubes, rods or flakes);
- Amount of nanomaterial used;
- Brief description of process in which nanomaterial is used and course of alleged exposure;
- Total duration of exposure.



**Figure 13.1** Schematic representation of protocol for dealing with accidental exposure to nanomaterials

An example of such a registration form is shown in Table 13.1.

*Care and support*

If the employee or student who is alleged to have been exposed to nanomaterials so wishes, he or she will be offered support from an occupational health officer or a doctor from the student medical centre, or will be offered assistance in finding sources of support outside the institute. If it is considered appropriate, a talk may be arranged later with the supervisor in the case of an employee or the central student counsellor in the case of a student.

*Waiver of statute of limitations*

Little is known about the effect of exposure to nanomaterials on health. If such effects do exist, it is reasonable to assume that clinical symptoms may not occur until long after exposure – in some cases long after the statute of limitations (the legal period after which claims for damages can no longer be brought) has elapsed. Research institutes often do not place any time limit on the bringing of claims by employees or students in such cases, even if they are no longer working or studying at the institute in question. This policy may vary from one research institute to another.

**Table 13.1** General structure of registration form for accidental exposure to nanomaterials and nanoproducts.

Date or period of activities performed	Name of employee or student	Name of nanomaterial	Details of activities	Duration of activities
Time a	Employee A	Chemical name or product name	<ul style="list-style-type: none"> <li>- Location</li> <li>- Worksite</li> <li>- Process / experiment</li> <li>- Amount of nanomaterial used</li> </ul>	<p>Overall duration of activities</p> <p>Duration of specific activities</p>
Time b	Employee A			
Time c	Employee B			
Time d	Employee C			

## References

1. Brouwer, D et al. (2012) Harmonization of measurement strategies for exposure to manufactured nano-objects: report of a workshop. *Ann. Occup. Hyg.* vol. 56, no.1;
2. California Nanosafety Consortium of Higher Education (2012) Nanotoolkit. Working safely with engineered nanomaterials in academic research settings;
3. Commission recommendation on the definition of nanomaterial, 2011/696/EU, 18 October 2011;
4. Compilation of the safety of nanomaterial exposure mitigation guidelines relating to laboratories, Organisation for Economic Co-operation and Development, 1 december 2010;
5. Cornelissen, R.T.M., Jongeneelen, F. en Van Broekhuizen, J.C. (2010) Guidance working safely with nanomaterials and nanoproducts. The Guide for employers and employees. Executed on behalf of the Dutch Social Partners FNV, VNO-NCV and CNV and was financed by the Dutch Ministry of Social Affairs and Employment;
6. Dekkers, S. en de Heer, C. (2010) Tijdelijke nano-referentiewaarden – Bruikbaarheid van het concept en van de gepubliceerde methoden. RIVM report 6010440001/2010;
7. Delft University of Technology, workgroup Nanosafety of the Faculty of Applied Sciences. Nanosafety Guidelines. Version 2 – September 2010;
8. Duuren-Stuurman, van, B., et al, Stoffenmanager Nano version 1.0: A web-based tool for risk prioritization of airborne manufactured nano objects, *Ann. Occup. Hyg.*, pp 1 – 17, 2011;
9. Flutters, M.F.J en Samwel-Luijt, M., RI&E Werken met synthetische nanomaterialen, intern rapport Faculteit W&N Universiteit Leiden, september 2011;
10. Geiser, M. (2005) Ultrafine Particles Cross Cellular Membranes by Nanophagocytosis Mechanisms in Lungs and in Cultured Cells, *Environmental Health Perspectives*, volume 113 (11);
11. Gezondheidsraad (2006) Betekenis van nanotechnologieën voor de gezondheid. Den Haag: Gezondheidsraad. publicatie nr. 2006/06;
12. Gezondheidsraad (2011) Nanomaterialen in afval. Rapport nr. 2011/14;
13. Giacobbe, F., Monica, L. and Geraci, D. (2009). Risk assessment model of occupational exposure to nanomaterials. *Human & Experimental Toxicology* 28, 401-406;
14. Golanski et al. 2009. Experimental evaluation of personal protection devices against graphite nanoaerosols: fibrous filter media, masks, protective clothing, and gloves. *Human and Experimental Toxicology* volume 28, pp 353-359;
15. Groso, A. et al. (2010) Management of nanomaterials safety in research environment. *Particle and Fibre Toxicology* 2010 7:40;
16. [http://www.inspectieszw.nl/Images/Arbeidsomstandigheden-in-de-afvalverwerking\\_tcm335-312358.pdf](http://www.inspectieszw.nl/Images/Arbeidsomstandigheden-in-de-afvalverwerking_tcm335-312358.pdf);
17. <http://www.rwsleefomgeving.nl/onderwerpen/afval/storten/> geraadpleegd 23 september 2013;
18. ICRP publication 66 (1994) *Ann. ICRP (UK)*, vol. 24, Nos. 1-3, Pergamon;
19. ISO/TR 13121, Nanotechnologies – Nanomaterials risk evaluation, 15 mei 2011;
20. Kabinetsvisie Nanotechnologieën. Van Klein Naar Groots, 2010;
21. Klein Entink et al (2011) How to statistically analyze nano exposure measurement results: using an ARIMA time series approach. *J Nanopart Res*;
22. Murdock, R.C., Braydich-Stolle, L., Schrand, A.M., et al. (2007) Characterization of nanomaterial dispersion in solution prior to in vitro exposure using dynamic light scattering technique, *Toxicol. Sci.*;



23. NanoNextNL. Safe Design of Nanomaterials – Paving the way for innovation (2012); Action plan and green paper;
24. National Institute for Occupational Safety and Health (NIOSH). General safety practices for working with engineered nanomaterials in research laboratories, publication number 2012-147, may 2012;
25. NPR-CEN-ISO/TS 27687:2008-08 en: Nanotechnologieën - Terminologie en definities voor nano-objecten - Nanodeeltje, nanovezel en nanoplaat;
26. OECD (2010) Series on the Safety of Manufactured Nanomaterials No. 28. Compilation of nanomaterial exposure mitigation guidelines relating to laboratories. ENV/JM/MONO(2010)47;
27. Ostiguy, C., et al. (2010) Development of a specific control banding tool for nanomaterials, ANSES, report;
28. Paik, S.Y., et al. (2008) Application of a pilot Control Banding tool for risk level assessment and control of nanoparticle exposure, *Ann. Occ. Hyg.*, vol 52, no 6, pp 419 – 428;
29. Park et al. (2011) Efficiency of protective dermal equipment against silver nanoparticles with water aerosol. *Journal of Nanoparticle Research*, volume 13, pp 3043-3049;
30. PD 6699-2:2007 Nanotechnologies – Part 2: Guide to safe handling and disposal of manufactured nanomaterials. British Standards. ISBN 978 0 580 60832 2. 2007;
31. Poland, C.A. et al. (2008) Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study, *Nature Nanotechnology*, 3, 2008, 423-428;
32. Poland, C.A. et al. (2013) Dermal absorption of nanomaterials. Danish EPA. Environmental Project no. 1504;
33. Rengasamy et al. (2011) Total inward leakage of nanoparticles through filtering facepiece respirators. *The Annals of Occupational Hygiene*, Volume 55. Number 3, pp 253-263;
34. Richtlijn Radionuclidenlaboratoria, Hoofdinspectie milieuhygiëne publicatie 94-02, september 1994;
35. Risk assessment of products of nanotechnology, SCENIHR, 2009;
36. Schaffer et al. (2009) Respiratory protection against airborne nanoparticles: a review. *Journal of Nanoparticle Research*, Volume 11, pp 1661 – 1672;
37. Schellekens, H., *Veilig werken met micro-organismen, parasieten en cellen in laboratoria en andere werkruimten*, 4<sup>de</sup> druk 2010;
38. Schulte, P., et al. (2008) Occupational Risk Management of Engineered Nanoparticles, *Journal of Occupational and Environmental Hygiene*, vol 5, pp 239 – 249;
39. Scislowicz, C., et al. (2012) Nanotoolkit – Working Safely with engineered Nanomaterials in Academic Research Settings, California Nanosafety Consortium of higher education;
40. Sociaal Economische Raad (2012) Voorlopige nanoreferentiewaarden voor synthetische nanomaterialen. Advies nr. 2012/01, maart 2012;
41. Takagi, A., et al. (2008) Induction of mesothelioma in p53+/- mouse by intra peritoneal application of multi-wall carbon nanotubes, *The Journal of Toxicological Sciences*, 33, 2008, 105-116;
42. The UK NanoSafety Partnership Group (2012) Working Safely with Nanomaterials in Research & Development;
43. Tsai et al. (2008) Airborne nanoparticle exposures associated with the manual handling of nanoalumina and nanosilver in fume hoods. *Journal of Nanoparticle Research*, Volume 11, Number 1, pp 147-161;

44. Van Broekhuizen et al. (2012) Exposure Limits for Nanoparticles: Report of an International Workshop on Nano Reference Values. *Ann. Occup. Hyg.* vol. 56 no. 5;
45. Vervoort, M.B.H.J. (2012) Risk Assessment of Occupational used Nanomaterials – A comparison of risk assessment methods in order to determine the risk of occupational used nanomaterials in a research environment- master thesis Netherland School of Public and Occupational Health (NSPOH);
46. Warheit, D.B., (2008) How meaningful are the results of nanotoxicity studies in the absence of adequate material characterization?, *Toxicol. Sci.*, 101, 183-185;
47. Zalk, D.M., et al, (2010) Control Banding and Nanotechnology. *The Synergist*, volume 21, issue 3, 2010, pp 26 – 29;
48. Zalk, D.M., Paik, S.Y. and Swuste, P. (2009) Evaluating the Control Banding Nanotool: a qualitative risk assessment method for controlling nanoparticle exposures. *J Nanopart Res* 11:1685–1704.