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French agency for food, environmental and occupational health & safety

Development of a specific Control Banding Tool for Nanomaterials

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French Agency for Food, Environmental
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Development of a specific Control Banding Tool for Nanomaterials

Request N°2008-SA-0407 relating to Control Banding

REPORT

Expert Committee (CES) on Physical Agents

December 2010

Key words

Hazard band, emission potential, continuous improvement, iterative process, uncertainty, exposure band, control banding, nanomaterials

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Abbreviations

AFNOR: French Standards Institute
ANSES: French Agency for Environmental and Occupational Health Safety
AM: Analogous material
ANSES: French Agency for Food, Environmental and Occupational Health & Safety
AST: Scientific and Technical Support
BM: Bulk material
CB: Control Banding
CES: Expert Committee
CL: Control level
CLP: Classification, Labelling and Packaging of Substances and Mixtures
CNT: Carbon Nanotube
CTS: Committee Responsible for the Solicited Request
EC: European Community
EP: Emission Potential
ERC: Full Risk Assessment
GER: Expert Rapporteur Group
GHS: Globally Harmonized System
HB: Hazard band
HSE: Health, Safety and Environment
INRS: French National Research and Safety Institute
ISO: International Organization for Standardization
PG: Project Group
WG: Working Group

Glossary

Agglomerate: collection of weakly bound particles or aggregates or mixtures of the two whose resulting external surface area is similar to the sum of the surface areas of the individual components.

Aggregate: strongly bound or fused particle whose resulting external surface area may be significantly smaller than the sum of calculated surface areas of the individual components.

Analogous substance: A substance or material with a similar composition and/or crystalline phase from the same chemical category and with similar documented physico-chemical properties (metal oxides, graphite, ceramics, etc.) as the substance of interest. An analogous substance can serve as a reference for the toxicological and chemical properties that may be of interest for risk assessment purposes.

Bulk material: A bulk material has the same chemical composition as the nanomaterial of interest and the same crystalline phase as the nanomaterial but its physical and biological properties may be substantially different and not at the nanoscale. The exclusion of the nanoscale is based on the ISO nano- core term definitions.

Chemical category (OECD definition): A chemical category is a group of chemicals whose physico-chemical and human health and/or ecotoxicological properties and/or environmental fate properties are likely to be similar or follow a regular pattern, usually as a result of structural similarity.

Classification & labelling: Any hazard information on a substance based on the principles of the GHS (Globally Harmonized System of Classification and Labelling of chemicals), or equivalent, and its transposition to the legislation of the country (e.g.: Regulation (EC) No 1272/2008 for the European Union).

Control banding (CB): A procedure designed to facilitate informed decisions on which to establish adequate control levels in order to improve workplace safety and protection of workers' health. It is based on simple input information regarding hazards and exposure to processes and the materials involved. CB is designed to allow quick decisions by local safety staff who are not necessarily experts on the specific risks at hand. It is therefore designed to tend towards elevated protection levels.

Exposure: contact with a chemical, physical or biological agent by swallowing, breathing, or touching the skin or eyes. Exposure may be short-term (acute exposure), of intermediate duration, or long-term (chronic exposure).

Full risk assessment/Full hazard assessment: Risk assessment is the determination of the qualitative and preferentially quantitative value of the risk related to a specific situation. In our field of discussions, it takes into account the hazards (toxicity) related to the nanoparticles (NPs) under study and the exposure of the worker in a specific task. A full risk assessment is defined in this context as a detailed risk assessment of specific workplaces and all other relevant work situations for a specific worker or group of workers involved. Risk assessment is an essential step in a risk management process. A full risk assessment is performed by an individual or a group of experts

highly knowledgeable in toxicology and industrial hygiene. It includes a full hazard assessment and a full exposure assessment.

- The full risk assessment is required when the band setting for both the hazard and the exposure requires a careful analysis that is not feasible with the proposed Control Banding model. In this context the full risk assessment requires the consultation of a specialist (industrial hygienist, occupational toxicologist).

- During the full hazard assessment, a specialist (toxicologist) provides a detailed evaluation of the hazard classification based on published literature and (if available) toxicological data provided by the manufacturers of the materials. Such a full hazard assessment can feed into a Control Banding process by providing a hazard band setting for substances for which insufficient information was available to the local health and safety staff.

Hazard: set of inherent properties of a chemical, physical or biological agent, mixture of agents or a process involving agents that, under production, usage or disposal conditions make it capable of causing adverse effects to organisms or the environment.

Particle: minute piece of matter with defined physical boundaries.

Risk: probability that a harmful event (death, injury or loss) arising from exposure to a chemical, physical or biological agent may occur under specific conditions.

Sensitisation: immune process whereby individuals become hypersensitive to chemical, physical or biological agents that make them develop a potentially harmful allergic response when they are subsequently exposed to the sensitising material.

State-of-the-art survey: A survey that ensures that the control strategy is based on the results of the risk assessment taking into account a) the evaluation of the hazard characterisation using the most up-to-date information available and b) the exposure using the best currently available techniques.

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BACKGROUND, PURPOSE AND METHODS USED FOR DEALING WITH THE REQUEST

1. Background

The properties of manufactured nanomaterials, i.e. those produced intentionally, are paving the way for a wide variety of promising technological developments.

There are many uncertainties associated with the quantitative assessment of hazards and exposure to nanomaterials, which will only be resolved through advances in scientific understanding of their properties. Indeed, their toxicity may turn out to be different to that currently known for the same materials on a larger metric scale, or it may even be entirely new in the case of materials with no equivalent at a larger scale. Similarly, the current occupational exposure limits[1] defined for dust are not necessarily appropriate when applied to ultra-fine dust[2] which, by definition, includes nanomaterials.

As part of the international standardisation work of the ISO Technical Committee (TC) 229 for Nanotechnologies, which began in 2005, a French standardisation committee on “Nanotechnologies” (AFNOR X457) was established, which led to the creation of a Working Group on “health, safety and environment” (HSE) standards. During its deliberations, the AFNOR standardisation committee expressed a wish to set up a project on the development of control bands based on the specific physico-chemical and toxicological properties of nanomaterials. Classifying nanomaterials in these hazard bands would ultimately provide producers and users of these substances with input data for risk management according to control levels, or “Control Banding”. At the ISO TC 229 (Nanotechnologies Technical Committee) plenary meeting in November 2008 in Shanghai, the French delegation requested that this project be included in the programme for standardisation work relating to the safety of nanomaterials. The Project Group 8 of the Working Group 3 (PG8/WG3) was officially approved by vote at the ISO on 3 March 2009. France has now been given three years to complete this pre-normative project.

In the current context characterised by a high level of uncertainty about the health risks associated with manufactured nanomaterials, the "Control Banding" method is presented as an alternative solution. It forms part of a comprehensive occupational risk assessment approach. It is intended to allow an appropriate level of risk control to be established, which can be reassessed according to developing scientific and technical knowledge of the products and processes involved. The methods of protection used for chemicals include some that are suitable for the handling of nanomaterials. For this reason, the Control Banding method can be applied to manufactured nanomaterials.

[1] Occupational exposure limits for chemicals in France (INRS, ED 984)

[2] Dust fractions for which the aerodynamic diameter of the particles does not exceed 100 nm

2. Purpose of the request

In a letter dated 7 August 2008, the Ministry of Health, in agreement with the Ministries for the Environment and Labour, requested that ANSES[3] conduct a collective expert appraisal specifically on Control Banding applied to manufactured nanomaterials. ANSES was asked to write a background document to which the HSE Working Group of the AFNOR Nanotechnologies Committee could refer in order to formalise a draft standard for submission to the ISO.

3. Working methods: resources used and organisation

ANSES decided to investigate this request with the help of an Expert Rapporteur Group (GER). This group informed the Expert Committee (CES) on "Assessment of risks related to physical agents, new technologies and major developments" of the status of the solicited request. Following the presentation of the solicited request at the CES meeting on 23 September 2008, a call for experts was launched on the ANSES website between 25 May 2009 and 1 September 2009.

ANSES's methodology will be adopted by AFNOR's HSE Working Group in October 2010, which will use it to present its Control Banding project for validation at the AFNOR Standardisation Committee meeting. After approval by this committee, AFNOR will present the project to experts from the other ISO delegations, who will approve, modify or reject the work proposed.

[3] Since 1 July 2010, ANSES has been incorporated in ANSES, following its merger with AFSSA. Consequently, certain methods of dealing with solicited requests have been modified, and the term 'Scientific and Technical Support' (AST) is no longer used.

CONTROL BANDING

1. Introduction to the Control Banding method

Like any tool, the method known as control banding and described in this report is applied within a specific field defined by its creators. The conditions of application must be complied with to ensure relevant results. The output data from such a tool should only be used for risk management if the regulatory environment in force in the country considered has been taken into account.

In light of these considerations, the regulatory framework governing occupational risk management in France is reiterated briefly, by way of example, in this introductory section. It thus highlights the technical challenges specific to the case of nanomaterials.

1.1. Nanomaterials and occupational risk assessment

1.1.1. General obligation for occupational risk assessment

Occupational risks expose employees to the threat of impaired health, either through illness or accident. The employer is responsible for establishing the appropriate means and techniques to ensure the safety of employees and protect their physical and mental health. This corresponds to the obligation to achieve a particular result.

Protection of employees is based primarily on the assessment of occupational risks and the implementation of adapted prevention policies, based on organisational and technical measures. Risk assessment, before the occurrence of malfunctions, accidents or occupational diseases, is the initial step of any prevention policy. It is based on a structured methodology for identifying hazards and conditions of use or exposure likely to generate a risk. French regulations stipulate that the results of this risk assessment must be recorded in a "single document" (Decree 2001-1016 of 5 November 2001).

1.1.2. Assessment of chemical risks

With chemical risks, the combination of exposure and hazard factors relating to the chemical enable a quantitative assessment of the risks to employee health and safety to be conducted, for each operation.

Identifying hazards involves an exhaustive inventory of all chemicals found in the establishment, followed by the compilation of accurate, detailed information on their potential hazards, mainly from labels and safety data sheets. Estimating exposure requires a study of the processes and procedures implemented, the quantities handled, the duration and frequency of operations, the properties of the chemical, etc. (24). Quantifying exposure levels requires either obtaining baseline data directly extrapolated to the case considered, or conducting atmospheric, biological or surface measurements.

Notwithstanding the obvious support they can provide to the prevention specialist, a recent study comparing the chemical risk assessment methods available on the French market highlighted the following points (25):

- limitations related to certain labelling deficiencies (with hazards therefore being inadequately taken into consideration);
- the need for the evaluator to possess a minimum level of expertise (the available software can only help the evaluator take into account actual work, field observations and a critical analysis of the results produced).

1.1.3. Assessment of chemical risks in the particular case of nanomaterials

In the particular case of manufactured nanomaterials, risk assessment is even more difficult due to the many uncertainties related to both the identification of potential hazards and the characterisation of exposure.

Regarding the hazards, toxicological data on nanomaterials are still largely incomplete. First, it appears to be impossible to perform tests on a case-by-case basis within a reasonable timeframe in view of the wide variety of nanomaterials. Second, existing toxicology results mainly come from studies with a limited scope, and their physico-chemical characterisation is often insufficient to distinguish one nanomaterial from another of the same type. Moreover, it is difficult to extrapolate the results obtained on cells or animals to humans. In short there are still fundamental and irreductible uncertainties in the current state of scientific knowledge.

Air measurements are sometimes taken in the vicinity of processes or operations using nanomaterials, either in companies or research laboratories, but to date, very little data have been published. In addition, no international consensus has been reached on any single measurement method for characterising occupational exposure.

Furthermore, given the current state of knowledge on manufactured nanomaterials, it is highly likely that many years will be needed before we know precisely which types of nanomaterials and associated doses represent a real danger to humans and their environment. Indeed, the assessment of potential health effects following exposure to a chemical must take into account the extent and duration of exposure, the biopersistence, and inter-individual variability, all subjects on which we have practically no knowledge for the field of nanomaterials.

It is therefore extremely difficult to conduct a quantitative risk assessment in most work situations involving nanomaterials with the currently available methods and techniques.

1.2. Alternative method known as Control Banding

The control banding method presented below is an alternative method to conduct a qualitative risk assessment and taking measures to protect workers exposed to manufactured nanomaterials.

1.2.1. Background

Control banding was developed in the pharmaceutical industry to ensure the safety of workers applying processes using products for which little information was available. These new products were allocated to "bands", mainly defined according to the hazard level of known products similar to those used, taking into account the assessment of exposure at the work station. Each band corresponded to a risk control strategy (10, 11). Shortly after, the UK Health and Safety Executive developed a banding method called COSHH Essentials (Brooke 1998; HSE 1999), that was easier to use and more accessible for small professional organisations that could not afford the expertise of a full-time occupational hygienist. A similar scheme to COSHH Essentials was described in a practical guide published by the "German Federal Institute for Occupational Safety and Health (34). The Stoffenmanager tool (8) proposes a further development by combining a hazard allocation scheme similar to COSHH Essentials and an exposure band allocation method based on a simplified exposure model that is easy for non-experts to understand and use.

Although control banding is a potential solution, there are few useable models adapted for use in activities related to the research, production or processing of these manufactured nanomaterials. A conceptual approach was presented by A. Maynard, which incorporated the same control schemes as the British HSE tool. More recently, Paik *et al.* presented a tool for management by control banding, which attempted to take account of current knowledge on the toxicology of nanomaterials and to use the control banding structure described in recent publications. On the whole these publications remain theoretical and the approaches are not really operational.

1.2.2. Presentation of the tool

Control Banding is an instrument that combines risk assessment and management. It is specifically proposed for conducting a risk assessment when input data are lacking. It takes into account existing information and the available technical and scientific data, and relies on a number of assumptions.

In this process, a risk assessment is associated with a risk control band proposing the minimum prevention methods to be implemented that are consistent with the estimated level of risk. Given the uncertainties regarding the toxicity of manufactured nanomaterials and the levels of exposure of employees handling them, the assumptions may relate either to hazards or exposure. Thus, the associated risk control band, and therefore the means of prevention to be implemented, will be based on ‘superimposed’ assumptions. These will be drawn from both the process’s input data and the prevention choices made by both the creators of the control banding approach used and its user, as was highlighted in the abovementioned study (25).

In the context of manufactured nanomaterials, control banding tends to overcome shortcomings in specific toxicological knowledge by taking into account the most easily accessible parameters,

such as the physico-chemical properties of the nanomaterials concerned and available data on the toxicity of materials of similar nature and physico-chemical form (parent material or analogous chemicals). Nevertheless, given the combined significance of all the uncertainties, it is not possible at the current time to guarantee predictions of the toxicity of nanomaterials on the basis of these different factors. Indeed, there is as yet no theoretical or empirical tool for estimating scientifically the toxicity of a type of nanomaterial based solely on the physico-chemical data and toxicological properties of the bulk material. The control banding approach is thus likely to be confronted by such irreducible unknowns as the intrinsic toxicity of a given type of nanomaterial (new health effects, new diseases, etc.). The example of carbon nanotubes (CNTs) is particularly telling in this respect: given the first scientific publications on CNTs (characterisation, toxicology, etc.) it does not seem to be reasonable for scientists to extrapolate the known properties for the closest non-nanometric carbon forms (graphite, diamond) to CNTs.

Concerning the characterisation of worker exposure, control banding can take into account the procedures implemented, the quantities handled, the duration and frequency of operations performed, and the intrinsic properties of the materials involved, particularly their physical form, etc.

Furthermore, vigilance is needed when taking into account these intrinsic parameters in order to avoid reducing the actual exposure of employees to the only emission potential of a single task or process.

It also seems important not to limit the prevention of occupational risks solely to the control banding approach. In other words, the proposed tool should not allow the employer to dispense with the necessary step of risk assessment and recommendation of preventive measures, and thus, the regulatory requirement to write the single document.

Knowledge of the risks associated with nanomaterials is constantly changing. It is therefore vital to update information regularly and continually improve the preventive approach on this basis. Thus, as new information becomes available, a new assessment must be conducted by integrating these new data into the control banding method used. Ultimately, the level of uncertainty should fall and the approach should move towards a more quantitative risk assessment. This is an iterative process aiming to refine risk assessment and the identification of necessary preventive measures as knowledge evolves. When all the required data become available, the control banding approach can be replaced by a quantitative risk assessment. A legitimate question remains however about the relevance of the results produced by a control banding method when the input data are too limited.

1.3. Scope and limits of Control Banding

The control banding method applied to manufactured nanomaterials requires assumptions to be formulated on information that is desirable but unavailable. To do this, the user should be proficient enough in chemical risk prevention (chemistry, toxicology, etc.), nanoscience and nanotechnology.

If control banding is implemented by companies without the necessary expertise, this could lead to incomplete results that will not meet the requirements for occupational risk prevention. Using this method without expertise, critical outlook or support may lead to false assumptions and therefore to unsuitable choices concerning preventive measures, which could put exposed people at risk.

Control banding can potentially be used in any work environment in which nanomaterials are manufactured or used (industrial workshops, research laboratories, pilot plants, etc.*).* It is intended to be applied only to regular handling and use at the work station, as part of the company's normal operations. Incidents involving accidental or degraded modes, failures, or risks of explosion and fire are all covered by other specific processes in the overall system of safety management at work.

Control banding can only be used to determine the risks to health. The approach does not address safety risks (fire-explosion risk) or risks to the environment. Nevertheless, just as with conventional dust clouds, it is reasonable to assume that clouds of nanomaterials may be explosive if their particles are capable of burning in air (aluminium, magnesium, lithium, etc.*).* The control banding approach should therefore be integrated into a wider process of chemical risk assessment, mainly to avoid disregarding fire-explosion risks and risks to the environment, or it should evolve to also include the determination of these risks, whose consequences may be severe for employees, the environment and the general population.

The control banding tool is required to be reasonable or even conservative. This is because while it is intended to manage an element of uncertainty, its use is currently restricted by two major limitations: the lack of toxicological data and the metrological limits for measuring exposure.

In addition, the user should always be able to assess the limitations of the method, which was developed for use in a laboratory or industrial production environment, and may be poorly suited to certain applications.

Thus, the method is not adapted to extreme situations, for example:

- if the nanomaterials are an extremely diluted component of the product used,
- or when handling large volumes, which requires special expertise.

Similarly, the method does not dispense the user from the usual/common sense individual protective measures. For example, applying the method to a nanomaterial that is toxic/hazardous but confined in a highly stable solid matrix (solid or viscous liquid, low volatility) will result in a recommendation for general or local ventilation, which should not prevent common sense measures being taken such as the wearing of personal protective equipment (goggles, gloves, protective clothing).

2. Control Banding process applied to manufactured nanomaterials

2.1. General points

The control banding tool described in this report should be an integral part of the overall system of health and safety management at work established by the employer. It requires input data, irrespective of the phase of the nanomaterial's life cycle, such as information collected at the work station through observation of actual work, toxicology data, etc. The output data generated by the control banding process will have an impact on other processes of the overall management system defined by the employer.

2.2. Operating principle

Figure 1 below shows how the control banding process is integrated in the overall risk management method, based on the PDCA (Plan, Do, Check, Act) model[4]. This section only covers the points specific to control banding of nanomaterials.

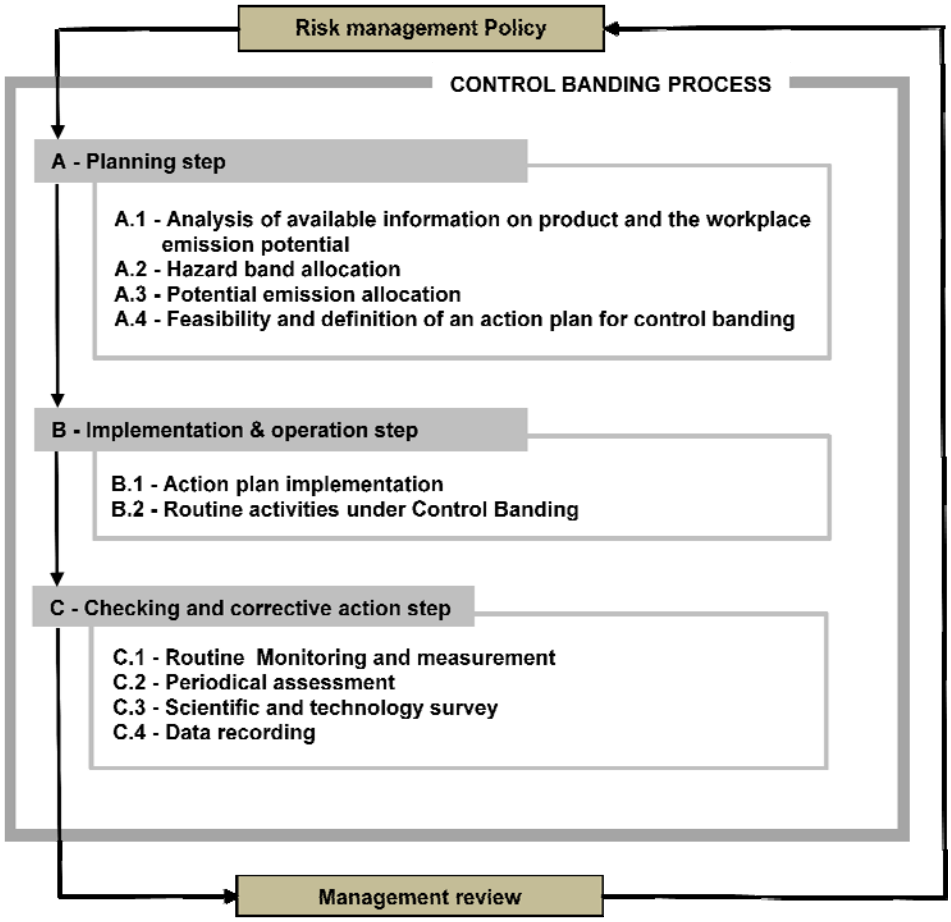

Figure 1: The control banding tool applied to nanomaterials, integrated in the safety management system

[4] OHSAS 18001 v2007

As shown in Figure 1, the general principle of the control banding method is an iterative process divided into several steps whose objectives are described below in order of operation.

2.2.1. Planning step

This planning step enables a nanomaterial or a product containing a nanomaterial to be allocated to hazard and exposure bands based on information gathered by the user. It also defines the feasibility and programme of the action plan for the control banding process for a given period.

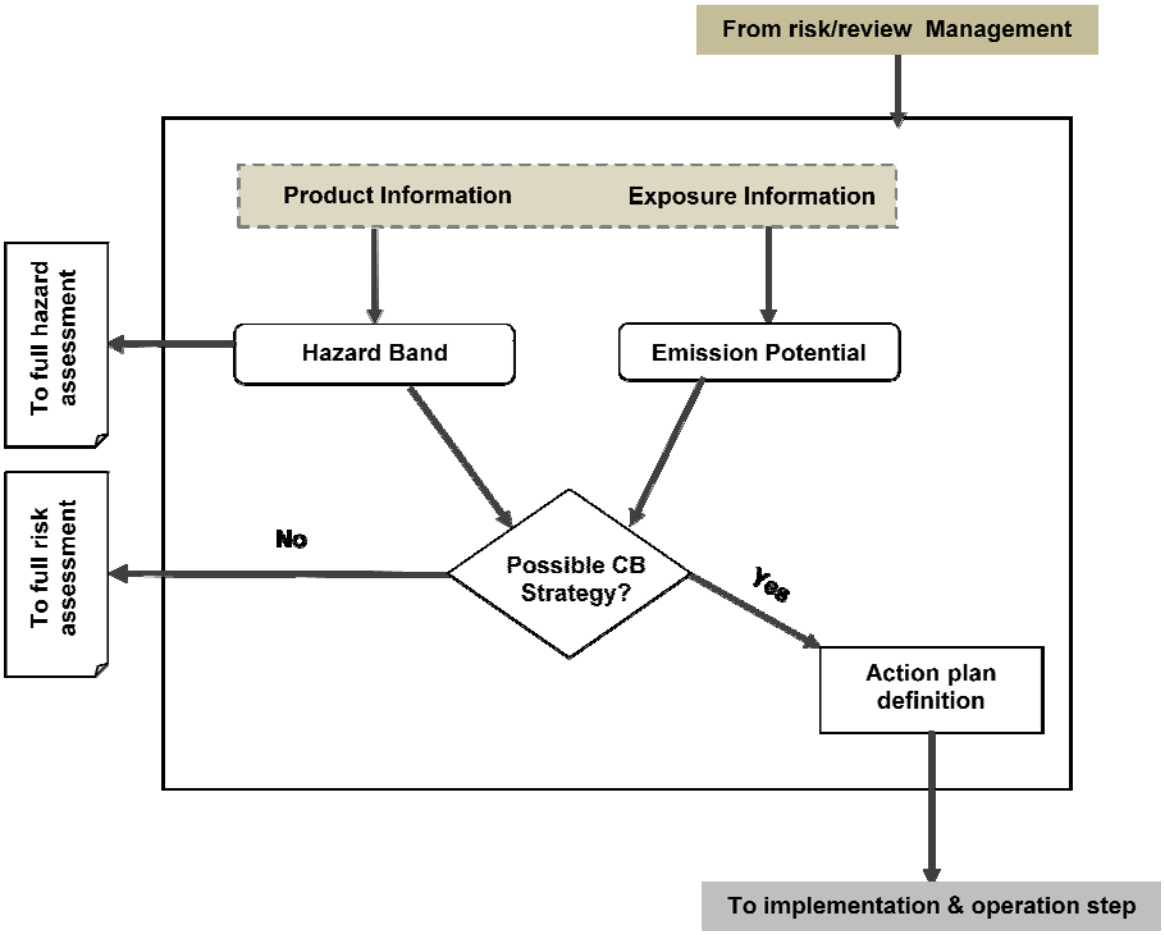

Figure 2: Control banding planning step

A.1 Information gathering

This consists in collecting and compiling the available information on the hazards of the manufactured nanomaterial being considered, as well as on the potential exposure of people at their work stations (field observations, measurements, etc.).

A.2 Hazard band allocation

The toxicological information collected on the nanomaterial considered or the product containing it enables it to be allocated to a hazard band. A specific hazard assessment must be conducted by an expert in the following cases:

- The user of the method considers that it has allocated a band that is too high for the known information;
- there are too many unknown factors, particularly concerning the toxicology of the nanomaterial or product.

A.3 Exposure band allocation

With regard to manufactured nanomaterials, the method of allocating an exposure band described in this document does not incorporate any quantitative variables (due to measurement difficulties). Exposure will be quantified after resolution of the current technical problems, as part of the process of continuous improvement.

The exposure band for the nanomaterial being considered or the product containing it is defined by the product's level of emission potential, taking into account its initial state, its natural tendency to evolve and the type of process used.

Notes: The allocation of bands will be systematically revised if new data appear on the product's toxicity, physico-chemical criteria or emission potential, or in the event of the use of a new product or any change to the work station.

A.4 Feasibility and definition of an action plan for risk control

Overlapping the previously-allocated hazard and exposure bands allows the level of risk control to be defined. It ensures that the most appropriate technical and organisational resources are implemented in order to maintain the risk at the lowest possible level.

An action plan is then defined to guarantee the efficacy of the preventive measure recommended by the control level selected. It takes account of existing preventive measures and reinforces them if necessary.

If the measures indicated by the level of risk control are not achievable, for example, for technical or financial reasons, a detailed risk assessment must be conducted by an expert.

2.2.2. Implementation and operation step

This step is intended to establish and ensure the effective implementation of the action plan outlined in the previous step.

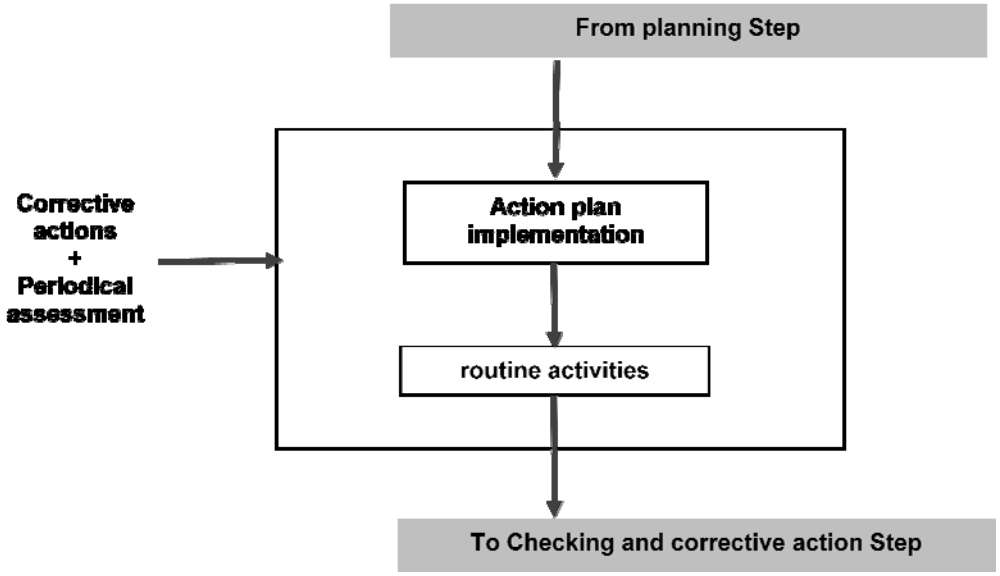

Figure 3: Control banding implementation and operation step

B .1 Action plan implementation

The implementation of the previously-defined action plan enables the level of protection recommended by the risk control strategy to be achieved. Once the technical, organisational and human means of prevention have been selected, the work stations concerned may be modified accordingly.

B.2 Routine activities under control banding

Verifying the performance of the resources applied compared to the predefined specifications in the action plan, and the correct operation of the security equipment helps ensures the efficacy of the control banding method.

2.2.3. Checking and corrective action step

The aim of this step is to monitor and update the control banding process according to the figure below. These two activities ensure that the means of prevention recommended by the control banding optimise its efficiency.

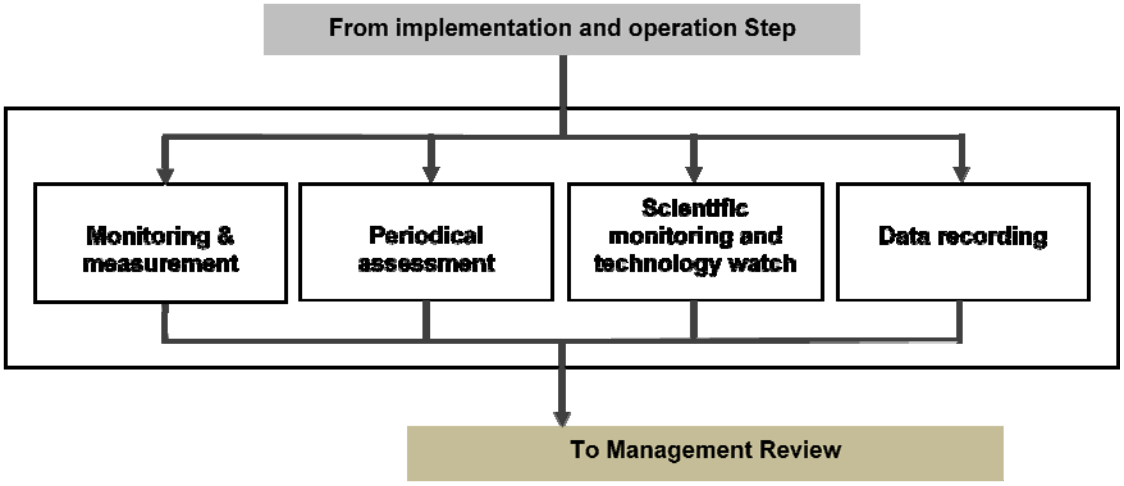

Figure 4: Control banding checking and corrective action step

This monitoring will be conducted:

- continuously by using performance indicators,
- periodically by organising an audit of the work stations within the scope of the control banding.

The process will be updated with the help of scientific monitoring and a technology watch, which will report any new knowledge on the hazards of the nanomaterials used and the technical means for characterising and controlling exposure (metrology, new equipment, new production processes, level of exposure measured, change in working method, etc.).

C.1 Routine monitoring and measurement

The objective is to continuously monitor the efficacy of the preventive measures implemented.

The user must define specific indicators and associated monitoring procedures to ensure the proper operation of the means of protection.

Ideally these indicators should refer to values obtained by measurement methods that characterise the actual level of exposure to manufactured nanomaterials at the work station. In the absence of a validated method, which is currently most often the case for nanomaterials, the indicators chosen will relate to the proper operation of the means of protection used (e.g. pressure level in a glove box, frequency of filter replacement, etc.).

Moreover, as technical advances and developments in knowledge occur, the indicators will be updated and applied to the monitoring of work stations, in order to move towards the quantitative assessment of exposure to nanomaterials.

C.2 Periodical assessment

The intervention of an industrial hygiene specialist is regularly scheduled to conduct detailed risk assessments on a sample of work stations. These are intended to verify the correspondence between the objectives set for occupational risk prevention and the means deployed, as well as the procedures implemented. Based on the results, these assessments should lead to measures being proposed to reduce any discrepancies identified.

C.3 Scientific monitoring and technology watch

The control banding method requires regular updating of scientific and technical knowledge in order to better adapt the means of prevention implemented.

Firstly, advances in scientific knowledge are likely to change the levels of the hazard and/or exposure bands initially allocated. Ultimately, the reduction of uncertainties regarding the toxicology of nanomaterials should lead to this method being abandoned: control banding is useful precisely because it assists the occupational risk prevention specialist in a context of high uncertainty associated with nanomaterials.

Secondly, monitoring the state of the art and best practices should allow more effective prevention devices to be established (new less emissive production processes, emergence of new techniques or more effective prevention equipment, etc.).

C.4 Data recording

The data used for conducting assessments and the conclusions of these studies must be recorded in a file for a certain period, which needs to be defined in compliance with national regulations. The results of all studies, regardless of their conclusions, should be included in the report. Additionally, all assumptions should be clearly articulated. The advantages and limitations of each test, measurement, model, or estimate employed should be identified and residual uncertainty due to the nature or source of the data — as well as data gaps and potential biases — should be noted.

The exact method used for archiving these documents needs to be specified clearly. It must be possible to retrieve key data relating to the assessment, such as:

- Type of activities
- Substances used
- Relevant data related to risk assessment
- Conclusions
- Actions to be put in place and follow-up

Data storage must be clear and easily accessible and must be understandable to anyone who needs to access the data.

2.2.4. Management review

The management review allows the system to be improved by developing new action programmes and undertaking corrective actions in response to potential malfunctions in the risk control system. This periodic assessment is also essential to identify and respond to any difficulties in the organisation's general activity which could hinder the efficiency of the control banding process, or to consider the evolution of scientific knowledge and risk control technology in the field of nanoscale materials.

The management review is not directly part of the control banding process. It is a part of the organisation's global risk management system which comprises many processes, including control banding.

3. Implementation of Control Banding

3.1. Gathering of information

This is an important step that allows the user to collect all the necessary elements to define the hazard level associated with the nanomaterials or products containing them, and to describe each of the work stations that fall within the scope of control banding.

Concerning the hazard assessment, other entry points should be added for a scientific watch on the nanomaterials used or related products, such as the analysis of safety data sheets, the contact with suppliers, the search for analogous substances, where relevant. The objective is to minimise the uncertainties surrounding the toxicity of the nanomaterial.

Concerning the exposure assessment, the user must obtain a clear description of the operations and processes taking place at the work station, or even better, must conduct field observations. He can begin by identifying the type of product used, then collecting information on how the product is processed (quantity of products used, duration and frequency of exposure, etc.).

All these parameters and information will influence decision making and the risk control strategy to be applied.

3.2. Hazard bands

3.2.1. Definition

These bands are defined according to the severity level of the hazard from a chemical resulting from the analysis of the available information, evaluated by competent persons[5]. This information may relate to various criteria for toxicity, described or suspected, in the literature or technical documentation (labelling, product classification).

In the specific case of manufactured nanomaterials, criteria such as the ability to cross biological barriers, the fibrous nature, or, more difficult to define, the concept of biopersistence, have been taken into account. These factors may also be linked to the material's physical and chemical properties, such as surface chemistry, crystalline form, particle morphology and size, etc.

3.2.2. Method of allocation to a hazard band (Fig. 2)

For the allocation of a hazard band we shall only consider for the moment the potential hazard of the present manufactured nanomaterial, whether raw or incorporated in a matrix (liquid or solid). In the case of nanoproducts, this choice is based on the fact that to date very few studies are available on the characterisation of nanomaterial emissions from a product containing them (e.g. nanosilica incorporated in tyres).

[5] A competent person is an individual who will properly perform a specific job. This person utilizes a combination of knowledge, skills and behaviour to improve performance. More generally, competence is the state or quality of being adequately or well qualified, having the ability to perform a specific role. (Wikipedia)

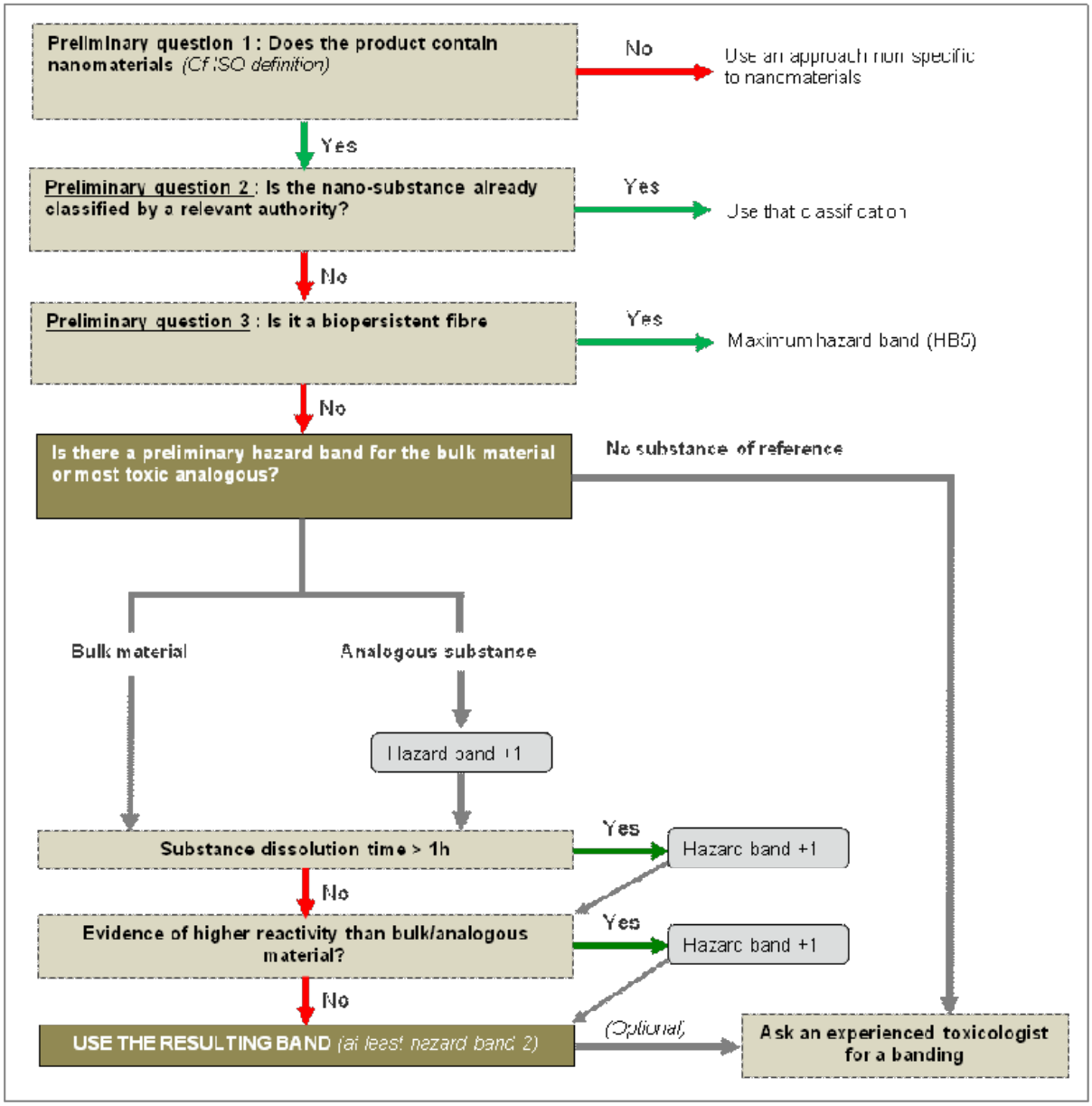

Figure 5: Diagram showing how a nanomaterial is allocated to a hazard band according to the level of knowledge of the nanomaterial

3.2.2.1 Preliminary questions

Before beginning the control banding process it is necessary to answer some preliminary questions:

- **Does the product contain nanomaterials[6]?** If not, the organisation will have the option of using either one of the control banding methods currently applied in some industries in the

[6] Definitions according to the ISO standards ISO/TS 27687 and ISO CD TS 80004-1 (26 and 27)

chemical or pharmaceutical sector, or any other risk assessment and control tool. If it does, the question below must be examined.

- **Has the nanoproduct already been studied with regard to regulations on classification and labelling?** If "yes" then the hazards of the material to human health will be clearly identified. A "no" then leads to the question below.

- **Is it a biopersistent fibre[7]?** If "yes" then the band is that of the maximum hazard, which requires a full risk assessment. If "no" then the control banding process can be applied to this nanoproduct in order to allocate it to a hazard band based on the assessment of its toxicity.

3.2.2.2 Toxicological parameters and hazard bands

Depending on the answers to the preliminary questions, the knowledge of the toxicology of the nanomaterial or product containing it will then be studied to enable its allocation to a hazard band. If this information is incomplete or nonexistent, the substance that is chemically closest to the nanomaterial should be considered: bulk material, analogous material. When the bulk material exists, it takes precedence over the analogous material. Finally, if there are several choices for the same bulk (analogous) material[8], the most toxic one shall be taken into account.

When there is a bulk material, the allocation of the nanomaterial to one of the five hazard bands (HB1-5) relates to the classification of the bulk material according to the CLP Regulation (see Table 1)[9].

In the case where there is no bulk material but there is an analogous material, the process is the same, the allocation of the nanomaterial to one of the five hazard bands (HB1-5) relates to the classification of the analogous material according to the CLP Regulation (see Table 1). To reflect the uncertainty added by the choice of an analogous material, the result obtained in Table 1 is incremented by one band.

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[7] Biopersistence is defined as the ability of a fibre to remain in the lung in spite of the lung's physiological clearance mechanisms. These defence mechanisms are:

a) transportation of entire particles by the mucociliary escalator and by alveolar macrophages,

b) dissolution of fibres, and

c) disintegration, where the fibre breaks into smaller particles that can be cleared.

Although the definition is qualitative, it is very important as the occupational health literature seems to suggest that all respirable and biopersistent fibres should be treated as asbestos unless evidence to the contrary is obtained. Hence the full hazard assessment required.

[8] For example, carbon = graphite or diamond, titanium dioxide = rutile or anatase, etc.

[9] Note: If the hazard from the bulk material or analogous material is recognised by the regulations on classification and labelling (CLP), the toxicity level then relates to the GHS classifications. As this document was originally produced in French, the experts decided to use only the GHS classifications as adopted by the European Union under the CLP Regulation.

If the toxicity of the nanomaterial is unknown, or it cannot be associated with any bulk or analogous material, then the control banding approach cannot be applied. A comprehensive risk assessment is then needed.

Finally, to account for deficiencies in terms of information on the nanomaterial's toxicity, increment factors are assigned based on certain characteristics specific to the nanomaterial and not those of the bulk or analogue material used to allocate the original band (see next section).

Thus, after analysing the product's toxicity criteria and referring to the hazard group allocation of the e-COSSH Essentials tool, the hazard levels adopted by the experts who participated in the method's development are presented as follows:

- HB1: Very low: No significant risk to health;
- HB2: Low: slight hazard – slightly toxic effects rarely requiring medical follow-up;
- HB3: Moderate: Moderate to significant health effects requiring specific medical follow-up;
- HB4: High: Unknown health effects or serious hazard: material highly toxic, sensitising, or with unknown effects on health or the environment. Emission or exposure in the environment requires a specific survey;
- HB5: Very high: Severe hazard requiring a full hazard assessment by an expert.

Note that the genotoxic nature is taken into account when classifying carcinogenic/mutagenic/reprotoxic substances. Particular attention is paid to sensitising substances, and to irritants/corrosives.

	Toxicity level labelling				
	HB1	**HB2**	**HB3**	**HB4**	**HB5**
Classification and labelling	 **Warning** Eye irrit. 2 Skin irrit. 2 And all H-phrases not otherwise listed	 **Warning** Acute tox. 4  **Warning** STOT-SE 2	 **Warning** Acute tox. 3  **Warning** STOT-RE 2  **Danger** Skin Corr. 1 Eye Dam. 1  **Warning** Skin sens. 1 STOT-SE 3 (resp. irritant)	 **Danger** Acute tox. 1-2  **Danger** STOT-SE 1 STOT-RE 1 Repro. Tox 1A - 1B  **Warning** Carc. 2 Repro. 2	 **Danger** Resp. sens. 1 Carc. 1A - 1B Muta. 1A - 1B  **Warning** Muta. 2

Table 1: Hazard band table based on the hazard group allocation of the e-COSSH Essentials tool

3.2.2.3 Increment factors

The control banding method developed then offers increment factors which aim to mitigate current uncertainties regarding the assumed toxicity of the nanomaterials. Particular attention is also paid to the criteria of solubility and reactivity. Thus, the uncertainty, the solubility and the reactivity of the material under consideration determine the allocation to a hazard band, as shown in Figure 6.

The hazard band can only be changed if new scientific evidence is produced or following the intervention of a toxicology specialist. This change will then be duly justified in a report.

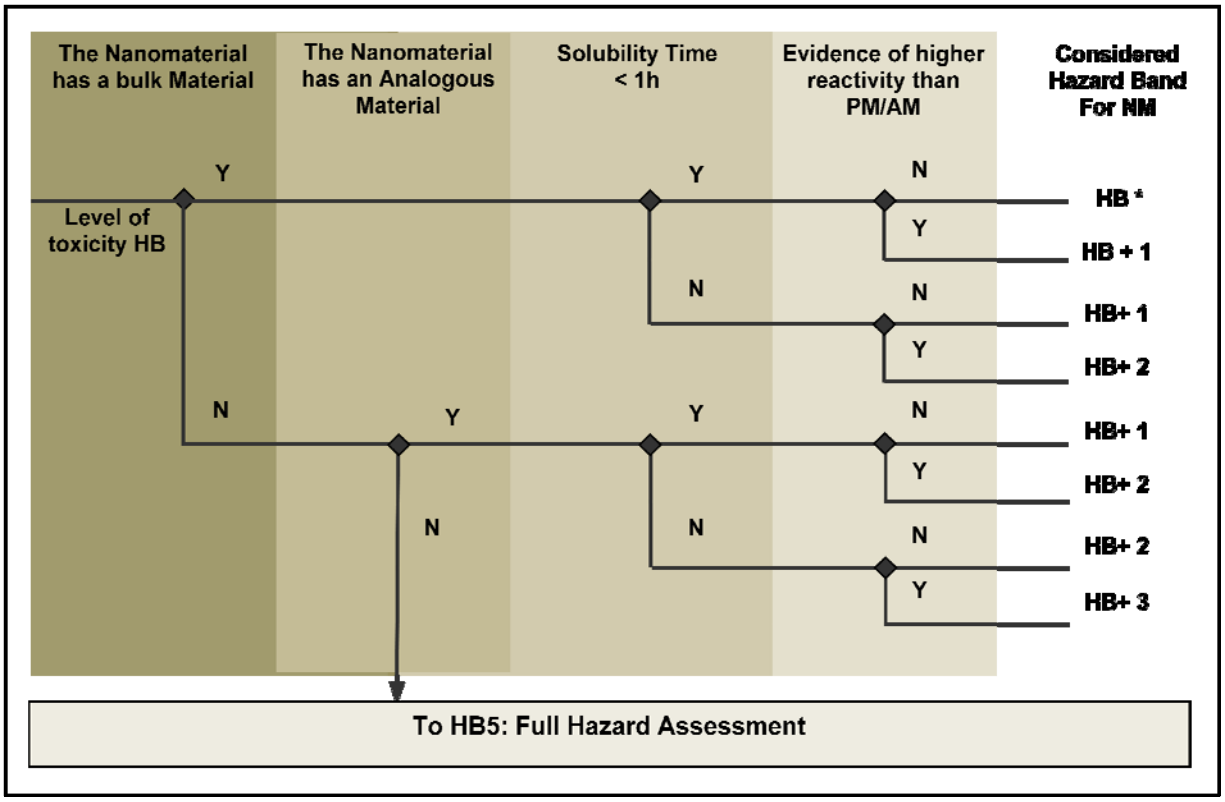

Figure 6: Increment in the toxicity level of a nanomaterial according to its reference material, its solubility or its reactivity — HB*: minimum level of 2 unless confirmed evidence of harmlessness (PM: parent material, AM: analogous material)

Solubility refers to the degree to which a material can be dissolved in another material so that a single, homogenous, temporally stable phase results. Solubility occurs when the material is surrounded by solvent at the molecular level.

It is important not to confuse solubility and dispersibility, as we are interested in the potential of a material to lose its particulate character and to change its form to a molecular or ionic form. This should be stressed, as this distinction may be difficult with colloidal suspensions of nanomaterials.

The measurand for solubility is the maximum mass or concentration of the solute that can be dissolved in a unit mass or volume of the solvent at a specified (or standard) temperature and pressure; unit: [kilogram/kilogram] or [kilogram/(meter)^3] or [mole/mole]). A possible method to assess the solubility of a nanomaterial can be derived from the OECD test guidelines TG105.

In the context of this document, the solubility of a nanomaterial is taken into consideration to assess its potential hazard. The rationale for choosing solubility as one of the main factors to allocate potential hazard levels to a material is related to the importance of the solubility of a material in evaluating its biopersistence or its biokinetics. An insoluble or poorly soluble nanomaterial will have the opportunity to be transported in the body from the entry compartment (lungs, gastrointestinal tract, skin, nose) to another (translocation) and be distributed in the body towards secondary target organs or tissues (accumulation) (12,15). If other factors hamper the transport of an insoluble or poorly soluble material, accumulation may occur at the site of entry (2). In both situations, there is accumulation in one site which enhances the risk of chronic hazardous effects (2,13). On the other hand, the potential hazard of a soluble material will be treated as an

ordinary toxicology problem of its solutes with no need to consider the peculiarities of the toxicology of particulate matter.

While it is commonly agreed that the solubility of a nanomaterial is important to assess its hazard level, there is almost no information on the solubility threshold that would be considered to describe a material as highly, moderately or not at all hazardous. We decided to increment the material by one hazard band if it does not completely dissolve in one hour, in water [OECD TG105, 14,22] or in a simulated lung lining fluid [e.g. in a natural porcine surfactant preparation (17;18)]. The limit of one hour is based on evidence that some insoluble nanoparticles may penetrate in the epithelial cells and deeper in lung tissues within one hour of exposure (3,4,20,21) and we focused on a model based on the airways because this is the major route for unwanted exposure.

Higher Reactivity: Higher reactivity with regard to the bulk material or analogous material. This idea covers different paradigms of the nanomaterials' chemical properties that are relevant for their potential impact on health. The basic definition of "reactivity" refers to the rate at which a substance tends to undergo a chemical reaction in time. Here we are mostly interested in the surface chemistry and the ability of the material to generate, directly or indirectly, reactive oxygen or nitrogen species. It is important in our context because for instance, a material with a higher specific surface area is expected to have a higher reactivity than a material of the same chemical composition but with a lower specific surface area. The reactivity can also be modified by the inclusion of contaminants that originate from the nanomaterial production processes, which differ from the bulk material.

3.3. Exposure bands

3.3.1. Definition

The exposure bands are defined according to the emission potential of the nanomaterial, whether raw or included in a matrix. They take into account the physical form in which it is used and, where applicable, the state of the matrix incorporating the nanomaterial. The physical form is a key parameter to consider, in order to assess the nanomaterial's emissivity from the product and hence the potential operator exposure level considered when it is handled. The number of workers, the frequency and duration of exposure, and the quantity used are not taken into account, unlike in a conventional chemical risk assessment.

3.3.2. Method of allocation to an exposure band

Before any allocation to a exposure band, each work station is identified in connection with its user.

The physical form to be considered is that of the material at the beginning of the process at the work station evaluated. Four categories of physical forms have been identified and are listed below in order of increasing emission potential:

- Solid: solid materials containing nanomaterials or having a surface that is nanostructured or covered with nanoparticles;
- Liquid: Suspension of free nano-objects and/or aggregates/agglomerates of nano-objects smaller than 100 nm in a liquid medium, regardless of its viscosity;

- Powder: mass of nanomaterials (free nano-objects and/or aggregates/agglomerates of nano-objects smaller than 100 nm);
- Aerosol: suspension of nanomaterials (free nano-objects and/or aggregates/agglomerates of nano-objects smaller than 100 nm) in a gas (including air).

To account for the tendency of certain materials to change from one physical form to another (friable solid yielding a powder, for example), exposure bands are increased by one or more emission levels according to the table below.

Finally, if the physical nature of the material changes as a result of the process used, then an increment in the exposure band is provided for by the following table.

Physical form	**Solid**	**Liquid**	**Powder**	**Aerosol**
Emission Potential	**EP1**	**EP2**	**EP3**	**EP4**
	Specific cases of band modification due to the natural tendency of the material			
	Friable solid[10] (+2 bands)	Highly volatile liquid[11] (+1 band)	High or moderate dustiness powder[12] (+1 band)	-
	Specific cases of band modification due to process operation			
	Dust generated by external forces[13] (+3 bands) Melting (+1 band) Dispersion in liquid (+1 band)	Powder generated by evaporation (+1/+2 band according to dustiness of the powder) Spraying (+2 bands) No generation of aerosol during process: (-1 band)	Spraying (+1 band)	-

Table 2: Emission potential depending on the physical form of the nanomaterial matrix and specific material transformations

Thus the physical form of the entry product and the transformation it undergoes with the process used at the workstation lead to the initial EP1 band being implemented.

[10] Material whose matrix is likely to release particles under low stress (Hansen et al., 2007)

[11] INRS ND 2233

[12] Respirable fraction according to EN 15051

[13] External forces such as for instance, mechanical forces, electrical forces, lasers, etc.

3.4. Allocation of risk control bands

Risk control bands are obtained by overlapping the hazard bands and emission potential bands previously defined by the expert authors of this work.

		Emission potential bands			
		EP1	EP2	EP3	EP4
Hazard bands	HB1	CL1	CL 1	CL 2	CL 3
	HB2	CL1	CL 1	CL 2	CL 3
	HB3	CL1	CL 1	CL 3	CL 4
	HB4	CL 2	CL 2	CL 4	CL 5
	HB5	CL 5	CL 5	CL 5	CL 5

Table 3: Matrix of control classes to be implemented with regard to the combination of the hazard level and the emission potential

Each control level corresponds to technical solutions for collective prevention to be implemented at the work station. They can be distinguished by the level of containment they offer to the user.

- **CL 1: Natural or mechanical general ventilation**
- **CL 2: Local ventilation:** extractor hood, slot hood, arm hood, table hood, etc.
- **CL 3: Enclosed ventilation:** ventilated booth, fume hood, closed reactor with regular opening.
- **CL 4: Full containment:** continuously closed systems.
- **CL 5: Full containment and review by a specialist required:** seek expert advice.

It should be noted that the wearing of personal protective equipment has deliberately not been taken into account. Indeed, personal protection should be limited to operations for which solutions involving substitution, technical change to a process or collective protection cannot be implemented.

The result of the approach presented in this report is contextual and should be reviewed as soon as circumstances change (process modifications, development of scientific knowledge or state of the art, etc.). In accordance with the principle of continuous improvement, the control banding approach deserves to be reiterated in order to update the result.

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ANNEXES

Annex 1: Solicited Request Letter

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

Ministère de la santé, de la jeunesse, des sports et de la vie associative

Direction générale de la santé

COURRIER REÇU LE
2800
07 AOUT 2008

DGS/EA1/N° 177

Paris le, 04

Le Directeur g

à

Monsieur le Directeur général par intérim de l'Agence française de sécurité sanitaire de l'environnement et du travail
253 Avenue du Général Leclerc
94701 Maisons-Alfort

Objet : Demande de prise en charge par l'AFSSET de la création et du suivi d'un projet de groupe d'experts portant sur les « bandes de danger» au sein de l'ISO TC 229 « nanotechnologies » via le groupe miroir de l'AFNOR

Copie : AFNOR

Dans le cadre des travaux internationaux de normalisation de l'ISO TC 229 relatifs aux nanotechnologies menés depuis 2005, une commission de normalisation française « nanotechnologies » de l'AFNOR a été mise en place, ainsi qu'un groupe de travail sur les standards de « santé, sécurité et environnement » (appelé HSE en référence au WG 3 relatif aux standards « Health Safety and Environment » de l'ISO). A ce jour, aucun projet de document technique ou norme n'est piloté par la France au sein de cet ISO.

Cependant, dans le cadre de ses dernières réflexions, la commission Nanotechnologies de l'AFNOR a exprimé le souhait d'initier un projet destiné à définir des niveaux (ou bandes) de danger en fonction des propriétés physico-chimiques et toxicologiques spécifiques des nanomatériaux. Le classement des nanomatériaux dans ces bandes de danger constituera, pour les producteurs et utilisateurs, une des données d'entrée permettant de définir les niveaux de protection à mettre en place en fonction des classes de danger (Control Banding).

Cette démarche de « Control Banding », fait l'objet d'un chapitre dédié de votre rapport « nanomatériaux et sécurité au travail » (p 74 à 77). Il indique que cette démarche généraliste permet une analyse des risques liés à l'exposition en milieu du travail, par une hiérarchisation des postes de travail. Cette hiérarchisation est fonction de différents paramètres tels que les caractéristiques physicochimiques, la toxicité et les niveaux de confinement. L'INRS a publié une telle démarche en 2005 et le Comité Technique de la Chimie, du Caoutchouc et de la Plasturgie l'a adoptée en tant que recommandation depuis 2004. Cette approche qualitative, non spécifique, peut être adaptée afin de contribuer à la gestion des risques liés aux expositions aux nanomatériaux.

Aussi, dans ce contexte, et en accord avec la DGT et la DGPR, il nous apparaît opportun que ce projet puisse voir le jour au sein du groupe de travail WG3 de l'ISO et nous vous sollicitons pour assurer la prise en charge de ce projet, à titre d'expert.

En effet, parallèlement aux différentes mesures menées pour le développement responsable des nanotechnologies afin de mieux prendre en compte les spécificités des nanomatériaux, l'élaboration, à un niveau international, d'un outil spécifique non contraignant permettrait de compléter le dispositif réglementaire envisagé dans l'objectif d'une prévention des risques pour le travailleur. Ce classement des nanomatériaux, par bandes de danger, serait effectué sous la responsabilité de l'industriel.

A titre d'information, l'Association pour la Prévention et l'Etude de la Contamination (ASPEC) a développé et présenté lors de la dernière réunion du groupe HSE un outil de maîtrise des risques comprenant des classes de danger (annexe C du référentiel 18101 sur les systèmes de management pour les laboratoires R&D, en cours d'évaluation par l'INRS).

Afin de respecter les procédures inhérentes à la normalisation ISO, nous vous demandons de rédiger un document comprenant le titre et le résumé du projet. Une présentation de ce document à la réunion du prochain groupe HSE prévue à l'AFNOR le 03 septembre 2008 permettrait que ce projet soit proposé officiellement lors la réunion plénière de l'ISO qui se tiendra en novembre 2008, en Chine.

Pour la réalisation de ce document, nous vous invitons à prendre contact avec Benoît Croguennec, chef de Projet en charge des travaux de la Commission de Normalisation X457 "Nanotechnologies"

Le Directeur général
de la santé

La directrice générale adjointe
de la santé

Sophie DELAPORTE

COPIE : DGT, DGPR

French Ministry of Health, Youth, Sport and the Voluntary Sector

Directorate General of Health

DGS/EA1/No. 177

MAIL RECEIVED ON 07 August 2008

Paris, on 04

The Director G

to

Acting Director-General of the French Agency for Environmental and Occupational Health Safety
253 Avenue du General Leclerc
94701 Maisons-Alfort

Subject: Request for ANSES to take charge of the creation and monitoring of a proposed expert group dealing with "hazard bands" within the ISO TC 229 "Nanotechnologies" through the AFNOR mirror group.

Copy to: AFNOR

As part of the international standardisation work of the ISO TC 229 on nanotechnologies, which began in 2005, a French standardisation committee on nanotechnologies was established by AFNOR, as well as a working group on "Health, Safety and Environment" standards (HSE, in reference to the ISO WG3 on Health, Safety and Environment standards). To date, no draft technical document or standard has been managed by France within the ISO.

However, during its recent deliberations, the AFNOR Nanotechnology Committee expressed a desire to initiate a project to define hazard levels (or bands) based on the specific physico-chemical and toxicological properties of nanomaterials. The classification of nanomaterials in these hazard bands will provide producers and users with input data to enable definition of the levels of protection to be set up according to the hazard classes (Control Banding).

This "Control Banding" approach is the subject of a chapter in your report, "Nanomaterials and Safety at Work" (pp. 74 to 77). It indicates that this general approach allows the analysis of risks related to exposure in the workplace, by ranking work stations. This ranking is based on various parameters such as physico-chemical characteristics, toxicity and levels of containment. The INRS published such an approach in 2005 and the Technical Committee for Chemicals, Rubber and Plastics has adopted it as a recommendation since 2004. This qualitative, nonspecific approach can be adapted to help manage the risks associated with exposure to nanomaterials.

Thus, in this context and in agreement with the DGT and the DGPR, it seems appropriate that this project be created within ISO's WG3 working group and we ask you to take charge of this project, as an expert.

Indeed, alongside the various measures undertaken for the responsible development of nanotechnologies, in order to better take into account the specific characteristics of nanomaterials, the development at international level of a non-compulsory specific tool would supplement the regulatory framework considered, with the aim of preventing risks to the worker. This classification of nanomaterials, according to hazard bands, would be conducted under the manufacturer's responsibility.

For information, the French Association for the Prevention and Study of Contamination (ASPEC) presented at the last meeting of the HSE group a risk management tool it has developed which comprises hazard classes (Appendix C of the reference 18101 on management systems for R&D laboratories, currently being evaluated by the INRS).

To comply with the procedures involved in ISO standardisation, we request that you write a document including the project title and summary. A presentation of this document at the next meeting of the HSE group scheduled at AFNOR on 3 September 2008 would then enable this project to be formally proposed at the ISO plenary meeting to be held in China in November 2008.

For the production of this document, please contact Benoît Croguennec, Project Leader for the work of the X457 Standardisation Committee on "Nanotechnologies".

The Director General of Health

The Assistant Director General of Health [Signature]
Sophie Delaporte

COPY: DGT DGPR

Annex 2: Table based on the hazard group allocation of the e-COSSH Essentials tool

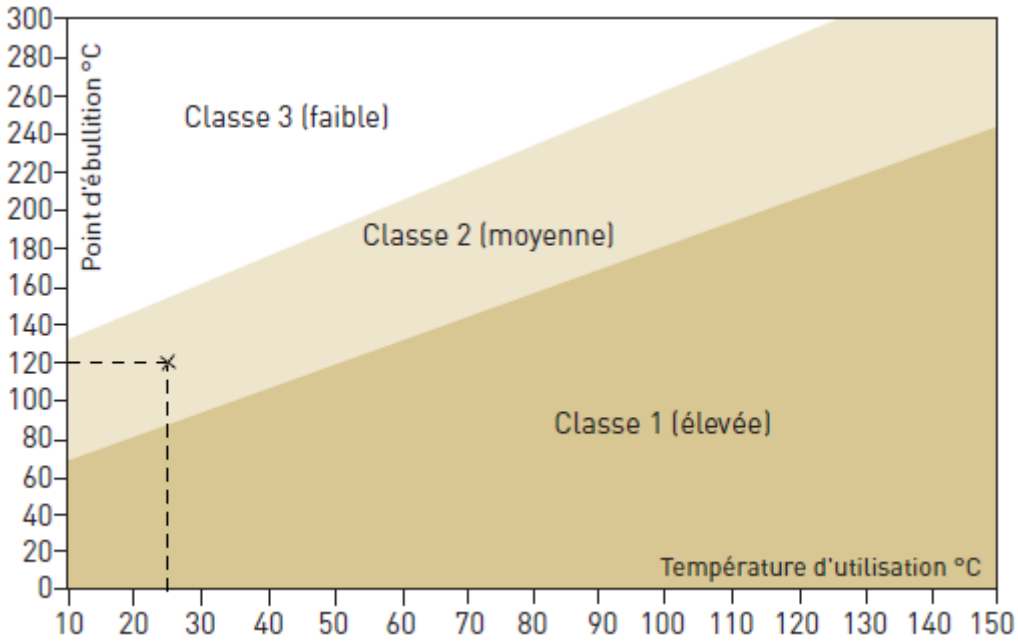
	Category A	Category B	Category C	Category D	Category E
	No significant risk to health	Slight Hazard – Slightly toxic	Moderate Hazard	Serious hazard	Severe hazard
OEL dust mg/m3	1-10	0.1-1	0.01 - 0.1	< 0.01	Seek specialist advice
Acute Toxicity	Low	Low / Moderate R20;R21;R22 Acute tox. 4	Moderate R23;R24;R25 Acute tox. 3	High R26;R27;R28 Acute tox. 1-2	
LD50 oral route mg/kg	> 2000 > 2000	200-2000 300-2000	25-200 50-300	<25 <50	
LD50 dermal route mg/kg	> 2000 > 2000	400-2000 1000-2000	50 – 400 200 - 1000	<50 <200	
LC50 inhalation 4H (mg/l) ***Aerosols/particles***	> 5 > 5	1- 5 1- 5	0.25 – 1 0.5 - 1	<0.25 < 0.5	-
Severity of Acute (Life-Threatening) Effects		Low/Moderate R68/Xn-R67-R65 STOT SE 2-3; Asp. Tox. 1	Moderate/High R39/T STOT SE 1	High (e.g. R39/T+) -	-
Adverse effects per oral route (mg/kg) (single exposure)	-	Adverse effects seen ≤ 2000 (Xn) ≤ 2000	Adverse effects seen ≤ 200 (T) ≤ 300	Adverse effects seen ≤ 25 (T+) -	-
Adverse effects per dermal route (mg/kg) (single exposure)	-	Adverse effects seen ≤ 2000 (Xn) ≤ 2000	Adverse effects seen ≤ 400 (T) ≤ 1000	Adverse effects seen ≤ 50 (T+) -	-
Adverse effects by Inhalation / 4H (mg/l) ***Aerosols/particles (single exposure)***	-	Adverse effects seen ≤ 5(Xn) ≤ 5	Adverse effects seen ≤ 1 (T) ≤ 1	Adverse effects seen ≤ 0.25 (T+) -	-

	Category A	Category B	Category C	Category D	Category E
	No significant risk to health	Slight Hazard – Slightly toxic	Moderate Hazard	Serious hazard	Severe hazard
Sensitisation	Negative	Slight cutaneous allergic reactions	Moderate / strong cutaneous allergic reactions (e.g. R43) Skin sens.1	-	Prevalent moderate to strong respiratory allergic reactions R42; R42/43 Resp. sens. 1
Mutagenicity/ Genotoxicity	Negative	Negative	Negative	Negative	Mutagenic in most relevant *in vivo* and *in vitro* assays. R68 (cat. 3) Muta 2 R46 (cat.1 -2) Muta 1A – 1B
Irritant/ Corrosiveness	None to Irritant R36; R38; R66 Eye Irrit.2; skin Irrit. 2 EUH 066	-	Severe irritant skin/eyes Irritant to respiratory tract R37; R41 STOT SE 3; Eye Dam. 1 Corrosive (e.g. R34;R35) Skin Corr. 1A – 1B	-	-

	Category A	Category B	Category C	Category D	Category E
	No significant risk to health	Slight Hazard – Slightly toxic	Moderate Hazard	Serious hazard	Severe hazard
Carcinogenicity	Negative	Negative	Some evidence in animals R40 cat.3 Carc. 2	-	Confirmed in animals or humans. R45; R49 (cat.1-2) Carc. 1A – 1B
Developmental/ Reproductive toxicity	Negative	Negative	Negative	Reprotoxic defects in animals and/or suspected or proved in humans R60;R61.R62;R63 (cat.1-2-3)) Repr. 1A, 1B, 2	
Likelihood of Chronic Effects (e.g. Systemic)	Unlikely	Unlikely	Possible R48/Xn STOT RE 2	Probable R48/T STOT RE 2	
Adverse effects per oral route (mg/kg-day) (90 day chronic study*)			Adverse effects seen ≤ 50 (Xn) ≤ 100	Adverse effects seen ≤ or 5 (T) ≤ 10	
Adverse effects per dermal route (mg/kg-day) (90 day chronic study*)			Adverse effects seen ≤ 100 (Xn) ≤ 200	Adverse effects seen ≤ 10 (T) ≤ 20	
Adverse effects by Inhalation / 6H (mg/l-day) Aerosols/particles (90 day chronic study*)			Adverse effects seen ≤ 0.25 (Xn) ≤ 0.2	Adverse effects seen ≤ 0.025 (T) ≤ 0.02	
Reversibility of Chronic Health Effects	Readily reversible	Readily reversible	Moderately reversible	Slowly reversible	Irreversible
IH/Occupational Health Experience	No evidence of adverse health effects	Low evidence of adverse health effects	Probable evidence of adverse health effects	High evidence of adverse health effects	High evidence of severe adverse health effects

Table 4: Table based on the hazard group allocation of the e-COSSH Essentials tool

Annex 3: Identification of volatility class for liquid products



Annex 4: Tracking of report updates

Date	Version	Page	Change description
27/10/10	Final		