Available online at www.sciencedirect.com
ScienceDirect
Regulatory Toxicology and Pharmacology 48 (2007) 171–183
Regulatory Toxicology and Pharmacology
www.elsevier.com/locate/yrtph

Limits and prospects of the "incremental approach" and the European legislation on the management of risks related to nanomaterials

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Received 21 November 2006
Available online 14 April 2007

Abstract

Scientific uncertainty involved in evaluating potentially harmful properties of engineered nanoparticles complicates and hampers the implementation of proportionate regulative measures by legislators. The European Commission has adopted a so-called "incremental approach", which focuses on adapting existing laws to regulate nanotechnologies, and therefore this paper aims to test the effectiveness of the "incremental approach". Three commercially available products containing fullerenes (C_{60} and carbon nanotubes) were analysed in a life cycle perspective in order to (1) map current applicable regulations, (2) analyse their applicability to nanomaterials, (3) identify their gaps, and (4) suggest proper solutions.

After mapping the life cycle of the three products, we analysed applicable regulations in the order in which they became relevant in their life cycle, i.e.:

- The Safety at Workplace Directives,
- Directive 61/1996 on the Integrated Pollution Prevention and Control,
- The European Union's Directive on the Registration, Evaluation, Authorization and Restriction of Chemicals, and
- The Waste Management Directives.

It was found that the applicability of environmental laws is limited due to difficulties in generating sufficient data on the nanomaterials residing in the products according to their life cycles. Further, metrology tools are unavailable; thresholds are not tailored to the nanoscale; and toxicological data and occupational exposure limits cannot be established with existing methodologies. We conclude that the "incremental approach" can only be applicable with the implementation of due amendments.
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Keywords: Nanotechnology; Risks; Regulation; Legislation; Incremental approach; Life cycle assessment

1. Introduction

Both the potential benefits of nanotechnology and potential hazards of some manufactured nanomaterials have been debated in recent years, especially following a number of studies which indicated that some nanomaterials can cause adverse effects on laboratory animals (Oberdorster, 2004; Lam et al., 2004). Data on nanoparticles, such as increasing production volumes and commercialization, capabilities to cross biological barriers, and increased biological activities of nanoparticles when compared to bulk counterparts, have worried some scientists about their potential impacts on the health and safety of both humans

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0273-2300/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.yrtph.2007.03.007

and ecosystems (European Commission, Health and Consumer Protection Directorate General, 2004). However, there still remains significant uncertainty on how nanomaterials differ from their bulk counterparts and corresponding risks.

In the last few years several legislative policies have been proposed and discussed by public institutions (i.e. European Commission, Health and Consumer Protection Directorate General, 2004; Royal Society & Royal Academy of Engineering, 2004, U.S. Environmental Protection Agency[1]) and non-governmental organizations (i.e. ETC Group[2] and Environmental Defense[3]). The different views on how to regulate nanomaterials vary substantially, ranging from a "laissez-faire" attitude to a total moratorium on nanotechnology research, development and commercialization. From a U.S. perspective, Davies (2005) advocates the establishment of a separate, specific regulation on nanomaterials, and argues that only a new legislation can be tailored to the unique properties of nanotechnology. However, as Davies (2005) acknowledges himself, issuing a new and specifically tailored environmental regulation on nanotechnology appears unlikely due to the political obstacles to passing new legislation. Similarly, Reynolds (2002) emphasized the ineffectiveness of a generalised prohibition and identified the need for a responsible approach coordinated by government agencies. Reynolds suggested a modest regulatory intervention based mainly on self-control mechanisms and research programs to address safety concerns. However, as Balbus et al. (2005) observes, voluntary programs cannot ensure that all companies actually take actions to safely manage nanomaterials. Rather, it can only ensure that the companies who participate in the voluntary programs are active in safely managing nanomaterials, and therefore "responsible" companies may have short-term disadvantages. Furthermore, even if voluntary programs would protect human and environmental health against potential risks of nanomaterials, it will not sufficiently foster public confidence (Kuzma, 2005), which is often a prerequisite for innovation.[4]

In Europe the identification of new risks among other calls for the application of the precautionary principle. In this context, a proportionate and effective regulation of the sector is essential to guarantee the safe development of nanotechnologies and to gain necessary public acceptance without stifling innovation. However, how to actually conduct this in practice is debated both within and outside of Europe. The European Commission (EC) has adopted an "incremental approach" which adapts existing environmental laws to the regulation of nanotechnologies in Europe, regarding it as the only realistic policy option. This approach is defined as the launch of a process which uses existing legislative structures (e.g., dangerous substances legislation, classification and labelling, cosmetic legislation, etc.) to the maximum, revisits them, and, when appropriate only, amends them in order to deal with nanomaterials. Among other things, this approach includes: issuing recommendations, commissioning studies, promoting risk assessment throughout the life cycle of a nanotechnology, encouraging actions of existing institutions, supporting observations of nanotechnologies; initiating a minimalist, appropriate and proportionate regulatory intervention, and setting-up a framework within which stakeholders can help shape the course of nanotechnologies (European Commission, Health and Consumer Protection Directorate General, 2004). Currently, the possibility of a specific regulation on nanomaterials is considered unfeasible in the European context, due to the difficulty of establishing links between strikingly different pieces of legislation and the need to negotiate internationally to establish a sensible specific, in-depth regulatory process (European Commission, Health and Consumer Protection Directorate General, 2004).

This study investigates the effectiveness of the incremental approach. In order to adequately determine the effectiveness, which is most likely product-specific, three commercially available nanoproducts were used in order to reflect the diversity of available carbon-based nanomaterials. The life cycle approach was chosen to capture all relevant aspects of human and environmental health related to nanoparticles during production, extraction and refining, manufacturing, use, and final disposal. The current regulations were mapped along the life cycle of each product in order to (1) analyse their applicability in relation to nanomaterials, (2) identify their gaps, and (3) suggest proper solutions. The analysis identified four relevant areas of legislation:

- The Safety at Workplace Directives,[5]
- Directive on the Integrated Pollution Prevention and Control,[6]
- The European Union's Directive on the Registration, Evaluation, Authorization of Chemicals,[7] and
- The Waste Management Directives.[8]

[1] Nanotechnology White Paper, available at: http://es.epa.gov/ncer/nano/publications/whitepaper12022005.pdf.

[2] The Big Down, available at: http://www.etcgroup.org/documents/TheBigDown.pdf.

[3] Getting Nanotechnology Right the First Time, available at: http://www.environmentaldefense.org/documents/4816_nanotechstatementNAS.pdf.

[4] The topic has been addressed by EurActiv, 2006, in: Stakeholders: public trust a prerequisite for 'nanoinnovation' EurActiv 2000–2005, available at: http://www.euractiv.com/en/science/stakeholders-public-trust-prerequisite-nanoinnovation/article-157904 (accessed 25 September 2006).

[5] e.g. EU Council Directives 31/1989, 24/1998.

[6] EU Council Directive 61/1996.

[7] European Parliament and the Council of the European Union, 2006. Regulation (EC) No. 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No. 793/93 and Commission Regulation (EC) No. 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. 30.12.2006 EN Official Journal of the European Union L 396/1.

[8] EU Council Directives 12/2006, 689/1991, 439/1975, 53/2000.

The analysis of these four areas of legislation follows the order in which it became relevant along the life cycle of the three products.

2. Materials and methods

In general, nanomaterials can be divided into three main categories:

- Materials that are nanostructured in the bulk. This can be either one or more materials that are nanostructured in three dimensions.
- Materials that have nanostructure on the surface. This can be (1) materials with surfaces structured on the nanoscale, but the surface and bulk consist of the same material; (2) nanoscale thick, un-patterned film on a substrate of a different material; (3) patterned film on a substrate, where the film is either nanoscale in thickness, or the pattern has nanoscale dimensions along the surface.
- Materials that contain nanostructured particles, defined as free structures that are nanosized in at least two dimensions (Hansen et al., submitted for publication).

The present study focuses on the third group of nanomaterials, materials that contain nanostructured particles, since they are considered as the most relevant fraction of products and applications in terms of safety issues.

The three commercially available products used in this study were chosen in order to reflect differences in regulation that might occur along the life cycle of three carbon-based products. These included a badminton racquet, and an oil lubricant containing C_{60} produced by Yonex and Bardahl respectively, and a baseball bat containing carbon nanotubes produced by Easton Sports. These products all use carbon nanomaterials but differ with respect to: (1) the structure of the nanomaterial and (2) whether the nanomaterial is suspended in a liquid or solid. The badminton racquet containing C_{60} and the baseball bat containing carbon nanotubes, both suspended in solids, were chosen in order to be able to compare the regulations of two carbon nanomaterials which have markedly different structure. The oil lubricant containing C_{60} was chosen in order to be able to compare the regulation of a product containing C_{60} suspended in a liquid to a product containing C_{60} suspended in a solid (i.e. the badminton racquet).

First, the life cycle of each product was mapped qualitatively. The life cycle overview served to map the applicable worker health and safety and environmental legislation as well as to provide the necessary technical information to discuss the legislations' suitability and gaps. Though the scope of the case studies is narrowed to carbon nanoparticles, the following discussion and recommendations are thought to be valid for all engineered nanoparticles. Very limited information could be gathered directly by contacting companies due to strict confidentiality policies. The collected information is mainly based on available scientific literature and information provided on companies' websites (i.e., product's description, technical reports, Material Safety Data Sheets).

3. Mapping the life cycle of the three products

In the following sections the three commercially available products used in this study are analyzed along the life cycle of the three carbon-based products. The results are presented in an arbitrary order which does not imply one product as more important or problematic than the others.

3.1. Badminton racquet and production of C_{60}

After more than a decade of research, the manufacture of carbon nanoparticles has become an industrial reality. The productivity of C_{60} manufacturing plants is measured by the tonnage and many products are already marketed.

In the case of the badminton racquet, C_{60} molecules are dispersed in a resin between carbon fibers in order to strengthen the structure of the composite. The first part of Fig. 1 presents an overview of the key elements of the life cycle of the badminton racquet. The supplier of C_{60} (Frontier Carbon Corporation) applies a combustion process for the synthesis of C_{60}, which uses hydrocarbons as a raw material to produce C_{60}. Toluene is fed together with oxygen to a low-pressure combustion chamber. The flame produces fullerene-enriched soot, which is extracted and filtered. The apparatus is a closed system, i.e. exhausted gas is cooled down in a heat exchanger and driven back to the inlet flow (Takeara et al., 2004). Fullerenes are then extracted from the soot by solvents (e.g. chlorobenzene and toluene) in a tank where the insoluble soot settle to the bottom while C_{60} are dissolved in the solution. Purified fullerenes are collected after the solvent has evaporated and appear as a black powder. The separation of single sized-fullerenes (C_{60}, C_{70}) and the degree of purity determine the price of the final product. Separation is typically performed by high-pressure liquid chromatography using solvents (Nano-C, 2002). As a whole, the system's outputs are the purified buckyballs and the residual soot, which still contains a few percent of fullerenes. Even though the residual soot can be considered a by-product it has a commercial value and hence no waste is produced (Ozawa, 2005).

Buckyballs are sold to the manufacturer of the racquet where C_{60} molecules are initially incorporated into an epoxy resin. For processing carbon fibers and epoxy resin into a composite material, the resin is put into a curing oven where it melts on the substrate (in this case, the carbon fibers). It then solidifies to form an insoluble plastic composite material, which does not melt again.[9] A certain amount of excess resin is always generated, and in this case, the hardened resinous waste contains fullerenes and will be considered hazardous waste by European legislation similar to normal resins.

The badminton racquet is produced in Japan while commercialized in the E.U. and in U.S. Since the nanoparticles (i.e., C_{60}) are fixed in a solid matrix, no fullerenes release is expected during the lifetime. Eventually the racquet becomes a waste, and it can be assumed that the racquet will be disposed off as a municipal solid waste at the end of its life.

3.2. Lubricant and the fate of free C_{60}

In the case of the lubricant, soot-containing C_{60} is mixed together with other chemical additives in order to improve the sliding between metallic surfaces and thereby enhance the performance of the lubricant.[10]

[9] See "Standard Operating Procedures for Handling and Use of Epoxy Resin Systems" by Thomas P. and Eckmann A., 1992, available at: http://psfcwww2.psfc.mit.edu/esh/epoxy.html (accessed 25 June 2006).

[10] Commercial information from Bardahl's website, available at: http://www.bardahl.it/tecnologie-set.htm.

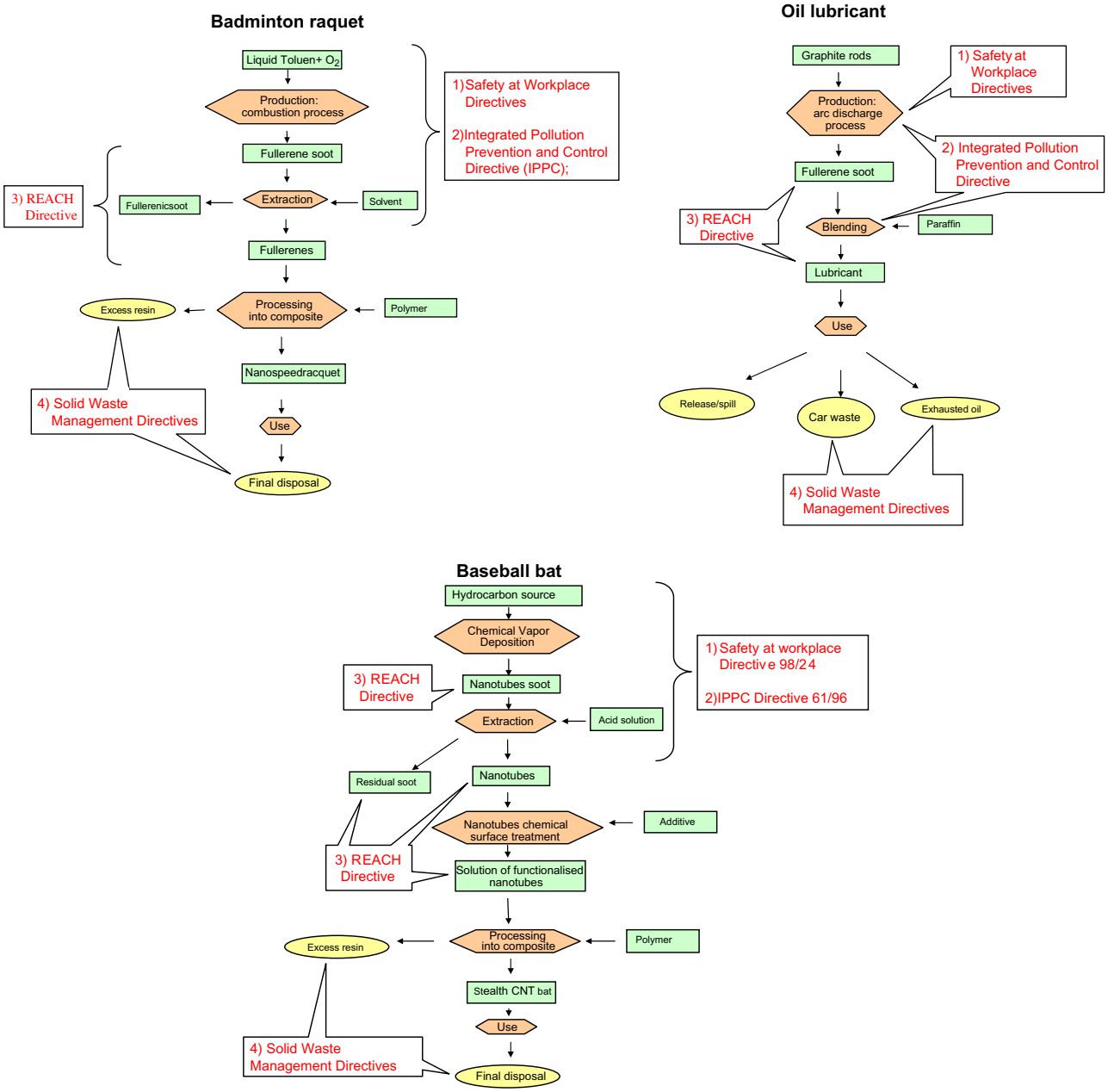

Fig. 1. An overview of the key elements of the life cycle of the badminton racquet, the oil lubricant, and the baseball bat and the applicable regulations along the life cycle of the three products.

The oil lubricant is imported to Italy from the U.S., and even though it has not been possible to identify the actual supplier of fullerenes, it is assumed that the fullerene soot is produced by the "arc method", most common and widely-used method to produce fullerenes. The process differs somewhat from the combustion method described above, since it uses graphite as the raw material. Electric current is led between two graphite rods in a helium low-pressure reactor chamber. The reactor is closed but the process is not continuous. When the graphite is consumed, the rods have to be replaced and the produced soot collected from the system. No other substances are involved in the process and no waste containing fullerenes is generated. The as-produced soot yields approximately 7% of mixed fullerenes and is sold without further treatment (Bogdanov et al., 2000).

The soot obtained by the arc method can be directly dissolved in the lubricant without any further extraction or purification step. Assuming a fullerenes concentration in the soot of 3.2% and soot content in the lubricant of 9.4%, we estimate that the concentration of C_{60} in the lubricant is about 3 g/kg (Huczko et al., 2003).

The manufacturer reports that fullerenes molecules work as micro ball-bearings along sliding surfaces. This suggests that the single molecules are at least partly free during use. Unintended release of free particles during

the lifetime of the product has to be considered in an exposure assessment. It is also reported that most of the fullerenes remain attached to the metallic surfaces of the motor even when the oil is removed. However, there is a lack of evidence and, hence, this question represents a large area of uncertainty in the life cycle of the lubricant. In addition, our knowledge of exposure and fate after release is very limited, and therefore the state of the fullerenes in the oil may not be relevant. Four possible fates of the fullerenes can be foreseen at this point, though any mass flow estimation cannot be done:

- Fullerenes may adhere to metallic components of the car and will eventually be incorporated in the end-of-life vehicle's waste,
- Fullerenes may be combusted if oil enters the engine during use,
- Fullerenes may be removed together with the oil if they remain suspended in the liquid phase when the oil is changed, and
- Unintended direct release occurring from oil spills or sublimation of fullerenes.

On the basis of the information available, two different waste-scenarios can be foreseen. (1) Either the fullerenes stay attached to metal surfaces as the producer claims and end-up as vehicle waste at the end of the vehicle's life cycle or (2) the fullerenes are dissolved in the exhausted oil, which is then removed from the motor when the oil is changed or at the end of the vehicle's lifetime. In the first scenario, fullerenes will follow the metallic waste and probably be degraded during recycling of the metal. Alternatively, they may transfer to liquid or solid wastes during treatment operations or be slowly released from landfills. In the second scenario, the exhausted oil is classified as a hazardous waste and should therefore be disposed of as such in order to avoid any leakage or spill to the environment. See second part of Fig. 1 for an overview for key elements of the life cycle of the oil lubricant.

3.3. Baseball bat and the thermal stability of carbon nanotubes

Similar to the manufacturing of the badminton racquet, the baseball bat investigated is manufactured in a process where carbon nanotubes are added to the resin between carbon fibers of the bat in order to increase the strength of the material. Several suppliers of carbon nanotubes have been identified in the baseball bat's production. The most frequently used process for the production of carbon nanotubes is based on chemical vapour deposition, which is currently regarded as the most promising method as well. See the third part of Fig. 1 for an overview of the key elements of the baseball bat's life cycle. Several hydrocarbons like methane, acetylene or ethylene can be used as a carbon source for the synthesis of nanotubes. The hydrocarbon molecules are introduced into a furnace at temperatures ranging between 650 and 900 °C. Consequently, molecules are cracked into single reactive carbon atoms which move towards the heated substrate coated with a metal catalyst. Atoms recombine in the form of carbon nanotubes on magnesium-supported iron catalyst together with impurities (Daenen et al., 2003).

The apparatus is a closed system and no substantial waste flow is generated. Once collected, the raw soot containing nanotubes is washed in an acid solution to remove the catalyst and other impurities,[11] mainly graphite sheets, amorphous carbon, metal catalysts and smaller fullerenes (short nanotubes). With respect to the total mass flow of the system, the most abundant element is the waste soot, often referred to as carbon nanofibres.

Carbon nanotubes possess unique electrical, mechanical, and thermal properties. In order to transfer these properties to useful materials, carbon nanotubes need to be homogenously dispersed in the host matrix. This has proven to be quite difficult because of the tendency of carbon nanotubes to cluster into larger aggregates.[12] An additional, chemical treatment is necessary to dissolve nanotubes into a functionalised additive which can eventually be blended into the resin. Unfortunately, information on the details of this treatment is not available since they are concealed by strict corporate non-disclosure policies.

The nanotubes enhanced resin can be incorporated into the structure of carbon fibre composites. Similar to the production of the badminton racquet, a waste stream consisting of the excess resin containing carbon nanotubes will be generated.

Due to the fixed nature of the nanomaterial within the bat, there seem to be little concern for exposure during the product's lifetime. Eventually the bat becomes a waste item and is disposed of in a similar way to the handling and final treatment of the badminton racquet, where it is treated as a municipal solid waste, disposed in a landfill or burnt in an incinerator. Interestingly, whereas the onset temperature reaction for C_{60} is very low (315 °C), carbon nanotubes display very low reactivity under combustion conditions (onset temperature = 820 °C) and hence may not breakdown in an incinerator (Cataldo, 2002). In theory, this means that they could end up in the gaseous effluent and released into the atmosphere. However, there has not yet been any scientific study assessing the impact of this potential exposure pathway compared to the present emission of airborne nanoparticles from incinerators.

4. Applicable regulations along the life cycle of the three products and subsequent identification of regulatory gaps

Four pieces of legislation were found to be of prime relevance in an analysis of existing applicable regulations along the life cycle of the three products:

[11] Information from Thomas Swan's website, available at: http://www.thomas-swan.co.uk/pages/nmframeset.html.

[12] Information from Zyvex website, available at: http://www.zyvex.com/Products/CNT_FAQs.html.

- The Safety at Workplace Directives,
- Directive 61/1996 on the Integrated Pollution Prevention and Control,
- The European Union's Directive on the Registration, Evaluation, Authorization and Restriction of Chemicals, and
- The Waste Management Directives (see Fig. 1).

However, there were important case-specific differences about the relevancy and applicability of the different laws. Each of the four pieces of legislation will be subsequently discussed with respect to its general applicability to nanomaterials and specific applicability to the three products.

4.1. Safety at workplace

There is no direct reference to the potential exposure of engineered nanoparticles in the Safety at Workplace Directives or in the communitarian and national legislation on the protection of workers' health at workplaces. The Frontier Carbon Corporation which produces C_{60} claim that exposure is irrelevant due to the use of closed systems (Ozawa, 2005). Very little is known about possible exposure during the production of carbon nanotubes as well as during the other handling operations in subsequent stages of the three products' life cycle. One study, however, conducted by the National Institute for Occupational Safety and Health (NIOSH) indicates that the airborne concentration of CNT material generated during handling of unrefined carbon nanotube soot is extremely low (Maynard et al., 2004).

The Framework Directive 31/1989 as well as Directive 24/1998 on the risks associated with chemical substances set guidelines to establish Occupational Exposure Limits (OELs) for workers, although three main problems arise at this point. (1) The establishment of OELs is typically based on a complete risk assessment procedure which presently is not possible for engineered nanoparticles, such as C_{60} and carbon nanotubes, because of the extent and profoundness of uncertainties involved and a general lack of scientific knowledge (European Commission Scientific Committee on Emerging or Newly Identified Health Risks, 2005); (2) nanoparticles are not easily detected by existing instruments; and (3) the most optimal parameter to determine the toxicity of nanoparticles is still undefined. With respect to the third point mentioned, it is widely agreed that the specific surface area is more relevant than the mass concentration to measure the toxicity of nanoparticles. However recent studies demonstrate that the reactivity of some nanoparticles is more likely to be related to the number of edges in the nano-structure of the particles rather than to the surface area (Dahl et al., 1999).

The problems related to setting specific OELs together with difficulties in monitoring particle concentrations create a gap in current regulations. Furthermore, the lack of any specific reference to engineered nanoparticles in existing laws on safety at workplaces creates a situation where companies are unprepared to tackle the issue sensibly. At the moment, manufactures refer to OELs set for metal dusts or dusts of other compounds (e.g. graphite or carbon black instead of fullerenes and carbon nanotubes). However given the recent concern about the toxicity of airborne fullerenes and carbon nanotubes, OELs defined for related bulk substances (e.g. graphite) are not representative and should not be used since properties displayed by nanoparticles differ substantially from those of their bulk material (Lam et al., 2004).

Problems associated with establishing OELs for C_{60} and carbon nanotubes are reflected in many of the Material Safety Data Sheets (MSDSs) made available by the producers themselves. For example, the MSDS delivered by Thomas Swan's for Elicarb® Single-wall lacks a Chemical Abstract Service (CAS) number and classifies carbon nanotubes as graphite, which is improper as stated previously. Lam et al. (2004) in particular have pointed out that the U.S. Occupational Safety and Health Administration's Personal Exposure Limit set for synthetic graphite dust should not be used to protect workers exposed to carbon nanotubes. In addition, a list of exposure control measures are recommended in the MSDS if "*engineering controls do not ensure that the OEL is not exceeded*", while the absence of any OEL is mentioned a few lines below. Furthermore the existence of such "*engineering controls*" is questionable.

These problems and inconsistencies reveal serious gaps in the Safety at Workplace regulation considering that the MSDSs are essential in passing information about risk and safety down the supply chain and they also provide workers and emergency personal information about the risks, protective equipment and proper handling of a substance. It has not been possible to locate a MSDS for C_{60} from suppliers to the producers of the badminton racquet and the oil lubricant, which in both cases are located outside the EU. However, just as in the case of carbon nanotubes, inconsistencies can also be found in the MSDSs for C_{60} made available by other producers. For example, a German manufacturer of 100% purified C_{60} refers to carbon black as the relevant OEL to be monitored.[13]

4.2. Integrated Pollution Prevention and Control

Directive 61/1996 on the Integrated Pollution Prevention and Control (IPPC) is the main environmental regulative tool on industrial and agricultural installations in Europe which focus on plants' processes and performances. It establishes an authorising regime for activities with a high pollution potential. The industrial activities encompassed are specifically listed. The performances of various processes must ensure a high level of protection, proper pollution preventive measures as well as comply with the notion of Best Available Techniques (BAT). The

[13] From the MSDS available on Alfa Asear's website at http://www.nd.edu/~exafs/msds/C60.html (accessed 25 June 2006).

BAT is defined as "*the most effective technology in achieving a high general level of environmental protection*", available "*under economically and technically viable conditions*" and "*reasonably accessible to the operator*".[14] The relevance of the IPPC Directive to manufacturing plants of nano-engineered substances and materials, such as C_{60} and carbon nanotubes, depends on whether they are encompassed by the list of industrial activities with a high pollution potential. Chemical installations for the production of a wide-ranging list of organic and inorganic chemicals are listed, however, there are no specific references to synthesised nanoparticles. Fullerenes can hardly fit in a category in the traditional chemical nomenclature. More specifically, C_{60} cannot be considered an organic chemical because an organic compound contains both carbon and hydrogen in its structure. Similarly, they do not fit in any category of inorganic chemicals, since traditionally they are defined according to the bulk composition which is merely pure carbon in this case.

In the life cycle of the badminton racquet, oil lubricant and baseball bat the following industrial installations were identified which were involved in the production of C_{60} and carbon nanotubes:

- Manufacturing plant of fullerenes (capability 40 tons/year),
- Manufacturing plant of carbon nanotubes (capability 24 kg/year),
- Chemical treatment of carbon nanotubes,
- Processing nanotubes containing additives into the composite structure of the baseball bat,
- Processing fullerenes into the composite structure of the badminton racquet, and
- Processing fullerenic soot into the motor oil lubricant.

Among these six industrial processes only the first two could be subjected to the Directive's requirements. There is no explicit reference to the synthesis of nanoparticles in the list of activities of Annex I, but the manufacturing of fullerenes and carbon nanotubes may be included as the list generically takes account of installations for the synthesis of chemicals. Since there is no mass production threshold for most of the chemical industry installations, the burden is merely on the interpretation of points 4.1 or 4.2 of Annex I.

Although the obligations to be met are the same, it is interesting to note that the supplier's situation differs in the case of C_{60} and carbon nanotubes. In the case of the baseball bat, the identified manufacturing plant of carbon nanotubes (i.e., Thomas Swan & Co. Ltd.) is a smaller installation of a larger existing chemical industry. In this case the chemical industry is already subjected to the IPPC Directive and the regulation applies if the installation for the synthesis of carbon nanotubes implies a "substantial change" of the site. In the case of the badminton racquet, however, the manufacturing plant for the synthesis of fullerenes (i.e., Frontier Carbon Corporation) is a new installation and requires a new application procedure.

The IPPC is managed by the IPPC Bureau which produces the Best Available Techniques reference documents (BREFs). Each BREF gives a comprehensive overview of materials, processes and techniques involved in a specific sector. It provides a "*a number of elements leading up to the conclusions of what are considered to be best available techniques in a general sense for the sector concerned*".[15] Considering the vast number of nanomaterials and the wide range of applications, establishing BREFs on nanomaterials seems a daunting task. However, it is important to remember that the IPPC Bureau has already faced difficult tasks for issuing BREFs, such as in the case of "Large Volume Organic Chemicals" or "Organic Fine Chemicals".

4.3. Registration, Evaluation and Authorization of Chemicals (REACH)

As of January 1, 2007 a new chemical legislation on the manufacturing and commercialization of chemical substances in the European market went into force. The new regulation, termed Registration, Evaluation and Authorization of Chemicals (REACH), establishes an authorizing system that requires the registration and evaluation of existing and new chemical substances. The Directive is expected to play a crucial role in the "incremental approach" and thereby also in managing risks associated with nanoparticles.

This study only considers the text of the Directive itself. The Technical Guidance Documents and methodologies used for risk assessment in support of the legislation on chemicals fall outside the scope of this study.

Even though the manufacturing of fullerenes used in the badminton racquet and the oil lubricant as well as the production of the baseball bat all occur outside Europe, it is interesting to discuss how the produced substances and products would be considered by REACH had they been produced in Europe. The first key question is whether the nanoparticles used in the three products fall under the scope of REACH. REACH considers a substance a "*chemical element (...) obtained by any manufacturing process, including (...) any impurity deriving from the process used*". This suggests that the annual production should be measured including impurities. A substance with a different degree of purity and composition can be classified as the same substance provided hazardous properties do not differ significantly. All carbon nanoparticles are typically produced as raw soot with a few percentage of purity. Produced or imported substances require a registration over the threshold of 1 ton/year, including impurities. This

[14] EU Council Directive 61/1996, art 2.

[15] From IPPC Bureau's description of BREFs available at: http://eippcb.jrc.es/pages/FActivities.htm (accessed 25 June 2006).

is not logical considering that hazardousness is proportional to the content of nanoparticles.

As mentioned, the regulation defines a substance as a chemical element including impurities and derived from the manufacturing process. Usually each substance is associated with a CAS- and EINECS[16]-number in order to be universally identified. It is not clear how this applies to the many different substances we are dealing with during the life cycle of the three products. For instance, raw soot, NanomBlack® and purified fullerenes from the C_{60} production at the Frontier Carbon's plant are isolated, but in theory they could all be classified within a single EINECS number provided the hazardous properties do not differ significantly.[17]

Tables 1–3 show the classification of substances and articles used in the life cycle of the badminton racquet, oil lubricant and baseball bat, respectively, in addition to obligations that the producers or importers would have to fulfil according to REACH. Tables 1–3 show that even if C_{60} and carbon nanotubes should fall under the scope of REACH, it is highly unclear whether this would involve any additional obligations from producers of C_{60} and carbon nanotubes as well as from producers or importers of the final products containing C_{60} and carbon nanotubes.

Although REACH obliges producers or importers to provide toxicological data and assess environmental exposure, requirements are based on mass thresholds. Hence, data sets are not required until production or imported volumes are above the threshold of 1 ton/year of substance. For many nanoparticles this threshold would hardly be reached, but for C_{60} produced in the case of the badminton racquet the threshold is greatly exceeded (>250 $ton_{raw\ soot}$/year). In the case of the baseball bat, carbon nanotubes are produced in very small amounts, and hence no registration would be necessary. Information on the quantity of C_{60} imported annually in the production of the oil lubricant was unavailable.

Furthermore, the usually low concentration of nanoparticles in the final article is likely to exclude many nanoengineered articles from the REACH legislation, since no registration is required when the concentrations of a substance is lower than 0.1% w/w. When considering the raw soot in the oil lubricant, the estimated concentration of nanoparticles was far greater than this threshold. However, the concentration decreases when it is calculated based on pure C_{60}. A lack of data did not allow performing the same estimation on nanoparticle concentrations in the racquet and in baseball bat.

4.4. Waste management

Wastes containing nanoparticles are produced at different phases of the life cycle, from by-products generated during manufacturing and purification processes to nano-engineered goods becoming wastes at the end of their lifetime. A case by case analysis of the behaviour of nanoparticles in waste products is recommended in order to identify potential pathways of exposure. Nano-wastes are tackled by waste management regulations in a non-specific way, because there are no specific references to engineered nanoparticles in existing laws. In general, nanoparticles will follow the material or the substance in which they are contained and their fate depends on the way these wastes are treated. In some cases the nano-waste can fall within a particular waste category, like the exhausted oil lubricant and excess resin containing C_{60} (see Table 4), which are specifically regulated. In other cases nanoparticles which are contained in products end-up in municipal solid waste.

Carbon nanotubes and C_{60} are produced in soot which is typically purified in order to produce a high value product and a residual by-product. The potential for these by-products to have a commercial value in the market is uncertain, and is reflected in the on-going debate at the European Court of Justice on the definition of waste. Particularly relevant is the distinction between "production residues" (considered wastes) and "by-products" (considered commercial goods). The use of C_{60} in the industry of lubricants is a good example of an effective use of low purity fullerene soot. How the carbon nanotube soot residues are handled is unknown.

Although recycling is not feasible from the composite of the sporting goods (i.e., racquet and baseball bat), it might be possible for the oil lubricant. Regeneration is recommended by Directive 439/1975 on the disposal of waste oil. If C_{60} are still dissolved in the exhausted oil it could be possible to recover them. In this case, the technical and economical sustainability of the process needs to be studied.

Wastes are typically disposed of in landfills or incinerated. Very little is known about the long-term behaviour of nanoparticles in a landfill. Release depends on the nanoparticles' mobility as well as on the degradability of the host material for fixed particles. When products are incinerated, the thermal properties of nanoparticles determine their fate. For example, a study by Cataldo (2002) demonstrated that C_{60} molecules are much easier to degrade than carbon nanotubes. Further, in a combustion chamber C_{60} behaves like graphite, while carbon nanotubes, similar to diamonds, are stable until very high temperatures (Cataldo, 2002).

If a certain nano-waste falls within the scope of Directive 689/1991 on the management of hazardous waste, more severe obligations would apply. Again, the lack of (eco)toxicological data makes it difficult to state if nanoparticles meet the criteria of hazardousness.

5. Recommendations

In the current paper, we tested the applicability of the incremental approach on three commercially available

[16] European Inventory of Existing Commercial Chemical Substances.
[17] REACH, preliminary note 31bis.

Table 1
Classification of substances and articles according to REACH in the case of the badminton racquet

Item	Description	Tonnage	Composition	Classification in the REACH	Obligations according to REACH[a]
Raw fullerene soot	As produced fullerene soot from the combustion synthesis	The manufacturing plant has a total capability of 40 tons of fullerenes per year	Black carbon: ~85%; fullerenes: ~15% (C_{60} ~50%, C_{70} ~25%, HF ~25%)[b]	On-site isolated intermediate	
Nanom Black®	Low purity by-product from the extraction process		Black carbon: 96%; fullerenes: 4%[c]	Substance A	
Nanom Purple®	Purified C_{60} fullerenes after extraction and separation		Fullerenes: 98% (C_{60} 98%, C_{70} 1%), impurities: <1%[c]	Substance B	
Nanospeed racquet[d]	Badminton racquet containing fullerenes in the composite material	n.a.	Fullerene content: n.a.	Article containing a substance	None (no foreseeable exposure)

[a] Only substances or products produced or imported to the community are considered; elsewhere blank spaces are inserted in the table.
[b] Estimations based on the pilot plant described in H. Takeara et al. (2004).
[c] Data from Frontier Carbon Corporation's website, available at: http://www.f-carbon.com/product.html (accessed 25 June 2006).
[d] The product is imported from Japan to the EU.

Table 2
Classification of substances and articles according to REACH in the case of the oil lubricant

Item	Description	Tonnage	Composition	Classification under the REACH	Obligations according to REACH[a]
Raw fullerene soot	As produced fullerene soot from the arc process	n.a.	Black carbon: ~93%; fullerenes: >7% (C_{60} ~75%, C_{70} ~22%, HF~3%)[b]	Substance A	
XTC_{60} oil lubricant[c]	Oil lubricant containing fullerene soot	n.a.	n.a.	Article containing a substance. Release is not intended but is reasonably foreseeable during the product's life cycle	If the substance in the product amounts to 1t/y and has a concentration >0.1% wt a notification is required

[a] Only substances or products produced or imported to the community are considered; elsewhere blanks spaces are inserted in the table.
[b] Data from MER Corporation's website, available at: http://www.mercorp.com/mercorp/fullbro.pdf (accessed 25 June 2006).
[c] The product is imported to Italy from the US.

Table 3
Classification of substances and articles according to REACH in the case of the baseball bat

Item	Description	Tonnage	Composition	Classification in the REACH	Obligations according to REACH[a]
Raw nanotubes soot	As produced CNT soot from the chemical vapour deposition process	n.a.	CNTs: 30%; soot: 70% (graphite sheets, amorphous carbon, metal catalysts and smaller CNTs) [b]	On-site intermediate	None <1 ton/year
Nanotubes fibres	Low purity by-product from the purification process	n.a.	n.a.	Substance C	None <1 ton/year
Elicarb® SWNT[c]	Purified single wall CNTs after extraction and separation	24 kg/year[d]	SWNTs: 70–90%; soot: 10–20%[d]	Substance D	None <1 ton/year
Nanosolve® additive	Solution containing chemically functionalised CNTs	n.a.	n.a.	Preparation	
Stealth CNT baseball bat	Baseball bat containing CNTs in the composite material	n.a.	n.a.	Article containing a substance	

[a] Only substances or products produced or imported to the community are considered; elsewhere blank spaces are inserted in the table.
[b] Estimations based on Daenen et al. (2003).
[c] The product is exported to the US.
[d] Data from Thomas Swans's website, available at: http://www.thomas-swan.co.uk/pages/nmframeset.html (accessed 8 April 2006).

Table 4
Characterization of identified nano-wastes

Type of waste	Waste classification in the existing legislation	Status of nanoparticles in the waste
Badminton racquet		
Excess resin	Included in the list of Annex I.A of Directive 689/1991 on hazardous waste	Buckyballs dispersed in the hardened resinous matrix
End of life racquet	Municipal solid waste	Buckyballs fixed in the composite
Oil lubricant		
End of life vehicle	Part of the end of vehicle waste regulated by Directive 53/2000	Buckyballs adhered to metallic surfaces
Exhausted oil	Included in the list of Annex I.A of Directive 689/1991 on hazardous waste. This waste is specifically regulated by Directive 439/1975 on the disposal of waste oil	Buckyballs dissolved in the oil
Baseball bat		
Waste soot	No specific reference	Smaller fullerenes present among other carbonaceous impurities in a dry powder
Excess resin	Included in the list of Annex I.A of Directive 689/1991 on hazardous waste	Carbon nanotubes dispersed in the hardened resinous matrix
End of life bat	Municipal solid waste	Carbon nanotubes fixed in the composite

Table 5
Limitations and suggested amendments in existing regulations applicable to nanotechnology

Framework	Task	Questions to be defined	Recommendations
Safety at work	Guarantee safety of workers to potential exposure to airborne engineered NPs	Impossibility to establish OELs based on complete risk assessment	Define standards for labs and other workplaces handling NPs
		Lack of metrology instrumentation	Promote research and development of usable tools
Integrated Pollution Prevention and Control (IPPC)	Establish a monitoring agency on nanotechnologies	Definition of the scope of the regulation for manufacturing plants of engineered NPs	Establish a Technical Working Group within the IPPC bureau to organise an exchange of information and issue BAT reference documents (BREF) on certain nanotechnologies
	Apply the concept of Best Available Technologies (BAT) on nanotechnology	Definition of BAT for the production and handling of NPs	
Registration Evaluation and Authorization of Chemicals (REACH)	Ensure safety of NPs to human health and the environment	Definition of new substance and classification of NPs	Adapt the Chemical Abstract Service (CAS) to properly classify NPs
		Suitability of thresholds based on mass units to NPs	Establish a specific regime for NPs within the REACH
Waste management	Avoid any release/exposure of NPs at the end of life of nano-engineered products/substances	Define the scope of the hazardous waste directive for engineered NPs	Add free NPs in the list of Annex II in Directive 689/1991 on hazardous wastes

products in a life cycle perspective and identified a number of significant limitations in the European legislation when applied to nanoparticles, such as C_{60} and carbon nanotubes. Table 5 summarises the main limitations identified in the Safety at Workplace Directives, IPPC Directive; REACH; and Waste Management Directives. Our recommendations on how to deal with these limitations are also included in the table.

In order to deal with the limitations of the Safety at Workplace Directives, we recommend that occupational exposure of nanoparticles is limited as much as possible, while international standards for the safe handling of nanoparticles in laboratories and other workplaces is developed. Currently, a great deal of international attention is given to the identification of potential exposure scenarios at workplaces, establishment of standard guidelines for workplaces and laboratories, identification of protection measures and development of efficient metrology infrastructures (NIOSH, 2006). For instance, the EU has funded a number of projects, such as NanoSAFE 1 and 2, with the main purpose of developing methods for detecting, tracking, and characterising nanoparticles along with risk assessment and management procedures to secure industrial production of nanoparticles. Another project, NanoDERM, studies the quality of human skin as a barrier against nanoparticles, which is highly relevant and timely for both workers and consumers (European Commission, 2007).

Because there is no reference to nanoparticles in the IPPC Directive, we recommend that the scope and coverage of the Directive is clarified in regards to manufacturing

plants of nanoparticles. In instances where such installations fall within the scope of the Directive, issuing a specific BREF would help apply the concept of BAT to certain engineered nanoparticles like C_{60} and carbon nanotubes. Although this might be time-demanding and complicated, given the rapid evolution of the processes applied, the procedure would enhance information exchange. We further recommend that the European IPPC Bureau is officially established as an institution that monitors the development of nanotechnologies.[18]

Many environmental laws (e.g. REACH, Directives on hazardous waste, etc.) are based on (eco)toxicological classification of substances. Terms like "toxic" or "persistent" are often used as triggering factors to establish specific regulations, set emission limits, prohibitions and other requirements. These rules acquire a consistent meaning only when (eco)toxicological data are available for a substance. Although work is underway in order to produce such (eco)toxicological data for nanoparticles, much of this work is just getting started. For instance the EU has funded a number of projects (e.g. IMPART-NanoTOX) that attempt to increase the understanding of toxicological impacts of nanoparticles on human and environmental health (European Commission, 2007).

A regulatory gap, on the other hand, emerges when there is insufficient scientific evidence or reliable data. In this context REACH will play a crucial role because it should provide the necessary information to make consistent use of other laws. For this reason we recommend that the incremental approach should be initiated by ensuring an efficient use of this Directive for nanoparticles. Our analysis of the applicability of REACH to the three different products shows that different thresholds and units than those given in mass terms would be more suitable.

The European Commission is considering the possibility of "*reexamining and, if necessary lowering the current 1 ton per annum threshold*" for engineered nanoparticles (European Commission, Health and Consumer Protection Directorate General, 2004). Furthermore, The Royal Society & Royal Academy of Engineering, suggests treating chemicals in the form of nanoparticles or nanofibres as new substances under REACH (Royal Society, 2004). The implementation of this suggestion requires a review of the definition of "new substance" under REACH: should a nanoparticle be defined as a "new substance" only because its dimensions are reduced to the nanoscale? From a chemical point of view, different engineered nanoparticles cannot be equally defined. Some, like fullerenes, can be classified as allotropes of a given substance (carbon) because they have a totally different chemical configuration. Others, like titanium dioxide, are manufactured by decreasing the particle size of a given substance to the nanoscale without altering the basic chemical structure. In the latter case it is incorrect to call it a "new substance". However, at the same time these particles can display extremely altered qualities.

In addition, the regulatory system identifies chemicals according to the CAS classification. The Danish Board of Technology (2006) proposes to classify nanoparticles separately when they display specific properties due to the nanoscale. This could be done either by giving a specific CAS number or by adding an additional code to identify nanoparticles of a given chemical (e.g. CAS-NP_{50}). The two options can be used alternatively in order to catch the differences between nanoparticles manufactured by the "bottom–up" and the "top–down" methodologies. This distinction is necessary to adapt the existing CAS classification to the nanotechnological phenomenon. It is reasonable to assign a new CAS number for those nanoparticles that are arranged in a unique atomic configuration, like C_{60} or carbon nanotubes, and an additional code to the other nanoparticles.

A specific regime should apply for nanoparticles within the REACH Regulation. Nanoparticles can be defined as "particles with at least one dimension <100 nm". A clear distinction between fixed and free nanoparticles is essential to sensibly differentiate obligations between the two cases. A nanoparticle can be defined as "fixed" when it is "embedded in a solid matrix and cannot move so that any exposure to humans or the environment can be excluded during the whole life cycle of the product", and "free" whenever an identified downstream user does not meet this criterion. As for fixed nanoparticles the existing regulations can apply, whereas registration should be required for free nanoparticles with the only exemption for research and development uses. Producers shall be in charge of the registration when they start to commercialise an engineered nanoparticles to a downstream user who makes use of it as free nanoparticles.

Waste management regulations require stricter protective measures for handling, treatment and final disposal of wastes according to their (eco)toxicological characteristics. Since there are reasons to suspect that nanoparticles can display hazardous properties when released into the environment, we recommend introducing "free nanoparticles" in Annex II of the Directive on hazardous waste, which lists the constituents of a waste that render it hazardous.

Despite the many gaps we have identified in this paper as well as gaps in current limitations of European legislation in relation to nanoparticles such as C_{60} and carbon nanotubes, the largest gap we have identified is the lack of access to key information along the life cycle of the products. We intended to take into account the specific properties of nanoparticles produced as well as specific circumstances during the manufacturing of the products in order to capture all limitations of current European legislation. This would require full access to all the relevant information during production, extraction and refining,

[18] As recommended by European Commission, Health and Consumer Protection Directorate General (2004), p. 26.

manufacturing, use and final disposal of the products. However, in several occasions, mapping the life cycle with sufficient detail was problematic due to manufacturers secrecies and non-disclosure policies. Therefore, it was not possible to obtain information on specific production volume of either C_{60} and carbon nanotubes, the number of product units, concentration of nanoparticles in final products, or evaluate the mass flows of nanoparticles from the raw material to the final product. Furthermore quantitative and qualitative characterizations of by-products, such as fullerenic soot and carbon nanotube fibres, as well as their fate could not be exhaustively described. Likewise, public authorities will also have to face the lack of access to key information to monitor the effectiveness of the incremental approach.

6. Conclusions

At the moment, issuing a specific long-term regulation on nanotechnology seems technically problematic and politically improbable. It is therefore necessary to make a consistent use of existing legislation when this can be easily applied as such or suitably amended. In Europe the incremental approach is considered the only practical method to tackle the risks caused by engineered nanoparticles, although no specific intervention has been made on existing regulation to date.

Based on our analysis of gaps within regulation along the life cycle of three different products containing carbon-based nanoparticles, we conclude that it is often unclear if nanoparticles are covered by current legislation. The main problems seem to be that metrology tools are unavailable, thresholds are not tailored to the nanoscale and are based on bulk material, and (eco-) toxicological data and limits cannot be established with existing methodologies. The difficulty to generate universally recognised data along the life cycle of commercially available products puts a limit on the applicability of many laws. An efficient use of the REACH regulation is essential to overcome these limits. Our study shows that particles' properties, (eco-) toxicological data and risk assessments are often necessary to determine the scope of many regulations. As long as there is uncertainty about how to determine these properties unequivocally, many environmental laws remain inapplicable to nanoparticles such C_{60} and carbon nanotubes. Moreover the specific properties of nanoparticles often render them unsuitable for regulation by existing laws. Concentrations given in mass terms are often used to establish thresholds even if a number of toxicological studies indicate that it is not accurate for nanoparticles, since their toxicity generally increases with decreased dimensions (European Commission, Health and Consumer Protection Directorate General, 2004).

We conclude that the "incremental approach" could work effectively, provided due explanations and amendments are taken where necessary.

We recommend that the Chemical Abstract Service is modified so that "bottom-up" engineered nanoparticles are classified separately as new substances and that "top–down" nanoparticles are classified as nanoparticles of existing substances. In both cases particles should be registered specifically under the REACH regulation. Free nanoparticles should be considered hazardous components in the regulation on waste management due to their high exposure potential and their unknown effects on human and environmental health. Finally, we recommend that the development of nanotechnologies is monitored by a working group within the IPPC bureau.

References

Balbus, J., Denison, R., Florini, K., Walsh, S., 2005. Getting nanotechnology right the first time. Issues Sci. Technol. (Summer), 65–67.

Bogdanov, A.A., Deininger, D., Dyuzhev, G.A., 2000. Development prospects of the commercial production of fullerenes. Tech. Phys. 45 (5), 1–7.

Cataldo, F., 2002. A study on the thermal stability to 1000 °C of various carbon allotropes and carbonaceous matter both under nitrogen and in air. Fuller. Nanotub. Car. N. 20 (4), 293–311.

Daenen, M., de Fouw, R.D., Hamers, B., Janssen, P.G.A., Schouteden, K., Veld, M.A.J., 2003.The Wondrous World of Carbon Nanotubes: a Review of Carbon Nanotubes Technologies. Eindhoven University of Technology. Available at: http://students.chem.tue.nl/ifp03/Wondrous%20World%20of%20Carbon%20Nanotubes_Final.pdf (accessed 25 June 2005).

Dahl, S., Bauer, E., Logadottir, A., Egeberg, A., Larsen, J., 1999. Role of steps in N_2 activation on Ru(0001). Phys. Rev. Lett. 83 (9), 1814–1817.

Danish Board of Technology, 2006. Regulering af Miljø-og Sundhedsaspekter ved Nanoteknologiske Produkter og Processer, konklusioner og anbefalinger fra en arbejdsgruppe under Teknologirådet. Danish Board of Technology, Copenhagen (in Danish).

Davies, J.C., 2005. Managing the effects of nanotechnology. Woodrow Wilson International Centre for Scholars, Washington, D.C. Available at: www.nanotechproject.org/file_download/30 (accessed 25 June 2006).

European Commission, Health and Consumer Protection Directorate General, 2004. Nanotechnologies: a Preliminary Risk Analysis on the Basis of a Workshop. European Commission, Brussels.

European Commission, 2007. Nanotechnology Emerging Needs. Available at: http://cordis.europa.eu/nanotechnology/src/pressroom_projects_nmp6.htm (accessed 27 January 2007).

European Commission Scientific Committee on Emerging or Newly Identified Health Risks (SCENIHR), 2005. The Appropriateness of Existing Methodologies to Assess the Potential Risks Associated with Engineered and Adventitious Products of Nanotechnologies. European Commission, Brussels Available at: http://files.nanobio-raise.org/Downloads/scenihr.pdf (accessed 24 June 2006).

Hansen, S.F., Larsen, B.H., Olsen, S.I., Baun, A. 2006. Categorization framework and hazard identification approach of nanomaterials. Environ. Sci. Technol. (submitted for publication).

Huczko, A., Lange, H., Drabik, J., Pawelec, E., 2003. Tribological characteristics of fullerene containing lubricants. AIP Conf. Proc. 591, 561–568.

Kuzma, J., (Ed.) 2005. The Nanotechnology-Biology Interface: Exploring Models for Oversight, Workshop Report. Center for Science, Technology, and Public Policy, Hubert H. Humphrey Institute of Public Affairs University of Minnesota, Minneapolis, MN.

Lam, C.W., James, J.T., McCluskey, R., Hunter, R.L., 2004. Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation. Toxicol. Sci. 77, 126–134.

Maynard, A.D., Baron, P.A., Foley, M., Shvedova, A.A., 2004. Exposure to carbon nanotube material: aerosol release during the handling of unrefined single walled carbon nanotube material. J. Toxicol. Environ. Health A 67 (1), 87–107.

Nano-C, 2002. Masters of Flame: Industrial Production of Fullerenes Becomes a Reality. Nano-C Inc., Westwood, MA.

National Institute for Occupational Safety and Health, 2006. Key Themes Emerge from 2nd International Nanotechnology Symposium. Available at: http://www.cdc.gov/niosh/topics/nanotech/keythemes.html (accessed 25 October 2006).

Oberdorster, E., 2004. Manufactured nanomaterials (Fullerenes, C-60) induce oxidative stress in the brain of juvenile largemouth bass. Environ. Health Persp. 112 (10), 1058–1062.

Ozawa, E., 2005. Nanomaterial Production and Application from Viewpoints of Health and Safety, Joint Workshop between Science Council of Japan and Royal Society of UK. The Royal Society, London. Available at: www.royalsoc.ac.uk/trackdoc.asp?id=2377&pId=3862 (accessed 25 June 2006).

Reynolds, G.H., 2002. Forward to the Future: Nanotechnology and Regulatory Policy. Pacific Research Institute, San Francisco. Available at: http://www.pacificresearch.org/pub/sab/techno/forward_to_nanotech.pdf (accessed 25 June 2005).

Royal Society & Royal Academy of Engineering, 2004. Nanosciences and Nanotechnologies: Opportunities and Uncertainties. Royal Society & Royal Academy of Engineering, London. Available at: http://www.nanotec.org.uk/finalReport.htm (accessed 24 June 2006).

Takeara, H., Fujiwara, M., Arikawa, M., Diener, M.D., Alford, J.M., 2004. Experimental study of industrial scale fullerene production by combustion synthesis. Carbon 43 (2), 311–319.