

Water governance challenges presented by nanotechnologies: tracking, identifying and quantifying nanomaterials (the ultimate disparate source) in our waterways

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ABSTRACT

Nanotechnologies are considered an enabling technology, as they enhance the functioning of a wide range of products and processes. They are increasingly appearing in consumer products, including sun creams, socks and outdoor paints, resulting in the potential for direct access of nanomaterials (NMs) into wastewater and the environment. As such, they could be considered as the ultimate disparate source, with multiple products and multiple routes into the environment, as well as numerous transformation pathways, such that the final form may bear little resemblance to the initially produced form. NMs thus represent a significant governance and regulatory challenge, for a number of reasons, related to their small size, which makes detection challenging, especially against a background of naturally occurring nanoscale entities (clay and sediment particles, etc.), and their large surface area and high surface energy which leads to very dynamic behaviour and a strong tendency to interact with (bind) anything they come into contact with. Some initial considerations of regulatory issues related to Registration, Evaluation and Authorization of Chemicals, the Water Framework Directive, and the potential for benign-by-design approaches exploiting the potential for recovery or recycling of NMs at the design phase are presented, aimed at reducing the risk of unintentional accumulation of NMs in our waterways.

Key words | governance, life cycle assessment, nanomaterials, regulation, tracking, Water Framework Directive

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INTRODUCTION

Nanotechnology is a rapidly evolving 'enabling' technology with the potential to revolutionize modern life. The term enabling is used to convey the fact that nanomaterials (NMs) and nanotechnologies are appearing in, and enhancing, a myriad of other technologies and cut across numerous industrial areas, such that it is difficult to identify an area where nanotechnologies are not present. Indeed, nanotechnologies are one of Horizon 2020's Key Enabling Technologies (European Commission 2013). NMs are already widely applied in several sectors: in consumer products (e.g., self-cleaning textiles, sunscreens, food

packaging), in medicine (e.g., as drug delivery vehicles and contrast agents for imaging), for environment friendly applications (e.g., as substitutes for hazardous chemicals), in environment remediation technology (e.g., iron oxide NMs are applied in soil and groundwater contamination) and other fields (see Figure 1 for a schematic overview of the application areas). The global market for NMs is estimated at 11 million tonnes at a market value of €20 billion, with the current direct employment in the NM sector estimated at up to 400,000 in Europe alone (European Commission 2011a). To date, the market is still dominated by materials

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their small size which allows them to reach sub-cellular organelles and cross biological barriers (Garbayo *et al.* 2014) and their unique electrical and conductance properties and enormous strength (Wang *et al.* 2014).

With increased use of nano-enabled products, increasing human and environmental exposure is inevitable. Indeed, as a result of the widespread use, including via consumer products, release of NMs into the environment from consumer products could be considered the ultimate disparate source, with tracking of which NMs came from which products/users almost impossible at present. Another difficulty comes from the fact that engineered NMs are not the only source of nanoscale particles in the environment: many industrial processes produce so-called anthropogenic nanoparticles, including combustion and mining, as shown in Figure 2. The combination of anthropogenic sources of nanoscale particles with the occurrence of natural colloids in the environment (such as clay particles and humic substances in aquatic systems)

makes detection of engineered NMs a significant challenge currently.

Despite the widespread use of NMs in consumer and industrial products, understanding of the health and environment safety aspects of NMs is still in its formative stage, and the applicability of existing risk assessment methods for use with NMs is still being validated for use with NMs (Kühnel & Nickel 2014). Indeed, regulation of NMs is in a critical state of flux currently, with the European Commission's 2011 definition of a NM for regulatory purposes reviewed in 2014 given the lack of methodologies to implement it (European Commission 2011b) (the outcome of which has yet to be published (March 2016), and indeed consultation is ongoing as to the need for modification of the Annexes of the main EU legislation for chemicals (Registration, Evaluation and Authorization of Chemicals (REACH)) for use with NMs. Indeed, it has been suggested that given the multiple application and exposure sources, regulatory authorities may need to

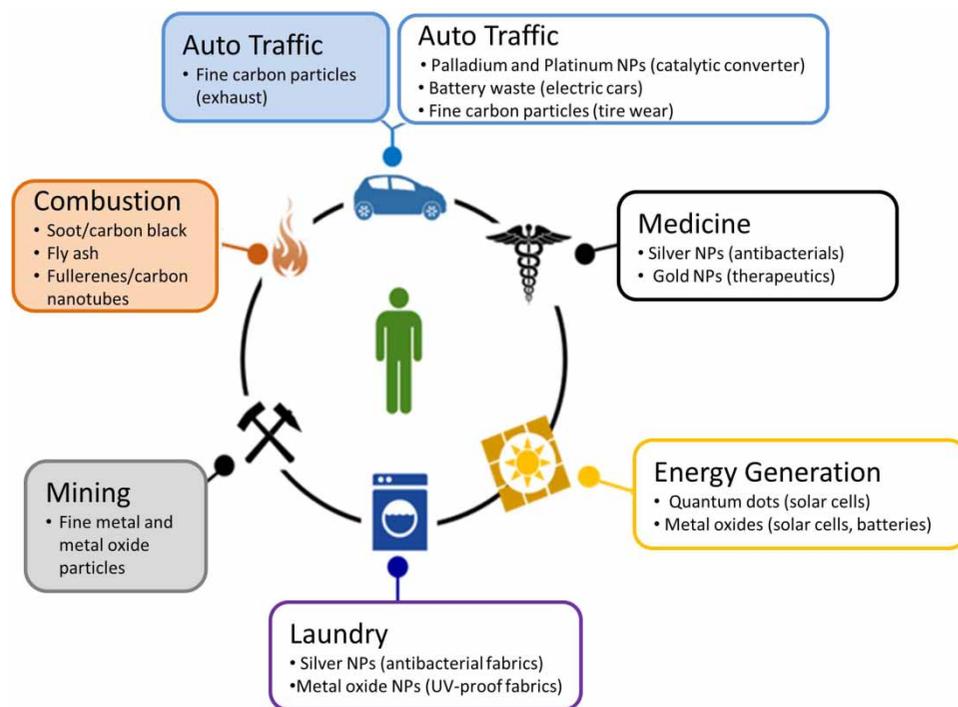


Figure 2 | Examples of major sources of NM release into the environment from nano-enabled products, as well as from anthropogenic activities (shaded boxes) such as mining and combustion, which also produce nanoscale particles. The term engineered NMs is used to distinguish those intentionally produced for specific applications or to exploit specific functions. In the case of Auto Traffic, anthropogenic particles are produced as a result of combustion to run the car, while intentionally added NMs (e.g., palladium catalysts, CNTs in tyres) can also be released during use. Release from consumer applications is typically into wastewater streams, while from energy generation, automobiles, paints, agricultural use, etc. is typically into surface water and from there into the ground, into freshwater bodies, or into wastewater treatment.

aggregate (e.g., add) drinking water exposure to other routes of exposure to come up with more accurate risk estimates (Tiede *et al.* 2016). A significant limitation of most of the ongoing work on nanosafety in Europe is the strong bias towards toxicology at the expense of ecotoxicology, and the lack of an integrated value-chain and ecosystem approach that considers whole life-cycle aspects, including product disposal and potential for NM recovery and reuse/recycling. Just as the development of ecotoxicology has lagged behind that of toxicology, nanoecotoxicological research has developed much more slowly than nanotoxicology: although the first nanotoxicology papers were published in the 1990s, the first nanoecotoxicology papers came out in 2006 (Kahru *et al.* 2013). Thus, an increasing body of scientific evidence would suggest that some materials in their nano-form may induce harmful biological or environmental effects through a variety of potential mechanisms, not all of which are fully understood or quantified as yet.

A consequence of the slow pace of development of nanoecotoxicology is that there is currently a gap in terms of understanding and awareness among both hydrologists (scientists), policy-makers and those charged with implementing the Water Framework Directive (WFD), the single most important piece of environmental legislation in Europe regarding water bodies and their quality. The current paper aims to highlight some of the challenges presented by NMs in terms of the WFD, and begin the processes of building stakeholder awareness and engagement with a rapidly emerging environmental/hydrological governance issue.

NM FATE AND TRANSFORMATION IN THE ENVIRONMENT: CHALLENGES FOR GOVERNANCE AND REGULATION

Due to their high surface area to volume ratio, NMs have a high surface energy that they seek to lower by binding to available macromolecules from their surroundings, be they inert components of product formulations (e.g., polymers, oils, etc.), the proteins or lipids in living systems, or the natural organic matter components of water or soil (Lynch *et al.* 2014). This ubiquitous phenomenon of formation of layer of bound molecules around NMs has been termed the protein

(Cedervall *et al.* 2007), biomolecule (Walczyk *et al.* 2010) or macromolecule corona (Lynch *et al.* 2014), and occurs instantaneously upon contact with available macromolecules, whatever their source (e.g., product formulation, living organisms or the environment). In the environmental context, interactions of NMs with environmentally relevant macromolecules (e.g., exopolysaccharides or humic substances) may be a significant source of NM transformations altering their surface properties and subsequent biological interactions, conferring an environmental identity to NMs, in analogy with the synthetic and biological identities defined for NMs in biological fluids/toxicological studies (Fadeel *et al.* 2013).

A recent review of the environmental transformation of NMs categorized the types of transformation reactions undergone by NMs as chemical (e.g., photooxidation and photoreduction), physical (e.g., agglomeration or dissolution), biological (e.g., oxidation and carboxylation) and interactions with biomolecules, including natural organic matter (NOM, a complex polydisperse polymeric mixture, whose properties echo their structural diversity, state of aggregation, conformation, and surface charge distribution), all of which ultimately influence NMs' persistence, bioavailability/biouptake, reactivity and toxicity (Lowry *et al.* 2012). An important consideration when considering NMs is that the form in which they are released can be quite significantly different from the form they had at the time of manufacture, as a result of interactions with their formulation and product components, which can change the state of agglomeration/dissolution and other interactions of the NMs, as illustrated schematically in the inner hemispheres of Figure 3 (Szakal *et al.* 2014). This increases the variability of NMs, and each of these product-transformed NMs can then undergo a range of further environmental transformations upon release into the environment during use or at the end of life, and following interaction with organisms present in the receptor (e.g., aquatic or sediment dwelling organisms in the case of release into aquatic environments), as illustrated in the outer hemispheres of Figure 3. The important thing to note here also is that as the matrix complexity increases, so also does the analysis challenges, in terms of detection of the NMs and their characterization (Szakal *et al.* 2014).

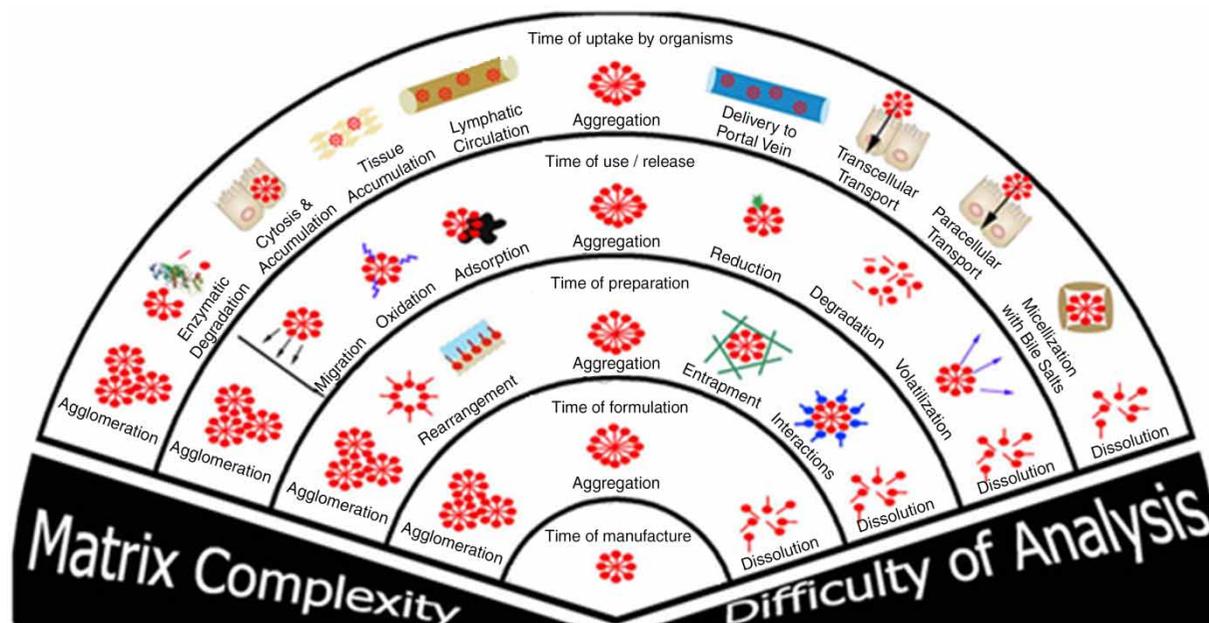


Figure 3 | Potential modes of destabilization through the lifecycle of a NM from the time of manufacture to potential biological interactions following uptake (by ingestion here although similar processes would occur following inhalation or intravenous exposure) and the complexity/difficulty of sample quantification and detection. Adapted from Szakal *et al.* (2014).

A key confounding factor in the fate and behaviour of NMs, unlike conventional chemicals, is thus that they are highly affected by their surroundings, transforming chemically, agglomerating, and/or acquiring an evolving coating of environmental or biological macromolecules, which provides them with an ‘environmental’ identity that is derived from their initial ‘synthetic’ identity. Factoring this context-dependence into assessment of the fate, behaviour and impacts of NMs is essential to move forward in terms of ensuring the safe implementation of nanotechnologies, and to facilitate the widespread application of NMs in environmental applications and for the improvement of ecosystems services. This context-dependence of NMs, resulting from their interaction with their surroundings, provides a useful way to identify key areas where NMs may behave differently from molecular species (conventional chemicals) from the perspective of governance and regulation (Malkiewicz *et al.* 2011), specifically in the context of REACH, but equally applicable to the WFD. As many NMs are metal based, it is important also to consider the extensive knowledge of metal environmental fate, and extrapolate as much as possible from this understanding. Table 1 summarizes some of the main differences between

NMs, and molecular chemicals, including the fact that interactions with their surroundings can lead to:

- Dramatic changes in NM size distribution, as a result of either particle aggregation (Yue *et al.* 2015) or improved particle dispersion (Metrevell *et al.* 2014) and thus the available NM dose.
- Changes in NM surface properties, including changes in surface molecule presentation, changes in zeta potential, changes in surface reactivity, etc.
- The potential for secondary toxicity effects resulting from, for example, nutrient deletion leading to organism starvation (van Hoecke *et al.* 2009), blocking of light due to NM sticking to organism surfaces and interfering with photosynthesis, and/or interference with assay read-outs as a result of adsorption of the reporter molecules to the NM surfaces (Kroll *et al.* 2012).
- The potential for ‘Trojan horse’ or co-operativity type effects, where other pollutant species adsorb to the NM surface and are transported into organisms they would not normally interact with, and where the resultant toxicity is not related to the nanoscale, but is a consequence of it (Auffan *et al.* 2012). An alternative form of this is the

Table 1 | A summary of the main differences between conventional chemicals and NMs as they relate to risk assessment under REACH and the WFD, extended from Malkiewicz *et al.* (2011)

Property	Molecular species	Metal ions	NMs
Interactions with surroundings	Limited	Extensive – affects speciation/solubility	Extensive – take on a ‘biological identity’
Cellular uptake mechanism	Diffusion	Several metals are selectively transported across membranes	Actively transported via energy-dependent, receptor-mediated processes
Cellular exit processes	Diffusion	Active transport via protein transporters	None identified as yet – cell division splits nanoparticle (NP) load equally between daughter cells Potential for specific exit signals to be added to particle surfaces
Potential for ‘evolution’	Metabolism	Speciation Adsorption	Dissolution Aggregation Metabolism? Biotransformation? Degradation Many of these changes not yet well understood
Mechanisms of action	Mostly known	Mostly known and related to bioavailable species	Unknown as yet – it is unlikely that NMs, which engage with the cellular machinery would have similar mechanisms of action as chemicals, although if dissolution occurs the free metal ions will behave as metals. Thus, a critical gap at present is the lack of validated positive and negative control NPs for a range of biological endpoints

lysosomal Trojan-horse effect, whereby localization of NMs in the lysosome and subsequent particle dissolution at the low pH of the lysosome leads to much higher local concentrations of ionic metals than would have occurred by direct uptake of the ionic forms (Sabella *et al.* 2014).

- Renewal or exchange of their biomolecule corona as they are actively transported from one location to another by organisms (e.g., as they pass through biological membranes via receptor mediated processes) (Lundqvist *et al.* 2011).
- Potential for interaction of NMs with signaling molecules (semiochemicals) secreted by organisms as part of intra- or inter-species signalling networks of attractants and repellents, e.g., pheromones, allomones, kairomones, etc. (Lynch *et al.* 2014).

Comparison between metal ions and (metal) NMs is also included in Table 1, since there are several metal uptake transporters, cellular exit pathways and specific protein interactions involved in their regulation within cells (Finney & O’Halloran 2003). Additionally, metal

speciation in the environment is very well understood, as well as the connection between species solubility and aquatic toxicity (Hughes & Poole 1991; Hartmann *et al.* 2014).

Many of the most toxic NMs to aquatic species are those metal and metal oxide NMs that undergo rapid dissolution and where the ionic form (the dissolution product) is toxic, e.g., silver (Yue *et al.* 2015), zinc oxide (Khan *et al.* 2013) and copper oxide NMs (Thit *et al.* 2015), and many quantum dots (Mahendra *et al.* 2008). From a regulatory perspective, once a NM has dissolved back to ionic or molecular components, classical approaches apply and the nano-form no longer needs to be considered (Kookana *et al.* 2014). For metals, toxicity mechanisms are well understood, as is environmental fate (Lopes *et al.* 2011). However, dissolution of NMs is complex, affected by NM properties such as size, agglomeration and surface coatings and bound corona, as well as solution properties such as ionic strength, pH and temperature (Misra *et al.* 2012; Izak-Nau *et al.* 2015), and natural precipitation (e.g., as hydroxides or via reduction) or

re-precipitation of dissolved metals (such as Ag^+ and Cu^{2+}) can also occur in the environment (Manoharan *et al.* 2014), further complicating matters. This suggests that precipitation as nanoparticles (NPs) is part of the natural cycle for Ag and Cu, and thus that biology has adapted mechanisms to deal with high concentrations of bioavailable cytotoxic ions. It is noteworthy that precipitation of excess and/or toxic misfolded proteins is a hallmark of several diseases (e.g., Alzheimer's) and it is likely that this is a conserved defence mechanism whereby in particulate form the metals are less toxic. This is consistent with the literature on NMs' aquatic toxicity, which has found generally that NMs are less toxic than the equivalent free ion, although exceptions exist (e.g., related to the Trojan-horse effect, or where the particulate form causes, for example, physical disruptions (e.g., blocking channels/gills, shading, impeding swimming, etc.) (Ma & Lin 2013). Thus, although classical models may provide guidance for understanding dissolution and aggregation of NMs in water, it is the detailed surface structure and surface chemistry that are needed to accurately describe the surface free energy, a large component of the total free energy, in order to fully understand these processes (Mudunkotowa & Grassian 2011). Without this information, it is difficult to develop a conceptual framework for understanding the fate, transport and potential toxicity of NMs.

WFD AND NMS

Water governance is the set of rules, practices and processes through which decisions for the management of water resources and services are taken and implemented, and decision-makers are held accountable (OECD 2011). Water governance addresses among other things:

- Principles such as equity and efficiency in water resource and services allocation and distribution, water administration based on catchments, the need for integrated water management approaches and the need to balance water use between socio-economic activities and ecosystems.
- The formulation, establishment and implementation of water policies, legislation and institutions.
- Clarification of the roles of government, civil society and the private sector and their responsibilities regarding

ownership, management and administration of water resources and services.

In addition to REACH, the EU WFD is the single most important piece of environmental legislation in Europe when it comes to dealing with NMs in the future given their widespread and dispersive use (Hansen *et al.* 2011). While REACH deals with the manufacturing and import of chemicals, the WFD is directed towards reducing the presence of dangerous chemicals (i.e., 'priority substances') in European waters (Hansen *et al.* 2011). The WFD has triggered the re-organization of water management by hydrological catchments, rather than by administrative borders, with the ultimate goal to improve the quality of surface water bodies (Hering *et al.* 2010). It has also resulted in a change of focus from pollution control to ensuring ecosystem integrity as a whole, with deterioration and improvement of 'ecological quality' being defined by the response of the biota, rather than by changes in (water) physical or chemical variables (Hering *et al.* 2010). The WFD was designed to focus on 'traditional stressors', such as eutrophication, organic pollution, acidification, toxic stressors and, to a lesser degree, hydromorphological pressure; however, other stressors have more recently come into focus, such as climate change, siltation, new toxic substances and alien species which may require adaptation of the WFD to encompass them (Hering *et al.* 2010).

A review of the overlap/complementarity of REACH with other significant EU legislation, performed by Milieu Ltd for DG Environment of the European Commission, identified important links between REACH and the WFD, as both focus on particularly hazardous substances – substances of very high concern (SVHC) under REACH and priority substances under the WFD (Milieu Ltd 2012). Additionally, REACH makes direct reference to the WFD as it states that it shall apply without prejudice to 'environmental legislation, including [...] Directive 2000/60/EC'. In other words, the application of REACH requirements should not permit circumvention of the requirements of the WFD, i.e., stricter conditions than REACH can be set up in permits for water discharge. This applies as well to the Environmental Quality Standards (EQS) Directive as a daughter directive to the WFD (Milieu Ltd 2012). In addition, the WFD recognizes that the selection of priority substances

should take into account information from REACH risk assessments (during registration or substance evaluation) or use REACH methodology: Article 16(2) of the WFD makes reference to Council Regulation (EEC) No. 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances which has been repealed by REACH. Pursuant to Article 139 REACH, references to the repealed acts shall be construed as references to REACH (Milieu Ltd 2012). Similarly, data derived while implementing the WFD can feed into the REACH process, for example, the monitoring data generated under the WFD can be used in carrying out REACH assessment and authorization in order to avoid double regulation (Milieu Ltd 2012). Where a REACH authorization concerns a substance considered as a priority hazardous substance under the WFD, authorization under REACH should not be granted if the use could lead to a breach of the legislation on water, as discharges, emissions and losses of these substances should cease or be phased out according to the WFD (Milieu Ltd 2012).

However, according to the report, there are some discrepancies between REACH and the WFD. For example, the various risk management measures set up by water-related legislation are not comparable with the risk management approach followed under REACH, although there are significant links, since information from registration and hazard assessment carried out under REACH can be used for setting or revising EQS for water (Milieu Ltd 2012). Most of the substances currently regulated under the WFD are also covered by REACH. However, a few cases were highlighted in the Milieu report, where the scope of the relevant water legislation exempts or covers substances that are themselves partially exempted from REACH, for example, active substances for plant protection products and biocides or substances used in medicinal products for human or veterinary use that are only partially covered by REACH (Milieu Ltd 2012).

Foss-Hansen and colleagues have assessed whether the WFD covered NMs as effectively as other pollutants, such as xenobiotic organic chemicals and heavy metals, and considers whether NMs could be considered as possible candidates for selection as priority substances (Hansen *et al.* 2011). However, given the enormous compositional and property variability of NMs, further sub-classification

is required, and thus the authors suggest that emerging (eco)toxicological evidence as well as the possibility of widespread environmental contamination of certain NMs (determined on the basis of systematic mapping of NM production volumes, product concentrations, market penetration, dispersive vs. non-dispersive uses) should be used to select priority substances (Hansen *et al.* 2011). This approach suggests 'upstream monitoring' rather than the traditional focus on environmental monitoring downstream which measures actual concentrations, in light of the numerous challenges highlighted above in terms of NMs' environmental transformations and difficulties in detection against a background of similarly sized naturally occurring colloids and particles.

A central tenet of the WFD is the establishment of a single EQS for specific priority pollutants, which specifies the maximum permissible concentration of a potentially hazardous chemical in an aquatic sample. To be sufficiently robust to allow establishment of EQS values, available data must not be subject to excessive uncertainty and, with some development, the analytical capacity should be adequate for compliance assessment purposes (EPA 2007). Substances that are toxic, persistent and liable to bio-accumulate or which give rise to an equivalent level of concern are considered as hazardous substances under the WFD, and as such are given priority substance status. To derive an EQS for a priority substance, the WFD outlines that test results from both acute and chronic ecotoxicological standard tests should be used for the 'base set' organisms, i.e., algae and/or macrophytes, crustacean and fish (Baun *et al.* 2009). As shown in the inset of Figure 4, the starting point for setting an EQS for surface water (defined as the maximum annual average concentration) is the Predicted No-Effect Concentration (PNEC), determined from lowest available effect concentration obtained using base-set organisms divided by an assessment factor taking into account the nature and quality of the available data, as described in the EU Technical Guidance Document for risk assessment of chemicals (European Commission 2003; Baun *et al.* 2009). An additional assessment factor may be used to taking account of the risk of secondary poisoning, related to substances' degradability and bioaccumulation.

Baun *et al.* (2009) assessed the likely scenarios if a NM should be considered a 'priority substance' in the WFD

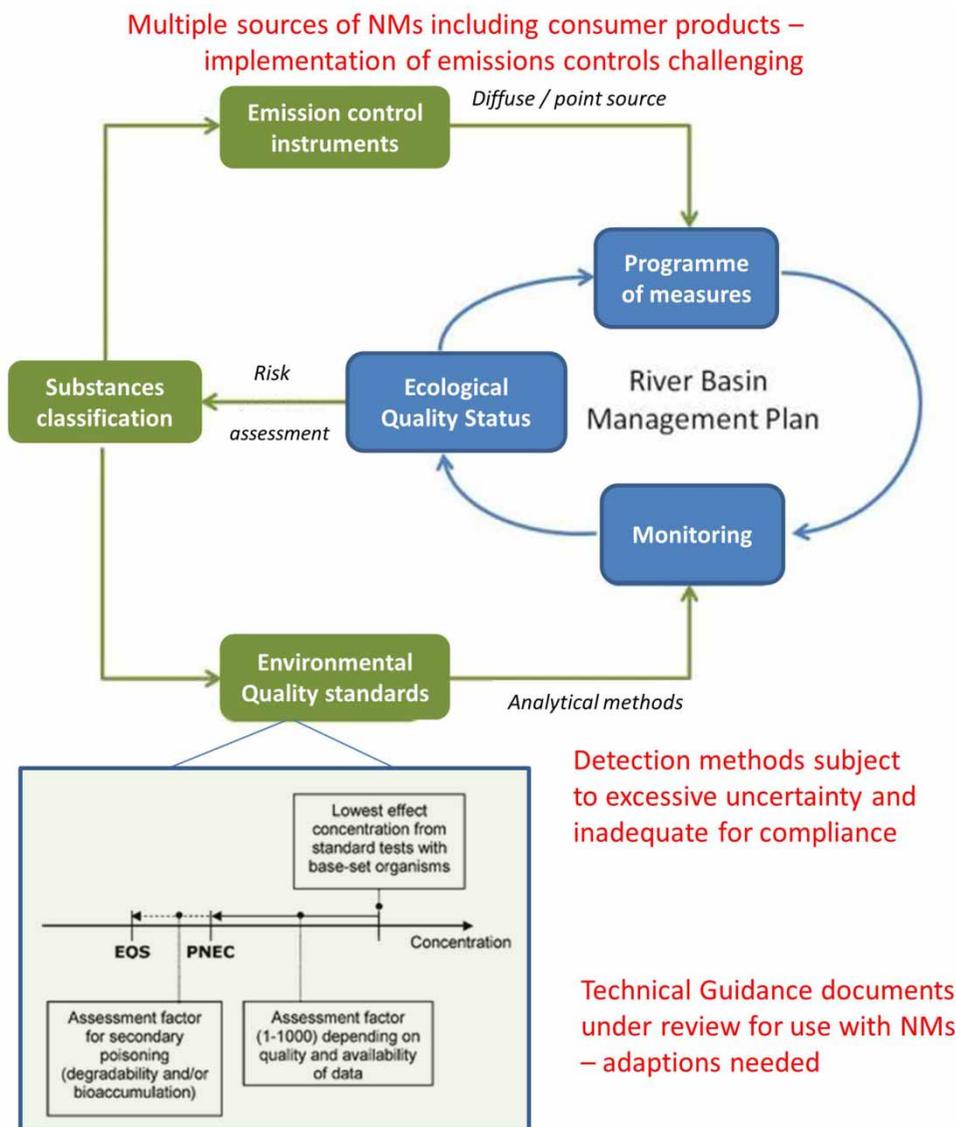


Figure 4 | The principle for setting EQS for surface water, based on predicted no-effect concentrations and using assessment factors from results of standardized ecotoxicity tests with fish, crustaceans and algae. The placement of an EQS in the overall implementation of the WFD is also shown, along with the challenges related to NMs from the monitoring perspective (limits of detection too high for environmentally realistic concentrations) and the emissions control instruments' perspective (lack of validated approaches and challenges to implement regulatory instruments) that would prevent NMs from being classified as a priority substance at present.

using literature on the aquatic toxicity of carbon- and metal-containing NMs and in light of principles to establish EQS. If a NM were to be included in the list of priority substances based on environmental occurrence or hazard information, an EQS would have to be defined (see Figure 4). The authors concluded that given the data available in 2009 it was impossible to set limit values for NMs in surface waters now and in the foreseeable future due to the extensive lack of knowledge not only in relation to

unknown toxic effects, degradability, and bioaccumulation of NMs in the aquatic environment, but also due to the questionable validity of test systems and methods to establish EQS (Baun *et al.* 2009). Indeed, the lack of validated methods and approaches for detection and quantification of NMs in products and in complex matrices has also been highlighted as one of the main challenges with implementation of the EU definition of a NM for regulatory purposes, which defines a NM as having >50% by

particle number of particles in the size range 1–100 nm (Roebben & Rauscher 2014). Baun *et al.* identified two fundamental challenges in regard to developing a feasible and effective monitoring methodology of NMs in environmental samples: that the detection limits for most methods are not sufficiently low to detect environmentally relevant concentrations of NMs in the range of ng L^{-1} – pg L^{-1} (Hassellöv *et al.* 2008) and the aforementioned challenges in terms of distinguishing between engineered NMs and the high background concentrations, since these may have different toxicological profiles. The challenges are summarized in Figure 4 which shows the stages in implementation of the WFD.

While significantly more ecotoxicology data are available now (see for example Table 2 summarizing the aquatic ecotoxicology data from 154 studies (Jackson *et al.* 2013)), the above challenges remain as evidenced by the extremely wide range of toxicities indicated. This also reflects the huge variability in the materials themselves, which can be functionalized in numerous different ways, and can be rigid or flexible, leading to hugely different toxicological effects (Nagai *et al.* 2011). Thus, while PECs and PNECs can now be determined, the issues regarding the suitability of standard chemical testing methods for use with NMs are still being assessed (as per the OECD Expert Group meeting in 2013 (Kühnel & Nickel 2014), and the subsequent and ongoing efforts to revise the OECD Test Guidelines for use with NMs). Additionally, given the pressure to fill knowledge gaps and facilitate risk assessment and regulation of NMs, there has been a convergence of testing using just the narrow range of OECD test species, detracting from the ability to perform species sensitivity distributions.

INTERPLAY BETWEEN WFD, REACH AND DRINKING WATER AND WASTE WATER DIRECTIVES

The Drinking Water Directive (80/778/EEC) sets standards for the quality of water intended for human consumption, and its implementation in the UK (for example) requires local authorities to take appropriate steps to keep themselves informed about the wholesomeness of public and private water supplies in their area and notify the water authority if not satisfied; and sets raw water standards for the quality of surface water to be used as sources of public water supply, among other requirements. A recent study, taking a worst case scenario approach, assessed whether, and how much, NMs might reach the drinking water supply following both advanced membrane-based reclamation and simpler conventional wastewater treatment: findings indicated worst case removal could lead to tap water concentrations of up to $3.3 \mu\text{g L}^{-1}$ (Ag), $13 \mu\text{g L}^{-1}$ (TiO_2) and $0.25 \mu\text{g L}^{-1}$ (ZnO) (Kirkegaard *et al.* 2015). Treated wastewater often ends up in recipients such as rivers, lakes and oceans, where it may, planned or unplanned (de facto), become an indirect source of drinking water supplies (Kirkegaard *et al.* 2015). Thus, water governance models, and directives related to water quality, need to begin considering sources, fate and implications of NMs, and engage in the ongoing dialogue proactively, rather than waiting until environmental health issues arise or using the data and methodology gaps as reasons not to engage.

Building awareness of these challenges among water governance and water quality professionals is central to ensuring that when companies approach environmental organizations, local authorities or water management companies with queries regarding how to handle/manage NM-exposed or

Table 2 | Summary of findings regarding aquatic ecotoxicity of different forms of carbon nanotubes (CNTs, single-, double- or multi-walled) from 154 studies (Jackson *et al.* 2013). Classification of the toxicity is according to European Commission Guidance 93/67/EEC

		Extremely toxic (<0.1 mg/L)	Very toxic (0.1–1 mg/L)	Toxic (1–10 mg/L)	Harmful (10–100 mg/L)	Not toxic (>100 mg/L)
SWCNT	Invertebrates	X	X	X		
	Vertebrates		X			X
DWCNT	Invertebrates		X	X	X	
	Vertebrates			X		X
MWCNT	Invertebrates		X	X	X	
	Vertebrates				X	X

containing wastewater, they receive appropriate expert advice. Informal conversations with small and medium-sized enterprises (SMEs) involved in production of NMs suggest that the relevant authorities currently have no idea what to do in these scenarios and have no advice to provide to companies.

BENIGN-BY-DESIGN CONSIDERATIONS

Emerging considerations of end-of-life cycle and waste treatment and potentially recovery of NMs, especially for high value NMs, has led to the concept of benign-by-design, whereby end of life aspects including the potential for recovery of components and recycling are included at the design phase. Coupling this with the more well-established toxicity-reduction approach of safe-by-design NMs, and an integrated approach to ecotoxicity assessment that focuses not just on individual species toxicity, but includes food chain effects and a more holistic approach to assessing ecosystems services impacts, results in an entirely new paradigm for ecofriendly NMs. This approach is applicable for NMs intended for wide-scale environmental use, in parallel with the safe-by-

design concept for NMs intended for use in medicine or consumer products. Figure 5 shows a typical product value chain (Porter 1988), i.e., the set of activities that a firm operating in a specific industry performs in order to deliver a valuable product or service for the market, mapped to the risk assessment framework paradigm, showing the interplay between human and environmental toxicities, confirming that safety and recyclability considerations can be developed in parallel as part of product development.

Porter's value chain model, which considers every aspect of a company's logistics as an arrow (see Figure 6) is a useful model to utilize for consideration of opportunities for multi-stakeholder approaches to benign-by-design aspects of NMs' production and subsequent use in, for example, consumer products. Thus, by connecting the inflows and outflows from NM manufacturers to producers of nano-enabled products (i.e., products containing or utilizing NMs) and identifying synergies and opportunities for re-use of waste NMs from one value chain as inputs to another, or indeed assessing opportunities for manufacturers and wastewater treatment operators to cooperate in recovery and re-use of 'released' or emitted NMs, new strategies for reducing

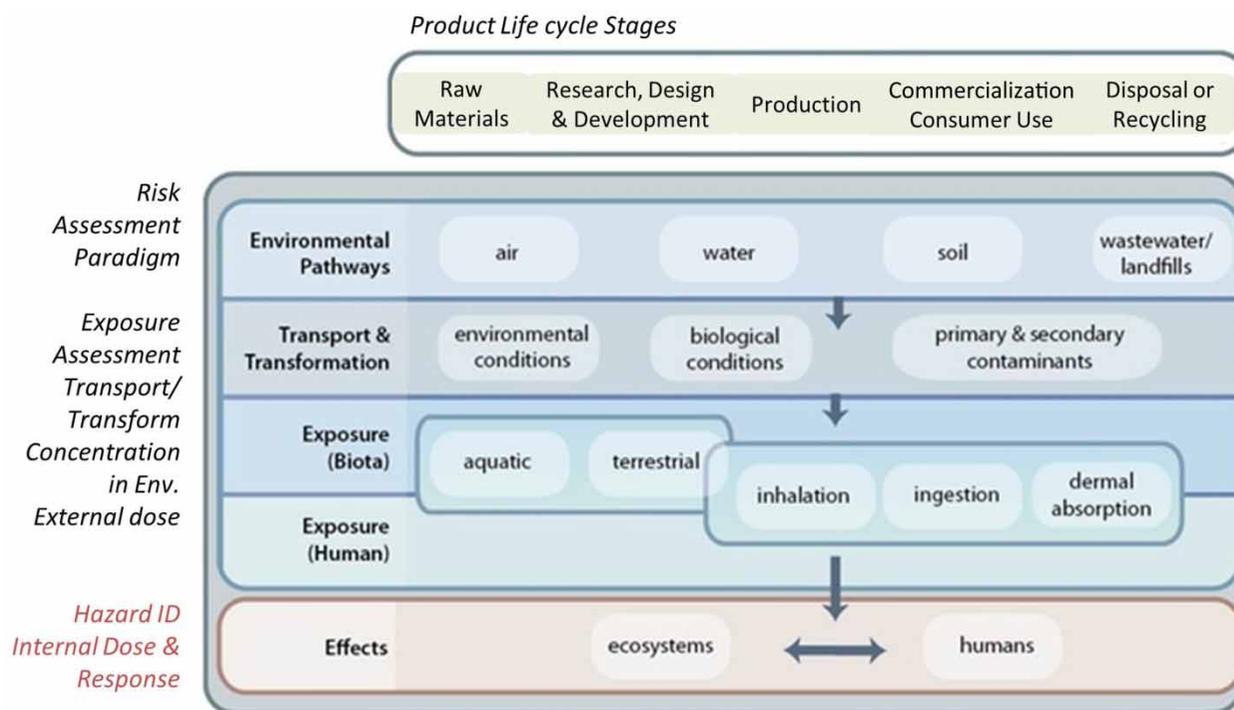


Figure 5 | A typical product value chain from raw materials, through production, product use and disposal, mapped to the risk assessment framework paradigm, showing the interplay between human and environmental toxicities.

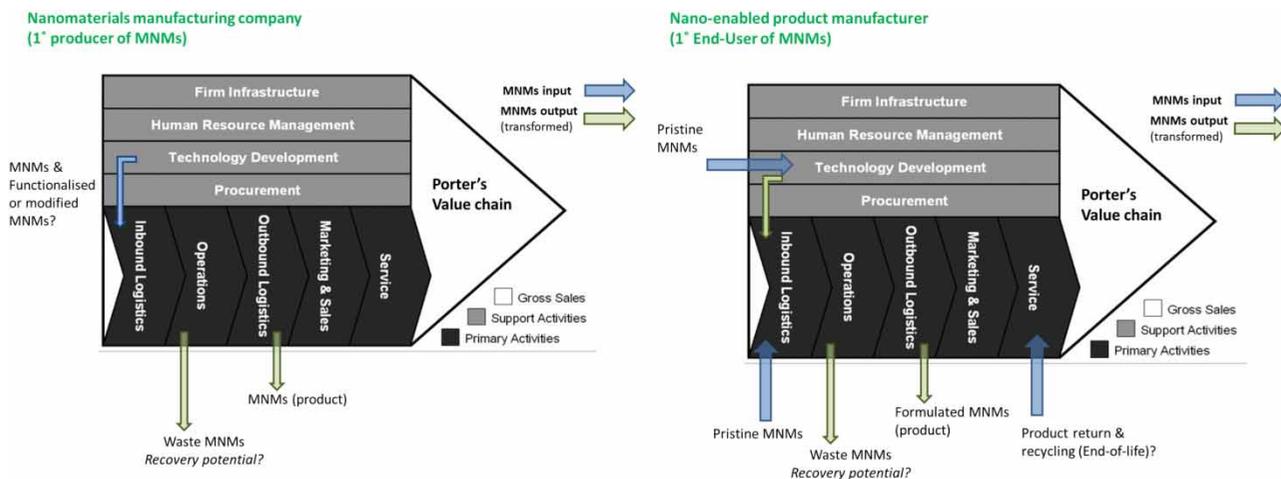


Figure 6 | Using Porter's value chain model, and giving examples of NM producers (left side) and a user of NMs who formulates NMs into another product or process (right side), we demonstrate where and how benign-by-design principles can be utilized to add value and ensure environmentally safe implementation of technologies. Further along the value chain, industry can also assess whether there is scope to build recyclability of NMs into their processes, which could even be considered as a partnership with local wastewater treatment plants for example, and/or include options for product manufacturers via product return schemes (such as operate very effectively for electronic products).

environmental footprints, and benign-by-design approaches emerge. Water governance and water quality management professionals could play a lead role in this, if presented as a means of value creation in partnership (i.e., the 'carrot' rather than using the regulatory 'stick').

Additionally, value chain considerations can include assessment of how NM synthesis or processing routes impact on the resulting structure and surface strain or energetics of the NMs, with the goal of obtaining a balance between function and safety. For example, it is emerging that flame-generated NMs (e.g., SiO₂) are much more reactive (toxic) than other forms of amorphous SiO₂, as a result of strained bonds at their surface (Zhang *et al.* 2012), and thus alternative routes, or use of a passivating shell layer while maintaining specific functional properties of their core material could be considered (Gass *et al.* 2013) and could result in safer NMs being supplied as the raw materials input stage for NM users (Figure 6, right). Similarly, consideration of sources of NM release during producing/processing can also facilitate consideration of where potentially transformational interactions may occur in order to mitigate against these, and more importantly, may identify opportunities where NMs may be recovered and recycled. Two examples of use of the value chain approach for identification of potential benign-by-design approaches to NMs and NM-enabled product development are given in Figure 6 for illustrative purposes. For example,

understanding that NM dissolution is a key driver of toxicity will allow NM manufacturers to develop NMs with slower dissolution, and NM users to assess whether slower dissolution alternatives of similar composition can be utilized to achieve the same desired effect. Additionally, this approach can be utilized to identify sources of interactions of NMs and assess whether these will result in conformational changes or membrane damage (for example) and whether alternative surfaces would mitigate this, etc.

Since many of the waste outputs may contain NMs, which are often discharged into wastewater or into ponds (for example), consideration of the recycling or re-use capability, or indeed the potential re-use of the NMs by manufacturers with lower grade technical specifications, could have significant impacts in terms of reducing NM concentrations and build-up in aquatic systems, and thus lowering the burden for WFD monitoring and compliance. Leadership in this approach could be driven via water governance considerations and be provided by water quality management professionals.

TOWARDS TRACKING OF NMs IN THE ENVIRONMENT

As indicated above, key challenges with detection of NMs in the environment are: (1) the multiple sources and applications of NMs in both consumer and industrial products

and processes, leading to them being an extremely disparate source which makes pinpointing specific sources difficult; and (2) the presence of high background concentrations of nanoscale particles/ionic components in the media. For example, *Dybowska et al. (2011)* showed that dietary Zn (NM) concentrations as high as $5,000 \mu\text{g g}^{-1}$ are required to detect Zn accumulation in freshwater snails beyond that of background. However, an exposure concentration of $5,000 \mu\text{g g}^{-1}$ represents a Zn concentration above even the highest observed in a polluted environment (e.g., close to a mining site) (*Luoma & Rainbow 2008*). The only circumstances under which such a concentration could be found naturally would be related to a large spill, for example, and here the source would be clear such that identifying it is not a challenge. Distinguishing from the background concentration could also be achieved by comparison to nearby areas unaffected by the spill. Thus, for the subsequent paragraphs, the focus is on potential approaches that could be embraced/supported as part of an overall water governance strategy to facilitate detection and quantification of NMs in field studies and/or monitoring programmes, and which could, in parallel or as a separate activity, be utilized to help determine provenance of NMs and allow tracing of NMs detected in water bodies to be tracked back to source (so overcoming the disparate sources challenge).

Thus, an important challenge encountered in detection and monitoring of metal-containing (e.g., metallic, metal oxides, metal sulphides) NMs is to differentiate between the background metal concentration and the newly accumulated metal resulting from exposure to NMs. This problem is especially acute for, although not limited to, those elements essential for organisms such as copper or zinc, which naturally occur in relatively high concentrations in biological tissues. One of the common approaches used to negate the contribution of background concentrations is to determine metal concentration in a subsample of unexposed organisms and subtract this 'background' from the concentration measured for each experimental organism; however this approach has several shortcomings, including the fact that individual variability in the background metal concentration is ignored, which can generate large errors. Another promising alternative, which has been used to conduct laboratory and field exposure studies using low concentration, is through

labelling techniques, where the NMs can be labelled with (i) dyes/phase contrasting agents, (ii) radio isotopes or (iii) an enriched stable isotope. Use of a label is especially appropriate if the goal is to work at the relatively low concentrations, which would be expected in real contaminated environments. Issues exist with the reliable attachment of certain labels to the NMs which can result in detection of uptake of the free label (*Tenuta et al. 2011*; *Mahon et al. 2012*), and with the handling of radioactive labels. The use of an enriched stable isotope, if successful, provides a powerful and reliable alternative for detection and quantification of engineered NPs following short time exposures even at environmentally realistic concentrations (*Dybowska et al. 2011*; *Khan et al. 2013*). An isotope can be defined as one of two or more species of atoms of a chemical element with the same atomic number and nearly identical chemical behaviour but with different atomic masses. Stable-isotope enriched NMs have been used for assessment of NM fate and behaviour in the environment and offer an important potential approach for detecting engineered NMs from background ones. While this approach increases the cost of the NMs significantly, it is likely that even a small proportion of a NM sample being stable-isotope enriched should be enough to facilitate confirmation of the presence of engineered NMs rather than naturally occurring ones, for monitoring and water quality compliance purposes, should NMs be added to the list of priority substance under the WFD in the future.

Another area of emerging interest, especially in light of increased focus on insurance and re-insurance concerns around NMs and nano-enabled products (*Mullins et al. 2013*), is the use of NM labelling strategies as bar codes. While much of the research focus in this area has been around development of NMs for use in anti-counterfeiting and anti-theft arenas (*Liu et al. 2011*), there is scope also for utilization for tracking of specific NMs and tracing their occurrence in the environment. Indeed, one suggestion could be that large-scale NM manufacturers might want to label their specific NMs with a unique signature or bar code that would enable them to prove or disprove the presence of their NMs in specific pollution or release incidents (even at very dilute concentrations and against a background of naturally occurring and/or similar composition particles produced by other manufacturers).

Doping, or chemical labelling, of NMs is a well-established approach for tuning the properties of NMs (including catalytic activity (Shah *et al.* 2002), contrast ability (Platas-Iglesias *et al.* 2002) and toxicity by tuning dissolution rates (George *et al.* 2011)) and facilitating their detection (Wang & Li 2003). Indeed, the concept of using NMs, specifically quantum dots, as bar codes for selective detection of proteins and biomolecules has been described (Zhao *et al.* 2011), as well as the use of solid-to-liquid phase change NMs with discrete and sharp melting peaks for use as a covert (invisible) bar code in a variety of objects, such as an explosive derivative, drug, polymer, and ink in order to track-trace objects, and authenticate documents (Figure 7) (Duong *et al.* 2014). While such approaches have not yet been proposed as a means to distinguish one manufacturer's NMs from another, this is an obvious next step, whereby manufacturer-specific bar codes could be a specific doping signature, a specific enrichment of a stable isotope, or a combination of these. Making the signature manufacturer-specific means that in the case of a large environmental impact or build-up (or as is likely to occur in the future a

convergence of NMs from disparate sources), manufacturers will be able to prove that it was not their version of the specific NM that was present at the site, offering strong legal protection to these manufacturers.

CONCLUSIONS

The fact that a significant route for NMs into surface water and groundwater is via consumer products means that nano-enabled products fall under the remit of REACH, as well as being of importance for those charged with implementing the WFD and its subsidiaries on drinking water quality and wastewater. This paper highlights some initial considerations around the current status of knowledge regarding NMs' fate and transformation in the environment, and the challenges presented by NMs in terms of their detection against a background of natural particles, which mean that currently detection methods are not sufficiently robust to allow for establishment of EQS for any NMs.

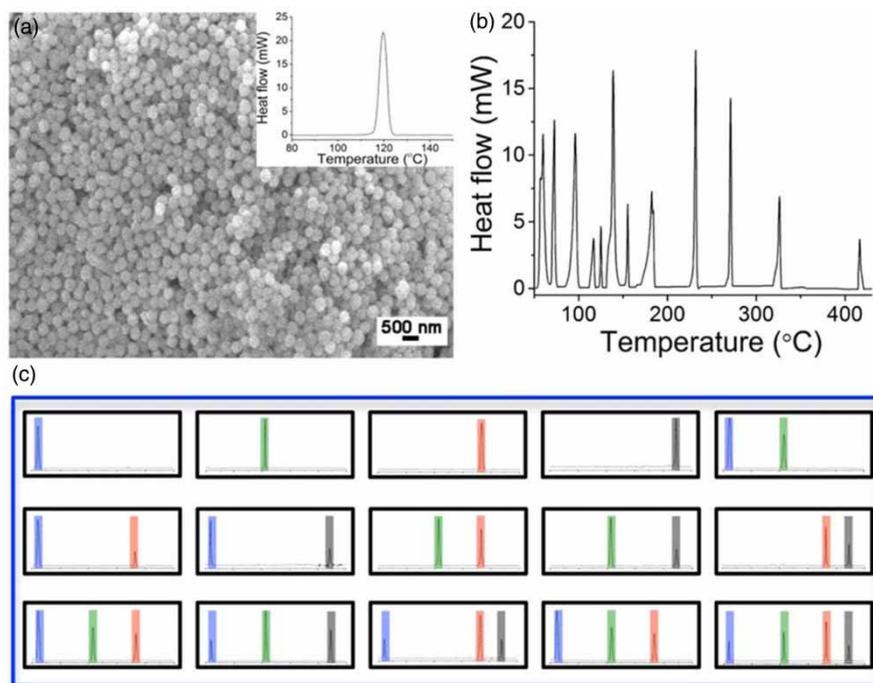


Figure 7 | Concept of the NM-based bar code utilizing melting points of NMs: (a) transmission electron microscopy (TEM) image and differential scanning calorimetry (DSC) (inset) profile of silica encapsulated indium-tin nanoparticles; (b) DSC of 12 types of nanoparticles collected from DNT debris; (c) a library of bar codes formed by four types of phase change nanoparticles (indium, tin, bismuth and indium-tin-bismuth eutectic alloy). From Duong *et al.* (2014).

The paper also discusses some emerging approaches for ensuring that NMs are not unnecessarily entering water systems, such as the use of a benign-by-design approach to nanotechnologies, via the application of value chain analysis and consideration of the potential for recovery or recycling of NMs already at the design phase, thereby reducing the risk of unintentional accumulation of NMs from a vast array of consumer products in our waterways. A final aspect considered is the potential for NM manufacturers to bar code their NMs as a way of tracking their fate in the environment and/or as a precautionary approach in the case of a large accidental release of NMs. Should a manufacturer's NMs have a specific isotope or chemical signature associated with them, this could be used to prove/disprove responsibility for the contamination.

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